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Review Article

Efficacy of radiosurgery with and without angioembolization: A subgroup analysis of effectiveness in ruptured versus unruptured arteriovenous malformations – An updated systematic review and meta-analysis

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ABSTRACT

Background: Congenital arterial defects such as cerebral arteriovenous malformations (AVMs) increase brain bleeding risk. Conservative therapy, microsurgical removal, percutaneous embolization, stereotactic radiosurgery (SRS), or a combination may treat this serious disease. This study compares angioembolization with SRS to SRS alone in ruptured or unruptured brain ateriovenous malformations (BAVM) patients.

Methods: We followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations for this study. Until September 2023, PubMed/Medline, Cochrane, and Clinicaltrials.gov were searched for literature. English-language studies comparing SRS alone to embolization with SRS on ruptured or non-ruptured AVMs that could not be operated on were considered. The Newcastle–Ottawa Scale assessed research study quality.

Results: Results included 46 studies with a total of 7077 participants. There was a greater obliteration rate in the SRS-only group (60.4%) than in the embolization plus SRS group (49.73%). Particularly in the SRS-only group, ruptured AVMs showed a noticeably greater obliteration rate than unruptured AVMs ($P = 0.002$). However, no notable differences were found in hemorrhagic events or radiation-induced changes between the two groups; however, the SRS-only group had a slightly greater, yet not statistically significant, mortality rate.

Conclusion: Our data showed that ruptured brain AVMs had a much greater obliteration rate than unruptured ones, mostly due to SRS alone, without embolization. The aggregated data showed no significant changes, whereas SRS alone decreased radiation-induced alterations and hemorrhagic rates but with increased mortality. SRS alone may have a higher risk-to-reward ratio for nidus obliteration in ruptured brain AVM patients, so it should be used without embolization, although more research is needed to determine the effects of immediate and late complications.

Keywords: Angioembolization, Cerebral arteriovenous malformations, Hemorrhagic events, Obliteration rate, Radiation-induced changes, Stereotactic radiosurgery

INTRODUCTION

AVMs, or cerebral arteriovenous malformations, are genetic anomalies that are characterized by aberrant arteries and veins without a capillary bed in between.[2] Epidemiological studies on brain AVMs have found the incidence of symptomatic cerebral AVMs to be 1/100,000[3], with unreported asymptomatic cases being a confounding factor contributing to the underestimation of AVM incidence.[2] Most cerebral AVMs are identified following intracerebral hemorrhage. However, a portion of them is found in individuals who experience seizures, headaches, and gradual neurological impairment.[4] Untreated cerebral AVMs have an annual rate of bleeding that ranges from 2 to 4%,[5-8] with a combined yearly morbidity and death rate of around 3%.[7] While surgical excision is still the mainstay of therapy for operable AVMs, inoperable AVMs may require alternate techniques to decrease the risk of bleeding and accomplish obliteration of the malformation.[9] A combination of techniques such as microsurgical resection, catheter-directed endovascular embolization, stereotactic radiosurgery (SRS), or conservative therapy with close observation are possible choices for treatment.[10,11] Figure 1 demonstrates the schema of management.

Endovascular embolization is frequently utilized as a preoperative adjunctive treatment option for major AVMs and can also serve as the primary therapy for smaller AVMs that are difficult to treat surgically.[12] Furthermore, radiosurgery, which was previously reserved for smaller, low Spetzler-Martin grade AVMs[13], has more recently shown better outcomes with high obliteration rates and low morbidity/mortality, even in larger AVMs.[14] SRS is a potentially effective therapy for managing AVMs that are not amenable to surgical excision. It provides accurate radiation delivery to the affected area while causing minimal damage to the surrounding tissues.[15] However, despite advances in SRS, the rates of total obliteration vary greatly, ranging from 30% to 85%.[15,16] One study reported that younger age, spherical shape of the AVMs, and improved dose planning were associated with better outcomes.[17] Hypofractionation has also been shown to improve obliteration rates although at a risk of increased complications.[18] SRS for cerebral AVMs can lead to complications such as hemorrhage during the latency period, detrimental radiation effects, neurological deficits, and radiation necrosis.[21,22] However, the overall rate of complications is relatively low, with radionecrosis and perifocal edema being the most common.[23] It is important to thoroughly evaluate the potential advantages and disadvantages of SRS, especially when dealing with large and non-ruptured AVMs.[21] Angioembolization, the selective blockage of feeding arteries supplying the central nidus of AVMs using endovascular procedures, has been proposed as an adjuvant therapy to enhance the effectiveness of SRS by altering growth and flow dynamics.[25] Recent research has emphasized that the combination of angioembolization with SRS may enhance the rates of obliteration and reduce the likelihood of hemorrhage recurrence.[27,29,30] However, opinions remain divided, with other studies reporting an increased risk of bleeding in patients who underwent angioembolization before SRS.[31,32] Other common complications following embolization include ischemia, headache, and equipment-related complications.[33]

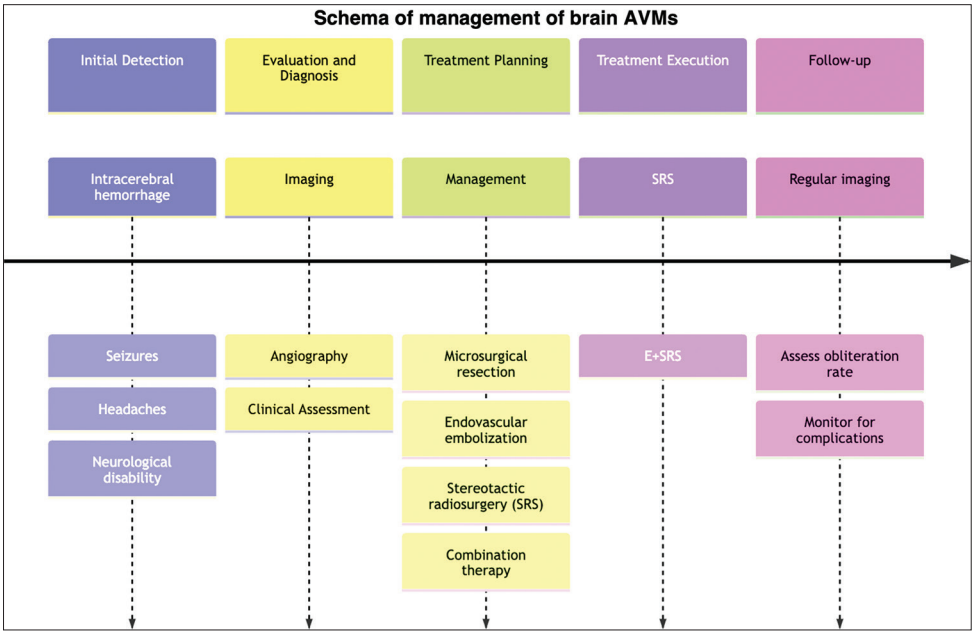

Figure 1: Schematic diagram of management of arteriovenous malformations (AVMs),E+SRS = Embolization + Stereotactic radiosurgery

With this review, we aim to assess the most up-to-date data to determine the efficacy of angioembolization as an additional therapy for SRS in in-operable AVMs. We also aim to conduct a subgroup analysis to evaluate the obliteration rate in ruptured and unruptured AVMs using "SRS only" or "embolization + SRS" treatment modalities, the segregation of which has not been a part of previous work such as by Chang *et al*.[12] Furthermore, we aim to assess the risk of bias in the articles, including newer research studies, to stratify the results further. Our goal is to present a thorough analysis of the existing evidence by integrating data from relevant articles, identifying possible trends or inconsistencies, and providing valuable insights into the therapeutic effectiveness of angioembolization for treating inoperable.

