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REVIEW

Does preoperative embolization improve outcomes of meningioma resection? A systematic review and meta-analysis

Fareed Jumah[1] · Anan AbuRmilah[2] · Bharath Raju[1] · Suhaib Jaber[2] · Nimer Adeeb[3] · Vinayak Narayan[1] · Hai Sun[1] · Hugo Cuellar[3,4] · Gaurav Gupta[1] · Anil Nanda[1]

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Abstract

Current evidence regarding the benefit of preoperative embolization (POE) of meningiomas is inconclusive. This systematic review and meta-analysis aims to evaluate the safety profile of the procedure and to compare outcomes in embolized versus non-embolized meningiomas. PubMed was queried for studies after January 1990 reporting outcomes of POE. Pertinent variables were extracted and synthesized from eligible articles. Heterogeneity was assessed using I^2, and random-effects model was employed to calculate pooled 95% CI effect sizes. Publication bias was assessed using funnel plots and Harbord's and Begg's tests. Meta-analyses were used to assess estimated blood loss and operative duration (mean difference; MD), gross-total resection (odds ratio; OR), and postsurgical complications and postsurgical mortality (risk difference; RD). Thirty-four studies encompassing 1782 preoperatively embolized meningiomas were captured. The pooled immediate complication rate following embolization was 4.3% (34 studies, n = 1782). Although heterogeneity was moderate to high (I^2 = 35-86%), meta-analyses showed no statistically significant differences in estimated blood loss (8 studies, n = 1050, MD = 13.9 cc, 95% CI = −101.3 to 129.1), operative duration (11 studies, n = 1887, MD = 2.4 min, 95% CI = −35.5 to 30.8), gross-total resection (6 studies, n = 1608, OR = 1.07, 95% CI = 0.8–1.5), postsurgical complications (12 studies, n = 2060, RD = 0.01, 95% CI = −0.04 to 0.07), and postsurgical mortality (12 studies, n = 2060, RD = 0.01, 95% CI = 0–0.01). Although POE is relatively safe, no clear benefit was observed in operative and postoperative outcomes. However, results must be interpreted with caution due to heterogeneity and selection bias between studies. Well-controlled future investigations are needed to define the patient population most likely to benefit from the procedure.

Keywords Embolization · Meningioma · Systematic review · Meta-analysis · Complications · Benefit

Introduction

Preoperative embolization (POE) of meningiomas has gained considerable interest in the past few decades since its initial description in 1973 [22]. Because meningiomas often tend to be highly vascular, resection can be complicated by significant, potentially life-threatening blood loss that may warrant transfusion [6]. Subsequently, endovascular embolization has emerged as an attractive adjunct to surgical resection. Devascularization of meningiomas before surgery induces necrosis which softens the tumor, potentially facilitating resection and reducing operative duration and blood loss [9, 14, 17].

Despite the touted benefits, there is widespread reluctance to adopt this procedure into standard clinical practice. Complications associated with POE are an important factor to take into consideration. The rate of embolization-related complications was reported to be 4.6% in a 2013 systematic review, with a mortality rate of less than 1% [30].

The purpose of this work is to provide an updated systematic review and meta-analysis in order to better characterize

✉ Anil Nanda
an651@rwjms.rutgers.edu

[1] Department of Neurosurgery, Rutgers-Robert Wood Johnson Medical School & University Hospital, Rutgers-New Jersey Medical School, New Brunswick, NJ, USA

[2] William J. von Liebig Center for Transplantation and Clinical Regeneration Mayo Clinic, Rochester, MN, USA

[3] Department of Neurosurgery, Ochsner-Louisiana State University Hospital, Shreveport, LA, USA

[4] Department of Radiology, Ochsner-Louisiana State University Hospital, Shreveport, LA, USA

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the benefit of POE in the management of intracranial meningiomas. In particular, we seek to provide answers to the following questions: (1) Is POE of meningiomas associated with superior outcomes compared to surgical resection alone? (2) What are the current indications in the literature for the presurgical embolization of meningiomas? (3) What is the safety profile of POE? In particular, we attempt to explore the nature and frequency of embolization-related complications as well as the mortality rate.

Methods

Data sources and study selection

This systematic review was performed in compliance with the PRISMA statement [24]. IRB approval was not required due to the nature of the study. PubMed was queried for articles published after January 1990 using the search string *("Meningioma"[Mesh] or meningioma) AND ("Embolization, Therapeutic"[Mesh] OR "preoperative embolization" OR "presurgical embolization" OR emboliz*)*, last updated on March 17, 2020. The bibliographies of the retrieved articles were manually searched for relevant studies that were not captured in the initial search. Our main focus is to capture studies that compared the outcomes of POE of meningiomas with direct surgical excision (i.e., without embolization).