METHODOLOGY

Search strategy

We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations in our research.[34] For a reliable, meticulous, and high-quality meta-analysis, we performed a comprehensive literature search using three databases, PubMed/Medline, Cochrane, and Clinicaltrials.gov, from database inception until September 19, 2023. The search strategy was established using the population, intervention, comparison, outcomes (PICOS) format to identify papers including information on individuals with AVMs who had various symptoms (either ruptured or non-ruptured AVMs). (P: Population) and undergoing SRS (C: Control) compared with embolization and SRS (I: Intervention) with subsequent post-treatment obliteration rates and complications of either intervention (O: Outcomes). Eight independent authors (HK, ABS, IA, AA, MKA, DS, SSS, and SAH) screened abstracts and subsequently evaluated the articles in full text; another author resolved the discrepancies (RN). The study protocol, ID: CRD42023464489, was prospectively registered with the international prospective register of systematic reviews (PROSPERO) registry of systematic reviews.

Inclusion and exclusion criteria

The parameters used as inclusion criteria for our study are as follows: (1) English-language publications, (2) randomized controlled trials (RCTs), quasi-experimental studies, cohort studies, retrospective cohort studies, (3) patients diagnosed with inoperable ruptured or unruptured AVMs, (4) studies conducted within the past 15 years, and (5) data comparing the use of SRS plus embolization versus SRS alone in patients with ruptured and/or unruptured AVMs. To reduce bias and maintain the reliability of the study, we excluded studies with the following parameters: (1) studies with arteriovenous fistulas, (2) non-comparative studies, qualitative studies (e.g., case series and case reports), (3) studies involving participants without a diagnosis of in-operable ruptured or unruptured AVMs, (4) studies not published in peer-reviewed journals (conference papers and unpublished data), (5) studies with ambiguous data regarding obliteration rates in the embolization + SRS group versus only SRS group, (6) studies evaluating non-intracranial AVM's, and (7) trials with a high risk of bias, as evaluated by the *Newcastle Ottawa scale (NOS)*.

Data extraction and quality assessment

A systemic search strategy was used to obtain reliable results from relevant research databases. Relevant articles were uploaded to Rayyan.ai for screening purposes. Duplicate studies were identified and removed. The remainder of the studies were screened using a two-step process. Originally, articles were assessed by scrutinizing the titles and abstracts of the research papers. Studies that did not fulfill the selection criteria were not included in the study. In the second phase of the screening process, a comprehensive examination was conducted of the complete texts of the remaining articles to determine their conformity with the selection criteria. The pertinent data from the chosen articles were extracted utilizing an Excel spreadsheet. The selected studies were used to gather demographic data, which included information such as the author, year of publication, location of the study, study period, study design, sample size, follow-up duration, mean or median age, and whether the presentation was hemorrhagic or non-hemorrhagic. The study collected data on numerous variables and outcomes, such as the average or median margin dosage, rate of AVM obliteration, occurrence of post-SRS hemorrhage, radiation-induced changes (RICs), and death. The quality of the selected studies was evaluated using the NOS *Observational Cohort and Case-Control Studies*.[35] The risk of bias is summarized in Table 1.

Statistical analysis

Statistics were done using RevMan 5.4 by Cochrane Library. The cumulative impact for all secondary outcomes as well as the odds ratio (OR) for each study was determined using the Mantel–Haenszel model. Heterogeneity was evaluated using I^2 and Chi-square test statistics. Heterogeneity was identified when the Chi-squared test statistic reached a significance level of 10% ($P < 0.10$). In addition, heterogeneity levels were categorized as low if the I^2 value was <40%, substantial if it was >50%, and considerable if it exceeded 75%.[36] Averages, standard deviations, and 95% confidence intervals (CIs) were provided in the data, which were pooled using *random effects models* in consideration of the heterogeneity and methodological diversity of the screened studies. The data for the meta-analysis are presented as a forest plot. Weights of the studies, based on sample size and variance, are also displayed within the forest plots. The Funnel plot was created to assess possible publication bias. Plotting the effect sizes against their

Table 1: Risk of bias summary for each study.

Study	S1	S2	S3	S4	C	E1	E2	E3
Yan *et al.* 2021	+	+	+	−	++	+	+	+
Chen Y *et al.* 2021	+	+	+	−	+	+	+	+
Winkler *et al.* 2020	−	+	+	+	+	+	+	−
Nerva *et al.* 2018	+	+	+	−	+	+	+	+
Chen *et al.* 2016	+	+	+	−	−	+	+	−
Paúl *et al.* 2014[74]	+	+	+	−	+	+	+	+
Izawa *et al.* 2009	+	+	+	−	−	+	+	+
Pulli *et al.* 2019[79]	+	+	+	−	+	+	+	+
Kawashima *et al.* 2020	+	+	+	−	+	+	+	+
Lee *et al.* 2015*	+	+	+	+	+	+	+	+
Lecavalier-Barsoum M *et al.* 2013	+	+	+	−	+	+	+	+
Darsaut *et al.* 2011[19]	−	+	+	−	+	+	+	+
Chen CJ *et al.* 2021	+	+	+	−	++	+	+	+
Andrade-Souza *et al.* 2007	+	+	+	−	+	+	+	+
Abecassis *et al.* 2017[1]	+	+	+	−	+	+	+	+
Yang *et al.* 2009	+	+	+	−	+	+	+	+
Nagy *et al.* 2012[67]	+	+	+	−	−	+	+	+
Nataraj *et al.* 2014	+	+	+	+	+	+	+	+
Schwyzer *et al.* 2012	+	+	+	−	+	+	+	+
Nagy *et al.* 2017	+	+	+	+	−	+	+	+
Erickson *et al.* 2022	+	+	+	−	−	+	+	+
Meng *et al.* 2021	+	+	+	−	+	+	+	+
Sun *et al.* 2011	+	+	+	−	+	+	+	+
Oermann *et al.* 2015	+	+	+	+	++	+	+	+
Back *et al.* 2008	+	+	+	−	−	+	+	−
Marciscano *et al.* 2017	+	+	+	−	+	+	+	+
Hasegawa *et al.* 2023*	+	+	+	+	−	+	+	+
Rajshekhar *et al.* 2016[80]	+	+	+	−	−	+	+	+
Loebel *et al.* 2022[56]	+	+	+	−	+	+	+	+

++ Two stars
\+ One star
− Zero stars

(Contd...)

Table 1: *(Continued).*

Study	S1	S2	S3	S4	C	E1	E2	E3
Thenier-Villa *et al.* 2017[91]	⊕	⊕	⊕	⊖	⊖	⊕	⊕	⊕
Link *et al.* 2018[55]	⊕	⊕	⊕	⊖	⊖	⊕	⊕	⊕
Kano *et al.* 2012*[42]	⊕	⊕	⊕	⊕	⊕	⊕	⊕	⊕
Arai *et al.* 2006	⊕	⊕	⊕	⊕	⊖	⊕	⊕	⊕
Faye *et al.* 2020[28]	⊕	⊕	⊕	⊖	⊖	⊕	⊕	⊖
Dumot *et al.* 2022[24]	⊕	⊕	⊕	⊖	⊕	⊕	⊕	⊖
Hoh *et al.* 2000	⊖	⊕	⊕	⊖	⊕	⊕	⊕	⊕
Lindvall *et al.* 2015[54]	⊕	⊕	⊕	⊖	⊖	⊕	⊕	⊖
Milker-Zabel *et al.* 2012	⊕	⊕	⊕	⊖	⊕	⊕	⊕	⊕
Mohr *et al.* 2020[62]	⊕	⊕	⊕	⊕	⊕⊕	⊕	⊕	⊕
Nagaraja *et al.* 2006[65]	⊕	⊕	⊕	⊕	⊕	⊕	⊕	⊕
Naoi *et al.* 2000[68]	⊕	⊕	⊕	⊖	⊕	⊕	⊕	⊕
Peres *et al.* 2017	⊕	⊕	⊕	⊕	⊕	⊕	⊕	⊕
Redekop *et al.* 1993	⊕	⊕	⊕	⊕	⊖	⊕	⊕	⊕
Kiran *et al.* 2007[48]	⊖	⊕	⊕	⊖	⊖	⊕	⊕	⊕
Schlienger *et al.* 2000	⊕	⊕	⊕	⊕	⊖	⊕	⊕	⊕
Bethanabatla *et al.* 2022	⊕	⊕	⊕	⊖	⊕	⊕	⊕	⊕

*Case–control studies; S: Selection, C: Comparability, O: Outcome, E: Exposure, E1: Assessment of outcome, E2: Was follow-up long enough for outcomes to occur, E3: Adequacy of follow up of cohorts, C stands for comparability, C= Comparability of cohorts on the basis of the design or analysis, S stands for selection, S1: Representativeness of the exposed cohort, S2: Selection of the non-exposed cohort, S3: Ascertainment of exposure, S4: Demonstration that outcome of Interest was not present at start of study

standard errors allowed us to observe the distribution around the pooled estimate, indicating whether it is a symmetric or asymmetric distribution.

RESULTS

Six hundred and thirty-six potential articles were found using our search method; 484 of these articles were eliminated during the preliminary screening and duplication phase because they did not meet the predetermined inclusion and exclusion criteria [Figure 2]. One hundred and forty-five articles were reviewed for full-text screening where further exclusion occurred with the removal of 54 articles that failed to mention the treatment modality of interest, ten articles that had other study designs, 23 articles that failed to mention the outcomes of interest, five articles due to publication in non-English languages, and eight articles due to mention of arteriovenous fistulas. We included four additional articles by searching through the citations. Our final search resulted in 46 articles with 8723 patients. However, 7077 patients were included in our analysis after our data extraction identified and excluded entries that failed to mention the definitive treatment modality of interest. Table 2 summarizes study characteristics and patient baseline information. Articles were assessed for risk of bias using the Newcastle Ottawa Scale [Figure 3].

Obliteration rate

Our analysis compared 46 studies to observe obliteration rates in either the "embolization + SRS" group (n = 2061) or the "SRS only" group (n = 5016). The "SRS only" group had a higher obliteration rate (60.4%, n = 3033) compared to the "embolization + SRS" group (49.73%, n = 1025) with a pooled OR of 0.65, 95% CI: 0.55–0.77, 95% CI, $P < 0.00001$, as shown in Figure 4. With $P < 0.00001$ and a low heterogeneity observed amongst records assessing the obliteration rates (I^2 value = 36%, P = 0.009), there is a strong likelihood of a significant difference in obliteration rates between the

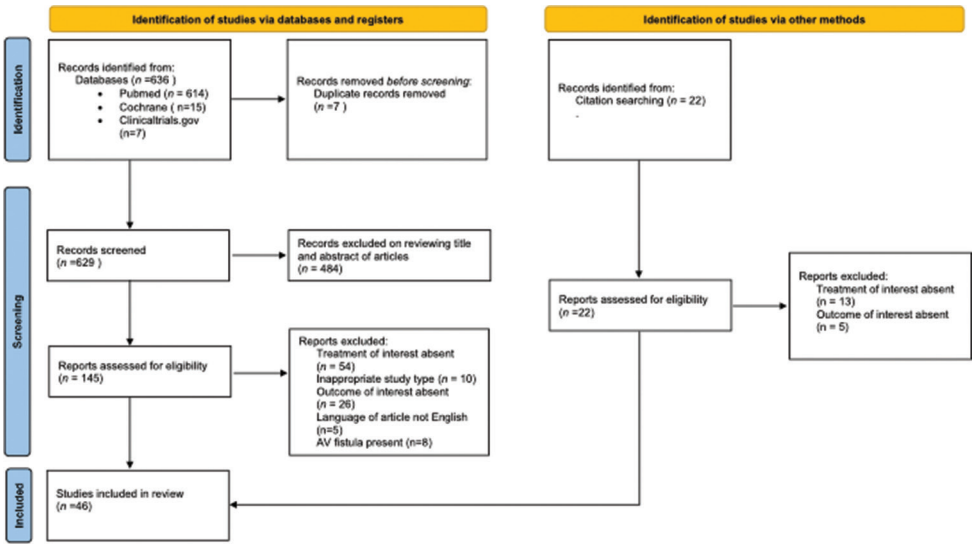

Figure 2: Literature review process according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

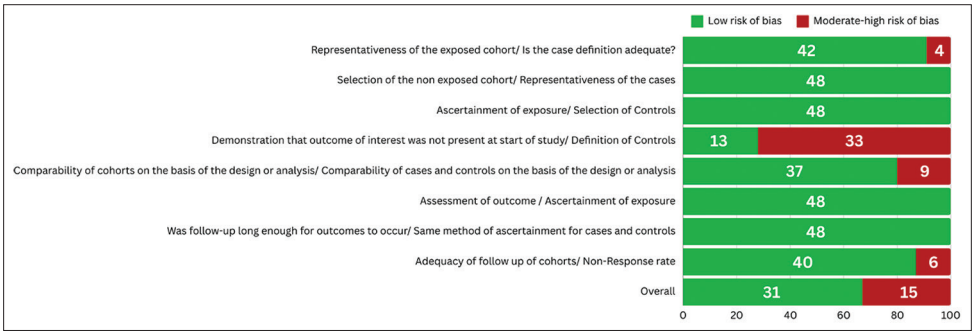

Figure 3: Newcastle–Ottawa scale risk of bias graph.

two interventions with good consistency amongst included articles. However, subtle differences may still exist.

Type of presentation: Ruptured or unruptured brain AVMs

We further assessed differences in obliteration rates based on the type of presentation, either ruptured or unruptured cases of brain AVMs. For our analysis, we included 186 cases for ruptured brain AVMs and 142 for unruptured brain AVMs. Overall, irrespective of the treatment modality of choice, the ruptured brain AVMs (81/186) had a better obliteration rate than unruptured brain AVMs (31/142) with a pooled OR of 2.41, 95% CI: 1.37–4.24, $P = 0.002$, as shown in Figure 5.

Based on the subgroup analysis, the "SRS only" treatment modality improved the obliteration rate for ruptured brain AVMs significantly than for the unruptured brain AVMs, with a pooled OR of 3.62, 95% CI: 1.89–6.94, 95% CI, $P < 0.0001$, as sown in Figure 5. For the "embolization + SRS" treatment modality, the subgroup analysis did not indicate a better obliteration for either intervention group and yielded a non-significant result with a pooled OR of 1.17, 95% CI: 0.50–2.76, $P = 0.72$, as shown in Figure 5.

Mortality outcome

Our analysis compared ten studies mentioning mortality outcomes in either the "embolization + SRS" group (9/374) or the "SRS only" group (24/896) and found no significant difference. The "SRS only" group had a slightly higher mortality (2.67%) as compared to the "embolization + SRS" group (2.45%) with a pooled OR of 0.85, 95% CI: 0.38–1.92, and $P = 0.7$, suggesting the results were non-significant, as shown in Figure 6. Although an I^2 value of 0% indicates a lack of heterogeneity among studies, a non-significant $P = 0.79$ suggests limited power to detect underlying variability.

RICs

We further compared nine studies mentioning RICs in either the "embolization + SRS" group (250/889) or the "SRS only"

Table 2: Study characteristics and data from 46 included studies.