The titles and abstracts of the retrieved articles were independently screened by two authors (AA and SM) using the population, intervention, comparison, outcomes, and study design (PICOS) criteria outlined in Supplementary Table 1. This was followed by a full-text examination of the selected studies in order to determine their final eligibility for data extraction. Discrepancies were resolved by discussion with a third author (FJ).

Data extraction

Following the selection of articles that met final eligibility, two authors (AA and FJ) extracted study, patient, and tumor variables, namely study design, sample size, gender, age, tumor volume, average maximum diameter, WHO meningioma grade, and tumor location. Parameters pertaining to embolization were also obtained, including embolic material, number of ICA feeders embolized, rate of complete devascularization, and days from embolization to surgery. The outcomes of interest were estimated blood loss (EBL), operative duration (OD), rate of gross-total resection (GTR), embolization-related complications, and postsurgical complications and mortality. Finally, the level of evidence of the included studies was assessed using the Oxford Centre for Evidence-Based Medicine (OCEBM) guidelines [23].

Data synthesis

Data synthesis was performed in two steps: (1) simple pooling of baseline characteristics and complication rate in the embolized patients across all studies and (2) meta-analysis in the double-armed studies to compare outcomes in the embolized versus non-embolized cohorts. Of note, in studies which split the embolized patients into 2 groups (e.g., different embolization materials), variables pertaining to these 2 groups were combined into one. Missing data were estimated using imputation methods; standard deviations were estimated from means and ranges using Wan et al.'s method [35], and means were extrapolated from the medias, quartiles, and ranges using Hozo et al.'s method [13].

Simple pooled analysis

Baseline patient characteristics, treatment parameters, and complication rates in embolized patients were combined across all studies and reported in the form of percentages, weighted means and standard deviations, and ranges. This was performed using Microsoft Excel 2019.

Meta-analysis

Meta-analyses were performed using double-armed studies (i.e., comparing embolized versus non-embolized cohorts) to evaluate five clinical outcomes: estimated blood loss (EBL), operative duration (OD), gross-total resection (GTR), postoperative complications, and postoperative mortality. EBL and OD were analyzed using meta-analysis of mean difference, and GTR using a meta-analysis of odds ratio. Because postoperative complications and postoperative mortality included studies with zero events, performing an odds ratio meta-analysis would overestimate the true difference. Thus, we felt that a meta-analysis of risk difference would be more appropriate in comparing embolized versus non-embolized cohorts. The pooled rates (95% confidence interval [95% CI]) of the outcome measures were calculated, with a $p < 0.05$ denoting statistical significance. The degree of heterogeneity between studies included in the meta-analysis was assessed using the I^2 index (≤25%: low, ~50%: moderate, ≥75%: high). Due to assumptions of heterogeneity between the included studies, the random-effects DerSimonian-Laird model was used in all meta-analyses [8]. The meta-analyses and corresponding forest plots were generated using RevMan v5.4.0.

Quality and bias assessment

The individual quality of the selected studies was evaluated independently by two authors (FJ and AA) using the National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tool. This assessment tool evaluates the internal

validity of studies using standardized checklists that assess parameters like selection, measurement, and outcome biases. Publication bias was assessed using funnel plots and the corresponding Harbord's and Begg's tests generated in StatsDirect v3.0.

Results

Study, patient, and tumor characteristics

The screening process revealed a total of 1782 preoperatively embolized meningiomas across 34 studies consisting of 6 (18%) prospective studies, 22 (65%) retrospective cohort studies, and 6 (18%) case series (Fig. 1). The aggregate sample was predominantly females (63%), with a mean age of 55.1 ± 11.4 (Table 1). The embolized meningiomas had a mean tumor volume of 150 ± 315 cm^3, with an average maximum diameter of 5.23 ± 4.87 cm (range 4.0-10.7 cm). The predominant meningioma location was convexity (30.3%) and parasagittal/falcine (20.3%), followed by middle, posterior, and anterior cranial fossae at 17.8%, 12.9%, and 6.2%, respectively. Table 2 shows a detailed breakdown of the location of the embolized meningiomas. Of all the embolized meningiomas, 79% were WHO grade I, 15.7% grade II, and 2.6% grade III.

Indications for embolization and the embolization technique

The overall rate of utilization of presurgical embolization of meningiomas was 23.4% (range 3.6-69.5%). However, the majority of studies (21/34, 62%) did not report the patient selection criteria or indications for embolization (Supplementary Table 2). Out of the 13 studies that reported indications for embolization, 3 (23%) cited the surgeon's preference and personal experience as the only indication [28, 29, 31]. The most frequently reported indication for embolization was a meningioma size ≥4 cm in diameter, reported in 4 (31%) studies [14, 19, 25, 27]. Iampreechakul et al. selected meningiomas with a blood supply that is difficult to secure intraoperatively, as well as patients with a history of excessive surgical bleeding. The remaining reported criteria were rather subjective in nature, such as a predominance of ECA supply defined as >50% on angiography [19, 25]. On the other hand, factors that deterred from preoperative embolization included skull base location, ease of vascular access intraoperatively, dangerous ECA-ICA anastomosis, presence of feeders to cranial nerves, ICA-predominant blood supply (>50% on angiography), and high tortuosity or narrowness of the feeding vessels [9, 25, 36, 38].