Author & Year	Location	Total patients in study	Treatment modality	Mean age	Patients per treatment modality	Median Or mean follow up time (in months)	Nidus size	Mean or median target vol (ml)	SM grade >3	Mean or median margin dose (Gy)	Obliteration rate (n/%)	Radiation induced changes (n/%)	mRS score	Post-SRS hemorrhage rate (*n*/%)	Mortality
Nerva *et al.* 2018	USA	70	E+SRS	32.425 (mean)	20	40.86 months (mean)	1.74 (diameter, cm) (mean) (22.1 ml)	NR	9	18.64 (mean)	Total: 12/60%, unruptured: 3 , ruptured: 9	NR	1.373	3/15%	NR
			SRS	38.812 (mean)	50	41.23 months (mean)	1.468 (diameter, cm) (mean) (13.3 ml)	NR	12	19.236 (mean)	Total: 31/62%, unruptured: 21 , ruptured 10	NR	1.023	3/6%	NR
Chen JC *et al.* 2016	USA	34	E+SRS	43.8	8	8 Years (median)	11.43 (diameter, cm) (mean) (overall)	NR	NR	35 (median)	2/25%	NR	1.6 (overall)	NR	NR
			SRS		26			NR	NR		7/26%	NR		NR	NR
Schwyzer *et al.* 2012	USA	944	E+SRS	32.9 (mean)	215	83.3 months (mean)	4.7 (volume,ml) (mean) 25.6mm (diameter)	NR	26 (overall)	19.6 (mean)	71/33%	NR	NR	NR	NR
			SRS	34.8 (mean)	729	78.4 months (mean)	2.8 (volume,ml) (mean), 20.3mm (maximum diameter)	NR		21.4 (mean)	444,/60.9%	NR	NR	NR	NR
Nataraj *et al.* 2014	UK	290	E+SRS	40.8 overall mean	17	NR	NR	NR	8	NR	12/70.6%	NR	NR	1/ 5.9%	0/0%
			SRS		37	NR	NR	NR	11	NR	25/67.6%	NR	NR	5/ 13.5%	4/10.8%
Nagy *et al.* 2012[67]	UK	564	E+SRS	29 (median) (overall sample)	97	NR	19.7 (volume, ml) (median) (overall)	NR	38 (overall)	NR	25/25.8%	NR	NR	NR	NR
			SRS		299	NR		NR		NR	113/37.8%	NR	NR	NR	NR
Yang *et al.* 2009	Korea	46	E+SRS	32.29 (mean) (overall sample)	25	74.3 months (mean)	32.4 (volume, ml) (mean)	NR	40 (overall)		8/32%	NR	NR	0/0%	NR
			SRS		21	76.6 months (mean)	26.5 (volume, ml) (mean)	NR			9/42.9%	NR	NR	8/32%	NR
Abecassis *et al.* 2017[1]	USA	114	E+SRS	NR	14	NR	NR	NR	0	NR	5/33.3%	NR	NR	NR	NR
			SRS	NR	40	NR	NR	NR	0	NR	13/30.2%	NR	NR	NR	NR
Andrade-Souza *et al.* 2007	Canada	94	E+SRS	39 (mean) (overall sample)	47	48 months (mean) (overall)	3.17, 2.49 (preembolization, post embolization) (diameter, cm) (mean)	7.42 (mean)	12	16.7 (mean)	22/46.8%	NR	NR	2/4.3%	2/4.3%
			SRS		47		2.42 (diameter, cm) (mean) (7.42 ml)	6.66 (mean)	4	16.7 (mean)	33/70.2%	NR	NR	5/10.6	0/0%
Chen CJ *et al.* 2021	Multicenter	202	E+SRS	39.1 (mean)	101	61.8 months (mean)	16.2 (volume, ml) (mean)	NR	NR		49/48.5%	31/31.6%	NR	8/8.3%	2/2%
			SRS	35.8 (mean)	101	68.1 months (mean)	4.2 (volume, ml) (mean)	NR	NR		55/54.5%	45/45%	NR	5/5%	4/4%
Darsaut *et al.* 2011[19]	USA	120	E+SRS	11.7 (mean) (overall sample)	17	NR	NR	21.4 (mean) (overall sample)	43(overall)		4, 24%	NR	NR	NR	NR
			SRS		25	NR	NR				5, 20%	NR	NR	NR	NR
Lecavalier-Barsoum M *et al.* 2013	Canada	43	E+SRS	37 (median) (overall sample)	31	23.5 months (median) (overall)	1.8 (diameter, cm) (mean) (3.05 ml)	NR	2(overall)		24, 92.3%	5/16.1%	NR	NR	NR
			SRS		12		1.8 (diameter, cm) (mean) (3.05 ml)	NR			9, 81.8%	1/8.3%	NR	NR	NR
Lee *et al.* 2015	Taiwan	75	E+SRS	42 (median)	25	24.1 months (median)	4.9, 3.5 (pre-embolization, post-embolization) (volume, ml) (mean)	NR	7(>1 SM grade)		6/24%	11/44%	NR	1/4%	NR
			SRS	40 (median)	50	25.7 months (median)	3 (volume, ml) (mean)	NR	21(>1 SM grade)		20/40%	25/50%	NR	3/6%	NR
Kawashima *et al.* 2020	USA	411	E+SRS	28 (median)	45	79 months (median)	4.1 (volume, ml) (median)	NR	28 (>2 SM grade)	20 (median)	34/75.6%	3/6.7%	NR	2/4.4%	NR
			SRS	30 (median)	306	111 months (median)	1.4 (volume, ml) (median)	NR	185 (>2 SM grade)	20 (median)	242/79.1%	22/7.2%	NR	23/7.5%	NR
Pulli *et al.* 2019[79]	USA	142	E+SRS	39.7 (mean) (overall sample)	7	61.2 months (mean) (overall)	NR	6.3 (mean) (overall)	14(overall)	14.8 (mean) (overall)	1/14.3%	NR	NR	NR	NR
			SRS		92		NR				37/40.2%	NR	NR	NR	NR
Izawa *et al.* 2009	Japan	396	E+SRS	35.3 (mean)	15	79.2 months (mean) (overall)	9.9 (volume, ml) (mean)	NR	NR	19.9 (mean)	10/66.7%	NR	NR	0/0%	NR
			SRS	30.1 (mean)	237		4.7 (volume, ml) (mean)	NR	NR	20.2 (mean)	130/54.9%	NR	NR	8/3.4%	NR
Paúl *et al.* 2014[74]	Spain	662	E+SRS	37.12 (mean) (overall sample)	239	132 months (mean) (overall)	6 (volume, ml) (mean) (overall)	NR	NR	18.9 (mean) (overall)	155/64.9%	NR	NR	NR	NR
			SRS		336						255/75.9%	NR	NR	NR	NR
Yan *et al.* 2021	China	152	E+SRS	29 (mean)	76	72 months (mean)	12 (volume, ml) (mean) (overall)	NR	37 (>2 SM grade)	NR	Total=24/31.6% ,ruptured=15 , unruptured= 9	NR	NR	7/9.2%	3/3.9%
			SRS	30.6 (mean)	76	76.8 months (mean)		NR	38 (>2 SM grade)	NR	Total: 34/44.7%, ruptured= 26, unruptured= 8	NR	NR	3/3.9%,	1/1.3%,
Nagy *et al.* 2017[66]	UK	84	E+SRS	37 (median) (overall sample)	6	NR	NR	NR	276 (overall)	17.5 (median) (overall)	3/50%	NR	NR	NR	NR
			SRS		38	NR	NR	NR			24/63.2%	NR	NR	NR	NR
Meng *et al.* 2021	China	96	E+SRS	27.5 (mean)	48	45.13 months (radiographic), 60.4 months (clinical) (mean) (overall)	7.5, 4.8 (pre-embolization, post-embolization) (volume, ml) (mean)	NR	16 (overall)	NR	36/75%	NR	NR	1/2.1%	NR
			SRS	25.6 (mean)	48		5.1 (volume, ml) (mean)	NR		NR	40/83.3%	NR	NR	1/2.1%	NR
Sun *et al.* 2011	USA	127	E+SRS	37 (median) (overall sample)	39	42 months (median) (overall)	7.3 (volume, ml) (median) (overall)	NR	NR	18 (median) (overall)	17/43.6%	NR	NR	NR	NR
			SRS		84			NR	NR		61/672.6%	NR	NR	NR	NR
Oermann *et al.* 2015	USA	484	E+SRS	32 (mean)	242	56 months (mean)	4.6 (volume, ml) (mean)	NR	32 (overall)	20 (mean)	115/47.5%	88/36.4%	NR	30/12.4%	NR
			SRS	30 (mean)	242	53 months (mean)	4 (volume, ml) (mean)	NR	43 (overall)	20 (mean)	163/67.4%	109/45%	NR	29/12%	NR
Erickson *et al.* 2022	USA	188	E+SRS	39.8 (mean) (overall sample)	6	42.7 months (mean) (overall)	NR	NR	0	17.5 (median) (overall)	6/100%	NR	NR	NR	NR
			SRS		182		NR	NR	19		85/46.7%	NR	NR	NR	NR
Bethanabatla *et al.* 2022	New Zealand	369	E+SRS	36.16 (mean)	37	NR	NR	NR	9	17.56 (mean)	26/70.3%	0/0%	NR	0/0%	0/0%
			SRS	38.82 (mean)	239	NR	NR	NR	26	17.69 (mean)	186/77.8%	5/2.1%	NR	10/4.2%	3/1.3%
Chen Y *et al.* 2021	China	60	E+SRS	26.3 (mean)	9	4.5 years (mean) (overall)	3.3 (cm) (not specified if diameter/ radius) (mean)	NR	NR	NR	Total=4/44.4%, ruptured= 3 , unruptured=1	NR	1.44	1/11.1%	1/11.1%
			SRS	30.1 (mean)	21		2.3 (cm) (not specified if diameter/ radius) (mean)	NR	NR	15.1 (mean)	Total= 13/61.9% , ruptured,= 10 , unruptured= 3	NR	1.2	3/14.3%	0/0%
Back *et al.* 2008	USA	150	E+SRS	33.9 (M) 35.3 (F) (mean) (overall sample)	21	NR	10.344 (volume, ml) (mean)	NR	NR	NR	13/61.9%	NR	NR	2/9.5%	NR
			SRS		73	NR	7.624 (volume, ml) (mean)	NR	NR	NR	55/75.3%	NR	NR	11/15.1%	NR
Marciscano *et al.* 2017	USA	42	E+SRS	24.5 (median) (overall sample)	22	9.5 years (median) (overall)	13.1 (volume, ml) (mean) (overall)	NR	16 (overall)	15.4 (median) (overall)	5/22.7%	NR	NR	2/9.1%	NR
			SRS		20			NR			11/55%	NR	NR	6/30%	NR
Winkler *et al.* 2020	USA	189	E+SRS	12.1 (mean) (overall sample)	2	49.2 months (mean) (overall)	2.95 (cm) (not specified if radius or diameter/ mean or median) (overall)	NR	49 (overall)	NR	Total= 2/100%, ruptured=2 , unruptured= 0	NR	NR	NR	NR
			SRS		56			NR		NR	Total=13/23.2%, ruptured=9 , unruptured= 4	NR	NR	NR	NR
Hasegawa *et al.* 2023	Japan	704	E+SRS	37.3 (mean)	111	76.9 months (mean)	10.3, 7.1 (pre-embolization, post-embolization) (volume, ml)(mean)	NR	NR	19.2 (mean)	58/52.3%	NR	NR	11/9.9%	NR
			SRS	36.6 (mean)	593	73.1 months (mean)	4.9 (volume, ml) (mean)	NR	NR	20 (mean)	362/61.0%	NR	NR	54/9.1%	NR
Kano *et al.* 2012[42]	USA	240	E+SRS	33 (median) (overall sample	120	70 months (median)	2.8 (diameter,cm) (mean) (11.5 ml)	7.1 (median) (overall)	NR	18 (median)	64/53.3%	11/9.2%	NR	4/3.3%	NR
			SRS		120	72 months (median)	2.8 (diameter, cm) (mean) (11.5 ml)		NR	18 (median)	85/70.8%	10/8.3%	NR	4/3.3%	NR
Link *et al.* 2018[55]	USA	86	E+SRS	43.6 (mean) (overall sample)	13	NR	2.7 (cm) (not specified if diameter/ radius) (mean) (overall)	NR	8 (>2 SM grade)	NR	10/76.9%	NR	NR	NR	NR
			SRS		9	NR		NR	6 (>2 SM grade)	NR	9/100%	NR	NR	NR	NR
Thenier-Villa *et al.* 2017[91]	Spain	195	E+SRS	37.64 (mean) (overall sample)	47	121.91 months (mean)	2.61 (diameter, cm) (mean) (overall)	NR	30 (overall)	16.75 (mean) (overall)	38/80.9%	NR	NR	NR	NR
			SRS		148	121.91 months(mean)		NR			120/81.1%	NR	NR	NR	NR
Loebel *et al.* 2022[56]	USA	123	E+SRS	39.8 (median) (overall sample)	54	48.1 months (median) (overall)	NR	3.4 (median) (overall)	31 (overall)	20 (median) (overall)	29/53.7%	NR	NR	NR	NR
			SRS		69		NR				38/55.1%	NR	NR	NR	NR
Rajshekhar *et al.* 2016[80]	India	69	E+SRS	14 (median) (overall sample)	9	22 months (median) (overall)	8.4 (volume, ml) (mean) (overall)		10(overall)	15 (median) (overall)	3/33.3%	NR	NR	NR	NR
			SRS		60						41/68.3%	NR	NR	NR	NR
Arai *et al.* 2006	Japan	13	E+SRS	41 (mean)	7	51.6 months (mean)	9.6, 4.8 (pre-embolization, post-embolization) (volume, ml) (mean)	NR	1	14.7 (mean)	5/71.4%	NR	NR	0/0%	NR
			SRS	40 (mean)	6	77.3 months (mean)	1.6 (volume, ml) (mean)	NR	1	14.5 (mean)	3/50%	NR	NR	0/0%	NR
Faye *et al.* 2020[28]	France	53	E+SRS	35.8 (mean) (overall sample	14	56.7 months (mean) (overall)	NR	1.43 (mean) (overall)	25 (overall)	22.9 (mean) (overall)	6/42.9%	NR	NR	NR	NR
			SRS		34		NR				14/41.2%	NR	NR	NR	NR
Dumot *et al.* 2022[24]	France	84	E+SRS	39.6 (median) (overall sample)	10	3.9 years (median) (overall)	2.5 (diameter, cm) (median) (overall)	NR	0 (overall)	NR	4/40.0%	NR	NR	NR	NR
			SRS		17			NR		NR	8/47.1%	NR	NR	NR	NR
Hoh *et al.* 2000	USA	40	E+SRS	1.5 (mean)	2	38.7 months (mean) (overall)	2.4 (diameter, cm) (mean) (7.24 ml)	9.9 (mean) (overall)	1	15.9 (mean) (overall)	1/50%	NR	NR	0/0%	0/0%
			SRS	12.1 (mean)	11		3.0 (diameter, cm) (mean) (14.1 ml)		5		5/45.4%	NR	NR	1/9.1%	1/9.1%
Lindvall *et al.* 2015[54]	Sweden	24	E+SRS	45.6 (mean) (overall sample)	16	NR	18.5 (volume, ml) (mean)(overall)	NR	NR	32.9 (mean) (overall)	11/68.8%	NR	NR	NR	2/12.5%
			SRS		8	NR		NR	NR		5/62.5%	NR	NR	NR	1/12.5%
Milker-Zabel *et al.* 2012	Germany	293	E+SRS	38.8 (median) (overall sample)	85	50.4 years (median) (overall)	3 (diameter, cm) (median)(overall) (4.1 ml)	3.1 (median) (overall)	20 (overall)	18 (median) (overall)	46/54.1%	NR	NR	11/12.9%	NR
			SRS		207						95/45.9%	NR	NR	25/12.1%	NR
Mohr *et al.* 2020[62]	USA	226	E+SRS	44.5 (mean) (overall sample, intervention arm)	23	48.5 months (mean) (overall)	NR	NR	8 (overall)	NR	6/26.1%	NR	NR	NR	NR
			SRS		33		NR	NR		NR	6/18.2%	NR	NR	NR	NR
Nagaraja *et al.* 2006[65]	UK	40	E+SRS	42 (mean) (overall sample)	9	NR	NR	NR	NR	NR	3/33.3%	NR	NR	NR	NR
			SRS		31	NR	NR	NR	NR	NR	6/19.4%	NR	NR	NR	NR
Naoi *et al.* 2000[68]	Japan	51	E+SRS	36 (mean) (overall sample)	11	42 months (mean) (overall)	1.7 (volume, ml) (mean) (overall)	NR	NR	19 (mean) (overall)	4/64.9%	NR	NR	NR	NR
			SRS		13			NR	NR		10/76.9%	NR	NR	NR	NR
Peres *et al.* 2017	Brazil	47	E+SRS	29.1 (mean) (overall sample	26	NR	NR	NR	9 (overall)	NR	12/46.2%	NR	NR	2/7.7%	NR
			SRS		21	NR	NR	NR		NR	11/52.4%	NR	NR	1/4.8%	NR
Redekop *et al.* 1993	UK	15	E+SRS	26.25 (mean)	4	123 months (mean)	50.75 (volume,ml)	NR	NR	44.55 (mean)	0/0%	NR	NR	0/0%	NR
			SRS	30.18 (mean)	11	88.32 months (mean)	19.97 (volume, ml) (mean)	NR		42.50 (mean)	2/18.2%	NR	NR	2/18.2%	NR
Kiran *et al.* 2007[48]	India	103	E+SRS	13.9 (mean) (overall sample)	4	26.4 months (mean) (overall)	2.4 (volume, ml) (mean) (overall)	NR	7(overall)	24.39 (mean) (overall)	3/75%	NR	NR	NR	NR
			SRS		35			NR			31/88.6%	NR	NR	NR	NR
Schlienger *et al.* 2000	France	169	E+SRS	33 (median) (overall sample)	65	NR	2.46 (volume, ml) (median) (overall)	NR	NR	29 (median) (overall)	35/53.8%	NR	NR	NR	NR
			SRS		104	NR		NR	NR		74/71.2%	NR	NR	NR	NR