The mean duration to surgery was 3.4 days, and in most studies, the duration between embolization and surgery ranged from 1 to 15 days. The most commonly embolized arteries were branches of the external carotid artery, particularly the middle meningeal artery. Out of all the embolized meningiomas, 34% were supplied by ICA feeders and 12% were predominantly supplied by ICA feeders. When present, ICA feeders were accessed and embolized in 33% of cases (Supplementary Table 3). The most frequently used embolysates were PVA (51%), nBCA (11%), porous beads (8%), and Embosphere (7%). Table 2 outlines all the embolization materials used.

Intraoperative outcomes and embolization-related complications

The mean estimated blood loss (EBL) was 627 ± 1729 ml, and mean operative duration (OD) 5.63 ± 9.9 h. Gross-total resection (GTR) was achieved in 649/986 (66%) of embolized meningiomas. The pooled rate of embolization-related complications in the included studies was 4.3% (0–25%). Minor or transient complications occurred in 2% of cases, and these included headaches and vomiting during the procedure (0.6%), transient motor or cranial never deficits (0.4%), or radiological exacerbation of edema (0.2%). Postprocedural scalp necrosis and groin hematomas were reported in a subset of patients (0.4%). On the other hand, serious complications occurred in about 2.3% of embolized patients. Common major complications were intratumoral hemorrhage (0.5%), visual field deficits (0.4%), and stroke (0.3%), followed by vessel perforation (0.2%), cranial nerve deficits (0.2%), and increased intracranial pressure (0.1%). Death related directly to the embolization procedure was reported in only 1 patient (0.06%) due to iatrogenic carotid occlusion. Postsurgical complications and mortality occurred in 35% and 0.8% of cases, respectively, and are outlined in detail in Supplementary Table 4. In ICA-supplied meningiomas, the aggregate complication rate was 4.3% in those that received ICA feeder embolization (pooled from 4 studies) [1, 3, 33, 38] compared to 3.8% in cases where none of the ICA feeders was embolized (pooled from 4 studies) [4, 12, 15, 39].

Meta-analysis of embolized versus non-embolized cohorts

Of the 34 included studies, 13 were double-armed, comparing meningiomas embolized preoperatively (n = 986) with non-embolized meningiomas (n = 1110) [1, 3, 7, 9, 14, 17, 20, 25, 27–29, 37, 38]. The baseline characteristics and treatment outcomes in embolized and non-embolized groups are shown in Table 3. Imputation of