NR: Not reported, SRS: Stereotactic radiosurgery, E: Embolization

group (496/1874) and found no significant difference. The "SRS only" group had a slightly lower frequency of RICs (28.1%) as compared to the "embolization + SRS" group (26.4%) with a pooled OR of 0.90, 95% CI: 0.62–1.33, $P = 0.61$, suggesting the results were non-significant, as shown in Figure 7. With $P < 0.05$, moderate heterogeneity was observed among records with I^2 value of 49%.

Hemorrhagic events

We additionally compared 23 studies reporting hemorrhagic events in either the "embolization + SRS" group (100/1306) or the "SRS only" group (217/3266) and found no significant difference in the observed rate of hemorrhage in either intervention. There were slightly more hemorrhagic events in the "embolization + SRS" group (7.65%) as compared to the "SRS only" group (6.64%), with a pooled OR of 1.03, 95% CI: 0.78–1.35, $P = 0.85$, indicating non-significance, as shown in Figure 8. Again, caution is advised when interpreting an I^2 value of 0% in the face of a non-significant $P = 0.80$.

Publication bias

A funnel plot was created using Revman 5.4 to indicate publication bias. Our results indicate a small-study bias, as shown in Figure 9.

DISCUSSION

Brain AVMs are congenital dysplastic groups of dilated blood arteries that bypass the capillary network and have a central nidus connected to an arterial feeder that empties into a vein.[37] According to epidemiological research, there are 0.89–1.34 instances of brain AVMs for every 100,000 patients.[38-41] Studies analyzing the presenting symptoms of brain AVMs have indicated a decrease in the rate of patients presenting with hemorrhages due to the development of non-invasive imaging modalities.[42] While various therapeutic approaches are described in the literature, there is currently no unanimous agreement on the safety and effectiveness of angioembolization before SRS, particularly in relation to the initial clinical presentation of brain AVMs, whether they are ruptured or unruptured. As a result, we carried out a thorough analysis of the literature to gather information on the frequencies of hemorrhage obliteration, mortality, and radiation-induced alterations. This was done for two groups: the "SRS only group," which received only SRS, and the "embolization + SRS" group, which received pre-SRS embolization followed by SRS. The data were obtained from 46 articles and included a total of 7077 patients. Our review incorporated 67% of studies that exhibited a low bias, as determined by a NOS score of 7 or higher.

One well-established method for treating cerebral AVMs is SRS.[1] Angioembolization is a possible beneficial addition to SRS. However, past studies that examined the impact of embolization before SRS on the rates of AVM obliteration have shown inconsistent findings. Angioembolization before SRS significantly decreases the total obliteration rates by reducing the nidus size before SRS.[43-47,49-51] Various factors associated with angioembolization, including unintentional promotion of angiogenesis, absorption or scattering of radiation beams by embolic agents, delayed recanalization during the latency period, and changes in the three-dimensional appearance of AVMs after embolization, as well as morphological factors such as the complexity of the central nidus' angioarchitecture and differences in nidus size among patients undergoing embolization, contribute to challenges in adjusting SRS dosage regimens.[44,47,51,52]

One such variable to consider is the use of different embolizing agents and their effect on clinical outcomes. Studies have highlighted potential causes of complications in different agents. Onyx is a well-researched embolizing material that has certain complications, including incomplete vessel occlusion, as it solidifies from outside inwards, creating a soft inner core that can prevent complete vessel occlusion.[95] Furthermore, N-butyl cyanoacrylate has also been noted to have certain complications, which include an increased chance of non-target embolization due to the rapid polymerization speed of the embolizing agent and heat production, which can damage surrounding tissue or cause inflammation.[95] Studies comparing postoperative outcomes when using N-butyl cyanoacrylate (NBCA) or Onyx have found the former to be associated with lower permeant complication rates, while the use of Onyx was associated with higher angiographic cure rates.[26] Studies analyzed in our analysis used a range of embolizing agents, including polyvinyl alcohol particles, lipiodol, NBCA, Onyx, and coils. The majority of the articles analyzed in this study did not mention the embolic agent used, but among the articles that did, the most commonly used agents included NBCA and Onyx.

Obliteration rates as per intervention of choice

Our analysis compared the effectiveness of two treatment methods for brain AVMs: SRS alone and SRS combined with angioembolization. We found that SRS alone resulted in a higher rate of AVM obliteration compared to the combination treatment (60.4% vs. 49.73%). The pooled OR was 0.65, with a 95% CI of 0.55–0.77 and $P < 0.00001$. In contrast, several other studies[43,53] have previously found that angioembolization before SRS has a significantly better obliteration rate than SRS alone. This is attributed to a reduction in volume and vascular density within AVMs. These findings are in contrast to the results reported by a previous study[57], which found that

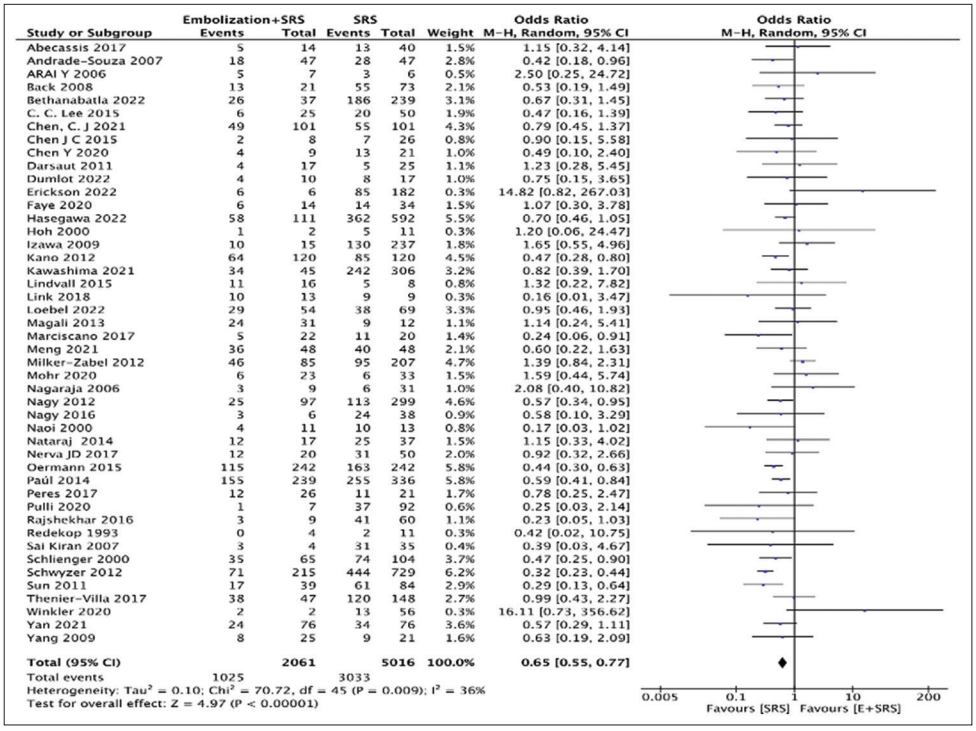

Figure 4: Forest plot comparing obliteration rates between the "Stereotactic radiosurgery (SRS) only" group and the "embolization + SRS" group in brain arteriovenous malformations. M-H: Mantal-Haenszel, CI: Confidence interval.