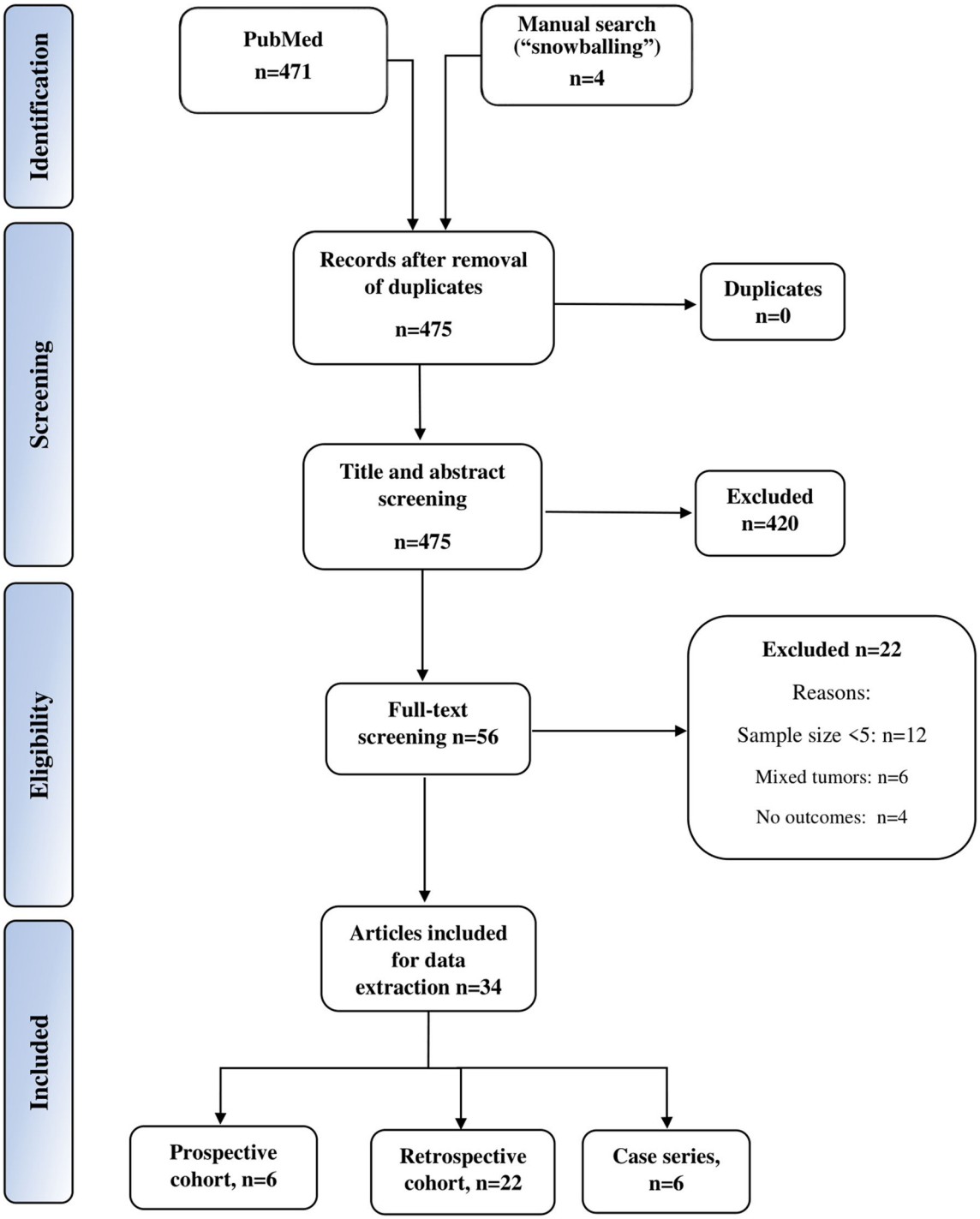


Fig. 1 PRISMA flow diagram outlining the article selection process

missing values was performed in 4 out of the 13 studies to obtain the standard deviations [9, 29, 37, 38]. Meta-analyses showed no clinically or statistically significant differences between embolized and non-embolized meningiomas with respect to any of the following clinical outcomes: estimate blood loss (mean difference = 14 cc; 95% CI −101 to 129 cc; p = 0.81; I^2 = 73%), operative duration (mean difference = 2.4 min; 95% CI −35.5 to 30.8; p = 0.89; I^2 = 86%), gross-total resection (OR = 1.07; 95% CI 0.77-1.47; p = 0.7; I^2 = 35%), postoperative complications (risk difference = 0.01; 95% CI −0.04 to 0.07; p = 0.62; I^2 = 86%), and postoperative mortality (risk

Table 1 The baseline patient and tumor characteristics and treatment outcomes reported in 33 studies

Author/year	Study design	Total meningiomas (n)	Selected for embolization (n)	Male (*n*, %)	Age (mean ± SD [range])	Tumor volume (cm^3, mean ± SD [range])	Average Maximum Diameter (mm, mean ± SD [range])	WHO grading (*n*, %)			Outcomes		
								I	II	III	Estimated blood loss (cc, mean ± SD [range])	Complete resection (*n*, %)	Operative duration (minutes, mean ± SD [range])
Grand et al. 1993	Case series	NR	15	7 (47)	47 ± 12.0	NR	NR	15 (100)	0	0	520 ± 215	NR	NR
Wakhloo et al. 1993	Prospective cohort	NR	32	10 (31)	60 ± 14.0	NR	NR	32 (100)	0	0	542 ± 572	NR	NR
Dean et al. 1994	Retrospective cohort	226	18	NR	NR	NR	57	NR	NR	NR	533 ± 353	NR	302.8 ± 138
Oka et al. 1998	Retrospective cohort	324	12	5 (42)	51 ± 14.0	NR	59 ± 15.3	NR	NR	NR	NR	6 (50)	780 ± 298
Bendszus et al. 2000	Prospective cohort	NR	60	20 (33)	60 ± 6.7	25 ± 14.0	NR	56 (93)	4 (7)	0	761 ± 198 (160-2550)	NR	NR
Bendszus et al. 2000	Prospective cohort	NR	30	12 (38)	56 ± 13.3	29.6 ± 25.4	NR	NR	NR	NR	636 ± 453	NR	310 ± 129
Gruber et al. 2000	Case series	833	63	21 (33)	54 ± 12.0	NR	NR	51 (85)	6 (10)	3 (5)	NR	50 (83.3)	NR
Chun et al. 2002	Retrospective cohort	NR	50	20 (40)	54 (9-83)	45 ± 66 (4-402)	NR	50	0	0	417.7 ± 397.6	NR	457.5 ± 192.97
Hirohata et al. 2003	Case series	NR	7	NR	52 ± 7.6	56 ± 45 (7-132)	45.6 ± 12.7	NR	NR	NR	421 ± 155	6 (86)	NR
Kubo et al. 2003	Case series	NR	13	7 (54)	57 ± 10.8	NR	NR	NR	NR	NR	NR	13	NR
Rodiek et al. 2004	Case series	NR	17	8 (47)	56 ± 12.7	NR	56.5 ± 12	13 (77)	3 (18)	0	749 ± 601	NR	229 ± 77
Kai et al. 2006	Retrospective cohort	203	141	58 (41)	56.6 (26-81)	NR	58 ± 9.8 (40-89)	NR	NR	NR	954 ± 373	NR	NR
Lee et al. 2006	Retrospective cohort	NR	13	NR	NR	NR	NR	NR	NR	NR	775 + 406	NR	1100 + 520
Russell et al. 2008	Prospective cohort	NR	9	6 (17)	60	NR	NR	NR	NR	NR	NR	9 (100)	NR
Yoon et al. 2008	Case series	NR	6	3 (50)	53	129 ± 43	58 ± 8.0	NR	NR	NR	305 ± 50.5	5 (83)	NR
Wu et al. 2009	Retrospective cohort	87	55	7 (31)	55.8 (13.4)	NR	49.2 ± 17.5 (25-90)	NR	NR	NR	733.3 ± 647.1	NR	371 ± 126
Kominami et al. 2012	Retrospective cohort	NR	31	12 (39)	56 ± 14.7	NR	49 ± 11.0	22 (71)	7 (23)	2 (6.5)	NR	27 (87)	NR
Borg et al. 2013	Retrospective cohort	NR	107	43 (40)	54 ± 8.2	NR	56 ± 4.7	68 (64)	26 (24)	0	NR	NR	259 ± 32
Nania et al. 2013	Retrospective cohort	NR	28	13 (46)	61	>4 cm	NR	23 (82)	5 (18)	0	NR	NR	204 ± 33.7
Singla et al. 2013	Retrospective cohort	NR	18	6 (33)	56	NR	56.4	14 (82)	3 (18)	0	574 ± 117 (300-1000)	11 (65)	258
Raper et al. 2014	Retrospective cohort	470	174	58 (33)	56 (17-82)	NR	45.6 ± 12.17 (16-89)	121 (75)	35 (22)	5 (3)	880 ± 450 [median 410, 0-2700]	116 (69.5)	233 ± 97.3 (55-639)
Ali et al. 2015	Prospective cohort	89	52	21 (40)	54 (30-78)	54 ± 38.6 cm^3	NR	NR	NR	NR	389.3 ± 428	38 (73.1)	309.1 ± 168

Table 1 (continued)

Author/year	Study design	Total meningiomas (n)	Selected for embolization (n)	Male (*n*, %)	Age (mean ± SD [range])	Tumor volume (cm^3, mean ± SD [range])	Average Maximum Diameter (mm, mean ± SD [range])	WHO grading (*n*, %)			Outcomes		
								I	II	III	Estimated blood loss (cc, mean ± SD [range])	Complete resection (*n*, %)	Operative duration (minutes, mean ± SD [range])
Ishihara et al. 2015	Retrospective cohort	105	56	22 (39)	60.6	90.7 cm^3	NR	48 (86)	8 (14)	0	516	52 (92.9)	345
Fang et al. 2016	Retrospective cohort	157	95	38 (40)	49 ± 5.7	NR	57.4 ± 16.3	68 (72)	25 (26)	2 (2)	681 ± 376	72 (76)	551 ± 165
Iacobucci et al. 2016	Retrospective cohort	191	64	34 (53)	58 ± 10.8	NR	48.8 ± 14	54 (84)	8 (13)	2 (3)	NR	NR	207.4 ± 79.5
Iampreechakul et al. 2016	Retrospective cohort	NR	18	6 (33)	46 ± 12.2	901.7 ± 83.6	NR	15 (83.3)	3 (16.7)	0	1350 ± 1044	12 (32.4)	NR
Jo et al. 2016	Retrospective cohort	NR	51	11 (23)	58 ± 11.4	58.3 ± 3.4	NR	NR	NR	NR	950 ± 227	NR	408 ± 77
Ohnishi et al. 2016	Retrospective cohort	NR	32	24 (75)	63 (38-83)	NR	50.9 ± 18.98 (21-83)	NR	NR	NR	NR	30 (93.8)	NR
Wen et al. 2016	Prospective cohort	NR	15	8 (56)	50 ± 12.0	118.5 ± 117.6	68 ± 23.0	13 (86.7)	NR	2 (13.3)	467.9 ± 355	NR	250.7 ± 85
Suzuki et al. 2017	Retrospective cohort	78	20	7 (35)	63 ± 11.0	NR	49.5 ± 13.3	NR	NR	NR	338 ± 251	18 (90)	301.5 ± 28
Arai et al. 2018	Retrospective cohort	NR	20	6 (30)	63 ± 14.0	NR	50.4 ± 16.7	18 (90)	1 (5)	1 (5)	410 ± 932	16 (80)	469 ± 220
Manaka et al. 2018	Retrospective cohort	183	69	30 (43)	62 (44-84)	40.6	NR	NR	NR	NR	214	NR	374
Wirsching et al. 2018	Retrospective cohort	779	337	103 (31)	57 (19-88)	NR	46 ± 16.5 (8-107)	258 (76.6)	63 (18.7)	16 (4.7)	NR	173 (51.3)	270 ± 128 (40-810)
Przybylowski et al. 2020	Retrospective cohort	1441	52	14 (27)	55.8 ± 13.1	NR	50 ± 14.0	52 (100)	0	0	660.4 ± 637.1	35 (67)	NR
Summary statistics			1782	640/1744 (36.7%)	55.1 ± 11.4	150 ± 315 cm^3	52.3 ± 48.7 mm	991/1253 (79.0%)	197/1253 (15.7%)	33/1253 (2.6%)	626.5 ± 1729	649/986 (66%)	337.6 ± 594