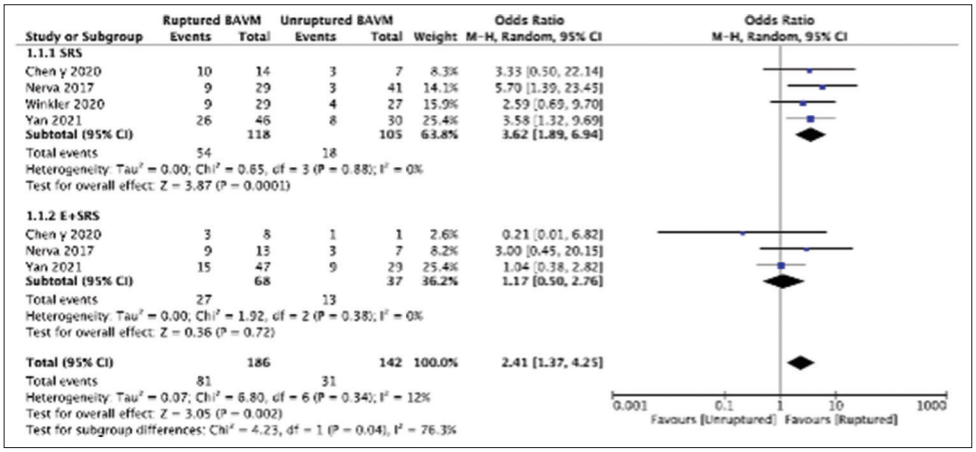

Figure 5: Forest plot comparing obliteration rates based on type of presentation (unruptured or ruptured brain arteriovenous malformations) and type of intervention ("Stereotactic radiosurgery [SRS] only" or "embolization + SRS"), E: Embolization, BAVM: Brain Arteriovenous malformation, M-H: Mantal-Haenszel, CI: Confidence interval.

obliteration rates in both patient cohorts, E + SRS and SRS, were similar. These findings were also replicated in studies with propensity score matching to alleviate the effect of extraneous variables on the results.[58-60] Previous meta-analyses have found pre-SRS embolization with SRS to have significantly worse obliteration rates than SRS alone, just as our pooled results indicate.[61,63,64,69,70] These contrasting differences can be explained by the time of publication, as multiple recent studies demonstrate more robust methodologies accounting for sources of bias.[58-60] The bias in our study can be explained by the inherent difference in angioarchitecture and AVM size in patients undergoing pre-SRS embolization with subsequent SRS. Embolization before SRS is conducted with the aim of decreasing the AVM size, making it more optimal for SRS;[20,44] hence, patients undergoing this multimodal therapy have larger AVM's than those undergoing SRS only. A large and

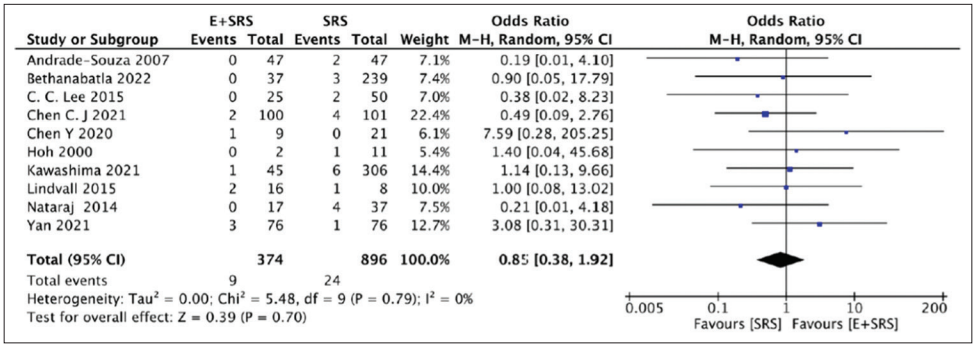

Figure 6: Forest plot comparing mortality outcomes in the "Stereotactic radiosurgery (SRS) only" and "embolization + SRS" groups. E: Embolization, M-H: Mantal-Haenszel, CI: Confidence interval.

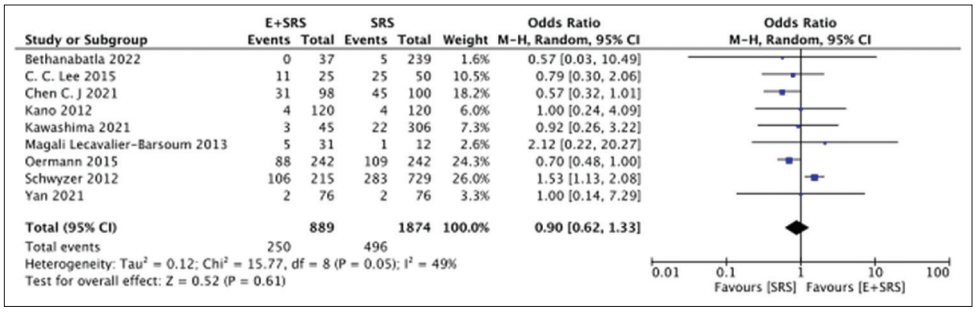

Figure 7: Forest plot comparing radiation-induced changes in the "Stereotactic radiosurgery (SRS) only" and "embolization + SRS" groups. E: Embolization, M-H: Mantal-Haenszel, CI: Confidence interval.

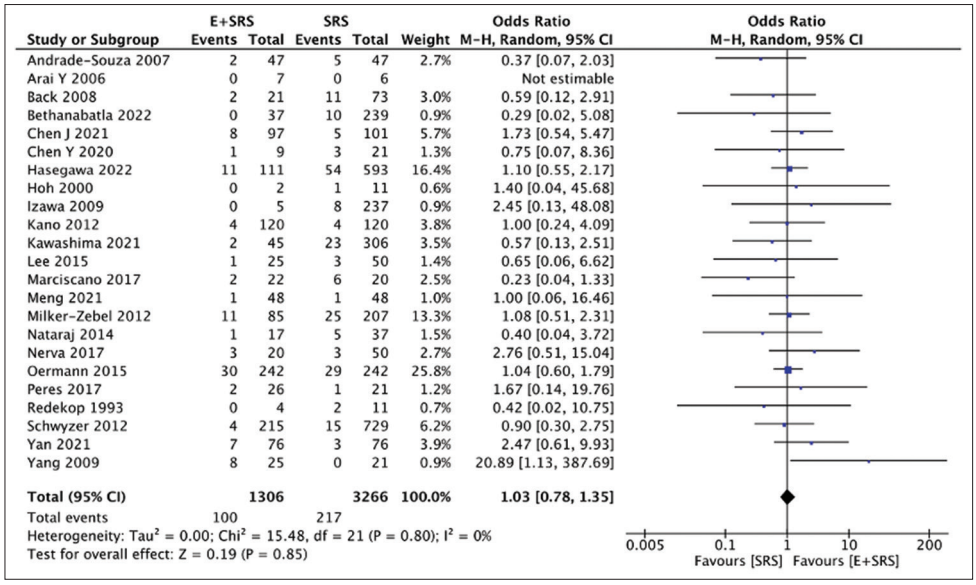

Figure 8: Forest plot comparing hemorrhagic events in the "Stereotactic radiosurgery [SRS] only" and "embolization + SRS" groups. E: Embolization, M-H: Mantal-Haenszel, CI: Confidence interval.