Table 2 Location of the embolized meningiomas and Embolization materials

Location	*n* (%)	Material	*n* (%)
Convexity	506 (30.3%)	PVA	878 (50.8%)
Parasagittal/falx	340 (20.3%)	nBCA	186 (10.8%)
Anterior cranial fossa	104 (6.2%)	Porous cellulose beads	141 (8.2%)
Olfactory groove	65 (3.9%)	Embosphere	117 (6.8%)
Tuberculum sella	8 (0.5%)	PVA + gelfoam	75 (4.3%)
Clinoidal	7 (0.4%)	Triacyl gelatin microsphere	60 (3.5%)
Unspecified	21 (1.3%)	Small particles	55 (3.2%)
Middle cranial fossa	297 (17.8%)	Glue	42 (2.4%)
Sphenoid wing/ridge	226 (13.5%)	Onyx	40 (2.3%)
Cavernous sinus	12 (0.7%)	Glubran	40 (2.3%)
Unspecified	59 (3.5%)	PVA + coils	38 (2.3%)
Posterior cranial fossa	215 (12.9%)	Gelfoam	23 (1.3%)
Tentorial	41 (2.5%)	Hydroxyapatite	13 (0.8%)
Petroclival	45 (2.7%)	Glue + particles	12 (0.7%)
Cerebellopontine angle	26 (1.6%)	EmboGold	6 (0.3%)
Unspecified	103 (6.2%)	Onyx + nBCA	5 (0.3%)
Intraventricular	6 (0.36%)	PVA + nBCA	3 (0.2%)
Other	142 (8.5%)	PVA + Onyx	3 (0.2%)
Skull base	131 (7.8%)	Onyx + particles	2 (0.1%)
Meningiomatosis	5 (0.3%)	Embozene microsphere	1 (0.1%)
Velum interpositum	1 (0.06%)	CeloNova	1 (0.1%)
Intraosseous	1 (0.06%)		
Unknown	4 (0.24%)		

difference = 0.01; 95% CI 0-0.01; p = 0.16; I^2 = 0%). Figure 2 shows the forest plots of the corresponding meta-analyses.

Results of quality and bias assessment

The quality assessment for each study is summarized in Supplementary Table 5. Out of 34 studies, 14 (42%) were rated as "good," 16 (47%) as "fair," and 4 (12%) as "poor". The funnel plot (Fig. 3) did not show signs of significant publication bias, which was additionally confirmed by Harbord-Egger's (bias = 0.55) and Begg's (0.2) statistical tests ($p > 0.05$).

Discussion

Summary of findings

This study was conducted in an attempt to explore the clinical benefit and safety profile of preoperative embolization of meningiomas. Meta-analyses did not show a clear benefit of embolization with regard to intraoperative bleeding, operative duration, rate of gross-total resection, and postsurgical complications and mortality. Pooled analysis of all the embolized patients (n = 1782) showed relatively low rates of procedure-related complications and mortality, at 4.3% and 0.06%, respectively. Additionally, 85% of studies did not report specific selection criteria for embolization of meningiomas.

Rationale behind the study

Despite meningiomas being one of the most commonly encountered and studied brain tumors, treatment continues to carry high rates of surgical morbidity especially in large, vascular meningiomas which can cause significant bleeding during resection [6]. The excision of stubborn, fibrous meningiomas further contributes to surgical morbidity resulting from the manipulation of critical neurovascular structures. These challenges have culminated in the conception of preoperative embolization which, since its initial description by Manelfe et al. in 1973, has been employed for the past 30 years as an adjunct to surgery [22]. Benefits of POE lie on the premise that devascularization induces histopathologic necrosis, inflammation, and fibrinoid changes which soften the consistency of the tumor, thereby facilitating its resection and

Table 3 Patient characteristics and clinical outcomes in embolized and non-embolized patients

Author/year	Study design	Treatment	Sample size (n)	Male (n, %)	Age (mean ± SD [range])	Outcomes		
						Estimated blood loss (cc, mean ± SD)	Gross-total resection (n,%)	Operative duration (minutes, mean ± SD)
Dean et al. 1994	Retrospective cohort	Embolized	18	NR	NR	533 ± 353	NR	302.8 ± 138
		Non-embolized	18	NR	NR	337 ± 100	NR	337.5 ± 100
Oka et al. 1998	Retrospective cohort	Embolized	12	5 (41.7)	50.7 ± 14	NR	6 (50)	780 ± 298
		Non-embolized	8	2 (25)	51.3 ± 11	NR	5 (62.5)	703 ± 262
Bendzus et al. 2000	Prospective cohort	Embolized	30	12 (37.7)	55.7 ± 13.3	636 ± 453	NR	310 ± 129
		Non-embolized	30	11 (36.7)	60.3 ± 17	646 ± 486	NR	234± 84.6
Lee et al. 2000	Retrospective cohort	Embolized	13	NR	NR	775 + 406	NR	283 + 90
		Non-embolized	23	NR	NR	1100 + 520	NR	271 + 105
Wu et al. 2009	Retrospective cohort	Embolized	55	7 (30.9)	55.8 (13.4)	733.3 ± 647.1	NR	371 ± 126
		Non-embolized	32	17 (21.9)	55.2 (16.9)	795.83 ± 688.73	NR	426.7 ± 173.8
Nania et al. 2013	Retrospective cohort	Embolized	28	13 (46)	60.5	NR	NR	204 ± 33.7
		Non-embolized	18	18	NA	NR	NR	256.1 ± 51.76
Raper et al. 2014	Retrospective cohort	Embolized	174	58 (33.3)	56 (17-82)	410 ± 450	116 (69.5)	233 ± 97.3
		Non-embolized	307	58 (18.9)	58 (18-90)	315 ± 367	228 (75.2)	219 ± 129.7
Ali et al. 2015	Prospective cohort	Embolized	52	40%	54 (30-78)	389.3 ± 428	38 (73.1)	309.1 ± 168
		Non-embolized	37	40%	54 (30-78)	270 ± 193	NR	291 ± 186
Ishihara et al. 2015	Retrospective cohort	Embolized	56	22 (39.3)	60.6	516	52 (92.9)	345
		Non-embolized	49	16 (32.7)	54.9	574	39 (79.6)	407
Fang et al. 2016	Retrospective cohort	Embolized	95	38 (40)	49 ± 5.7	675 ± 374	72 (76)	477 ± 129.6
		Non-embolized	62	23 (37)	49	900 ± 520	44 (71)	547 ± 182.2
Iacobucci et al. 2016	Retrospective cohort	Embolized	64	34 (53.1)	58.4 ± 10.8	NR	NR	207.4 ± 79.5
		Non-embolized	70	28 (40)	59 ± 11	NR	NR	226.9 ± 117.6
Wirsching et al. 2018	Retro cohort	Embolized	337	103 (30.6)	57 (19-88)	NR	173 (51.3)	270 ± 128.3
		Non-embolized	404	130 (32.2)	59 (18-87)	NR	210 (52.0)	210 ± 119.2
Przybylowski et al. 2020	Retrospective cohort	Embolized	52	14 (27)	55.8 ± 13.1	660.4 ± 637.1	35 (67)	NR
		Non-embolized	52	13 (25)	55.3 ± 11.9	509.2 ± 422.0	39 (75)	NR

minimizing blood loss [18, 26]. The initial interest in this technique was subsequently fueled by the rapid advancements in endovascular and embolysate technology that ensued over the last decade.

Many studies have assessed the benefits of POE of meningiomas, but the conflicting results have precluded the integration of the procedure into standard clinical practice. The resulting lack clear of guidelines has subsequently led to a huge variability in the utilization of POE across institutions, a notion further supported by our findings (3.6-69.5%). Multiple systematic reviews were performed in order to distill the available literature into more concise metrics that can guide clinical practice and decision-making. Shah et al. found a 4.6% pooled complication rate in 459 embolized meningiomas across 36 studies, closely resembling our 4.3% [30]. Ilyas et al., on the other hand, analyzed treatment outcomes of 403 skull base meningiomas embolized preoperatively, revealing a higher complication rate of 12% [16]. Only one meta-analysis exists to date, which compares operative outcomes in 510 embolized versus non-embolized meningiomas, showing that POE significantly reduced blood loss and operative duration, contrary to our findings [5]. However, the current updated meta-analysis sought to improve on some of the methodological limitations found in the previous studies. For example, the current meta-analysis included 5 additional studies meeting the selection criteria that were not included in previous meta-analyses [1, 5, 25, 27, 29, 37]. Omitting relevant studies in a systematic review can have a considerable impact on the study findings that is sometimes enough to change statistically insignificant findings to significant. Therefore, we have attempted to address these limitations in our meta-analysis by including all relevant studies within the search date range as well as by following appropriate statistical methodology (e.g., clarification of imputation methods) in order to increase the reproducibility of the results and minimize bias.