diverse sample of patients was analyzed to mitigate the effects of the aforementioned confounders. Data on pre-embolization AVM size, which was only mentioned in a limited number of studies[46,59,71-73,75], can aid in addressing this confounding variable and analyzing the effect of presenting AVM size on obliteration rates in different treatment modality groups. Many studies have suggested using post-SRS embolization to address residual AVMs[76-78,81], which may lead to higher obliteration rates. Furthermore, the authors highlighted the presence of larger AVMs in the post-SRS embolization group

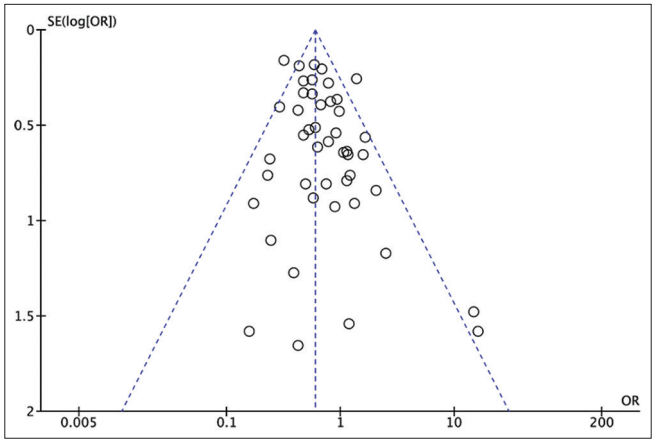

Figure 9: Funnel plot for publication bias. OR: Odds ratio, SE: Standard error.

as a potential confounder influencing the results. Research, such as the study conducted by Meng *et al*.,[60], has indicated that targeted embolization may be advantageous due to its higher rates of obliteration compared to volume reduction embolization.

Obliteration rates as per type of presentation

The presenting status of brain AVMs, ruptured or unruptured, is a potential confounder when analyzing the obliteration rates in patients undergoing different treatment modalities. This finding aligns with other research examining the rates of obliteration in individuals undergoing SRS with either ruptured or unruptured AVM presentations.[82-84] Nevertheless, our research showed that compared to unruptured brain AVMs, ruptured brain AVMs had a considerably greater obliteration rate with any treatment approach (43.55% vs. 21.83%). with a pooled OR of 2.41, 95% CI: 1.37–4.24], $P = 0.002$, and SRS alone seemed to be responsible for that, while pre-SRS embolization with SRS did not show any significant advantage. This is supported by Schwyzer *et al*.,[85], who studied a cohort of 17 patients with ruptured AVMs and found that angioembolization had no advantage over SRS alone. Therefore, SRS alone may confer a substantial benefit with a greater risk-to-reward ratio in achieving significant obliteration of nidus in patients presenting with ruptured brain AVMs. These findings were also present in studies analyzing pediatric patients[86], indicating that SRS alone, without any adjunct embolization, should be used in patients presenting with ruptured AVMs. Regarding pre-SRS embolization with subsequent SRS, several variables could explain why obliteration rates were similar in both the unruptured and ruptured cohorts. First, embolization reduces nidus size and flow, boosting the effectiveness of SRS, which contributes to consistent obliteration rates in both ruptured and unruptured AVMs.[46] Second, advances in neuroimaging and SRS techniques have improved targeting precision and radiation dose delivery, leading to comparable outcomes for ruptured and unruptured AVMs.[87] Finally, careful patient selection and tailored treatment planning with standardized dosing regimens help offset variations in outcomes.[11]

Other outcomes

Hemorrhagic rate

Our findings indicate that there was no statistically significant disparity in the incidence of hemorrhage between the two interventions. This is consistent with prior extensive studies that have been published on the same subject.[70,71,88] The overall results of our analysis were in line with the individual OR found in most of the studies included in our comprehensive study.[31,47,53,58-60,71-73,75,89,90,92-94,96-101] In contrast, other studies have reported increased hemorrhage rates following pre-SRS embolization,[32,102] with authors hypothesizing that the elevated hemorrhage rates might be attributed to sudden hemodynamic shifts caused by embolization, which could be exacerbated by the irregular endothelium present in the AVM vasculature. This abnormal endothelium may result from elastic and medial degeneration due to prolonged exposure to high flow-induced mechanical stress. Our findings contradict these findings and instead suggest that embolization may not be a significant contributor to elevated hemorrhage rates. Our hypotheses suggest that the primary cause of hemorrhage may not be the hemodynamic shifts caused by embolization. Instead, the irregular endothelium of the AVM vasculature, which is a result of the degeneration of the elastic and medial layers due to prolonged exposure to high flow-induced mechanical stress, may play a more significant role in the development of hemorrhage.[102] Numerous larger-scale studies carried out by Chen *et al*. (1258 participants), Oermann *et al*. (484 participants), and Milker-Zabel *et al*. (292 participants) also support our results.[13,61,71]

RICs

The pre-SRS embolization may protect patients from RIC;[58,103] however, our results found no significant protective advantage against RICs using either intervention. Previous meta-analyses conducted by Russell *et al*.[82] and Xu *et al*.[47,58,73,94,101,104] found pre-SRS embolization to confer protection against RIC. The study by Oermann *et al*., which involved 242 patients in each cohort and utilized a propensity score-matched analysis, found that Pre-SRS embolization resulted in decreased radiographic induced risk of changes.[71] The decreased occurrence of RIC may be attributed to the embolic agent acting as a barrier against radiation, potentially reducing gliosis and endothelial disruption and attenuating the risk of radiation-induced

vasculopathy and subsequent tissue damage.[44,89,105] In addition, the embolization procedure itself may also mitigate the development of radiation-induced arteriopathy, which can lead to a decreased blood supply to the affected area and subsequently reduce venous congestion.[44,105] There is a need to incorporate more studies to establish this association.

Mortality rate

Our investigation showed that the mortality results for the two treatments did not vary statistically significantly. Previous meta-analysis comparing the outcomes between patients undergoing only SRS and those that underwent embolization before SRS found mortality rates to be higher in patients undergoing only SRS, but no information regarding the statistical significance of these results was mentioned.[64] Other studies[73,101] that compared death rates between the two treatment modalities yielded comparable findings to our meta-analysis, indicating no statistically significant difference in mortality rates between the two groups. A propensity score matching study comparing mortality between patients undergoing either only SRS or embolization and SRS also found no significant difference between the mortality rates between the two groups ($P = 0.981$).[60]

Limitations and future implications

The study has limitations, including potential small-study publication bias, heterogeneity in patient demographics, AVM characteristics, treatment techniques, and follow-up durations, and limitations in the design, sample size, and methodological rigor. Furthermore, limited or incomplete data reporting constrains the depth of our analysis. Further research comparing obliteration rates in ruptured and unruptured brain AVMs while controlling for confounding variables, including post-embolization nidus size, treatment modality, intranidal aneurysms, and venous drainage pattern, is required to confirm whether ruptured AVMs have higher obliteration rates than unruptured AVM's. Future studies with data regarding these factors can help mitigate bias and provide more reliable results.

CONCLUSION

From data from 46 studies, with 7077 patients with brain AVMs, a significantly higher obliteration rate was found with ruptured brain AVMs than unruptured brain AVMs, mainly accounted by SRS alone, with no protective advantage of embolization. While no significant differences were seen in the pooled findings, there was a tendency toward a decrease in the frequency of radiation-induced alterations and hemorrhagic rates following SRS alone, but with an increase in mortality. Therefore, SRS alone may confer a substantial benefit with a greater risk-to-reward ratio in achieving significant obliteration of nidus in patients presenting with ruptured brain AVMs, and therefore should be used without any adjunct embolization. Further investigation is necessary to fully understand the effects of pre-SRS embolization on both immediate and long-term consequences, including radiation-induced alterations, hemorrhaging, and mortality. These studies should consider confounding variables such as AVM angioarchitecture, patient variability, and the lack of standardization in techniques and regimens.

Consent

As this was a systematic review and meta-analysis, no consent was required.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

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Conflicts of interest

Abdul Basit Sangah has contributed the same amount of work as the first author.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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