Clinical implications

Upon re-evaluation of the literature, we have identified a clear disagreement regarding the benefits of POE on clinical outcomes in meningioma patients. Some studies support its efficacy in reducing blood loss during tumor resection [7, 9, 17, 25, 27], especially if complete devascularization is achieved [4, 10, 15, 29]. In a comparison between embolized (n = 56) and non-embolized (n = 49) meningiomas, Ishihara et al. reported a significant reduction in intraoperative blood loss and blood transfusion, especially in meningiomas with an ECA-dominant blood supply [17]. Meanwhile, others have shown that efficacy of embolization depends on the size of meningioma. Oka et al. reported a positive outcome in meningiomas <6 cm in diameter [27]. To the contrary, Wu et al. showed that embolization is more effective in reducing bleeding at larger tumor sizes, albeit without a clear cut-off due to sample size limitations [38]. While the aforementioned studies supported the role of POE, others showed no clear benefit in reducing intraoperative blood loss [1, 3, 28, 38].

Few studies have reported shortened surgical duration in embolized meningiomas compared to their non-embolized counterparts [9, 21], especially with extensive devascularization [14]. Yet, others found no difference in the operative duration between the two groups [1, 3, 7, 29, 38], and some even reported a paradoxical 60-min increase in the embolized cohort [37]. Nonetheless, there seems to be an agreement on delaying surgical resection after embolization, with varying degrees. Some recommended performing surgery at least 24 h post embolization[6], while others recommended a delay of at least 7 days in order to achieve the maximum tumor softening possible [19, 25]. Furthermore, the US healthcare system's emphasis on value-based care puts the true cost-effectiveness of this procedure into question. We found only one study that directly assessed the cost-effectiveness of POE, showing a lower average total cost in embolized patients ($29,606 versus $38,451), although that did not reach statistical significance [7].

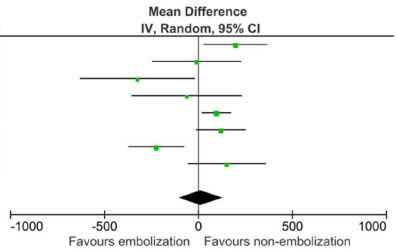
Embolization of meningiomas can carry potentially serious complications [3, 11, 17, 19, 21, 34, 36]. Establishing the likelihood of complications is vital for a sound risk-to-benefit analysis. Our results show that approximately 1 in every 20 patients will suffer an immediate complication, and 1 in 50 will experience a serious complication such as permanent hearing loss [19], coma [36], or death [11]. That being said, embolization can be favorable in certain situations such as in a large meningioma primarily supplied by the ECA. Embolization is also useful in skull base meningiomas where vascular pedicles are hard to reach, and can only be accessed after a significant portion of the tumor has been debulked [12].

In meningiomas predominantly supplied by the ICA or VA, embolization of ECA feeders could trigger a compensatory increased flow from the unembolized ICA or VA branches, thereby negating the original purpose of embolization [9]. At the same time, embolizing ICA/VA feeders can be risky and technically challenging due to their narrowness and tortuosity [2, 30, 32], and is therefore not routinely performed. Our findings support this notion, where ICA feeders, when present, were embolized in only 33% of cases. Out of the 34 included studies in this analysis, only two assessed the clinical value of embolization strictly in ICA branches. Hirohata et al. reported safe, complete devascularization in 42% of ICA feeders of petroclival meningiomas [12]. Similarly, Yoon et al. reported a complication-free embolization of the ICA feeders in 6 meningiomas in mixed locations [39].

a

Study or Subgroup	Embolized Mean	SD	Total	Non-embolized Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Dean et al. 1994	533	353	18	337	100	18	13.5%	196.00 [26.51, 365.49]	1994
Bendzus et al. 2000	636	453	30	646	486	30	10.6%	-10.00 [-247.74, 227.74]	2000
Lee et al. 2006	775	406	13	1,100	520	23	8.1%	-325.00 [-631.38, -18.62]	2006
Wu et al. 2009	733	647	55	796	689	32	8.5%	-63.00 [-356.64, 230.64]	2009
Raper et al. 2014	410	450	174	315	367	307	17.6%	95.00 [16.54, 173.46]	2014
Ali et al. 2015	389	428	52	270	193	37	15.3%	119.00 [-12.91, 250.91]	2015
Fang et al. 2016	675	374	95	900	520	62	14.5%	-225.00 [-374.70, -75.30]	2016
Przybylowski et al. 2020	660.4	637.1	52	509.2	422	52	11.8%	151.20 [-56.50, 358.90]	2020
Total (95% CI)			**489**			**561**	**100.0%**	**13.90 [-101.32, 129.12]**	

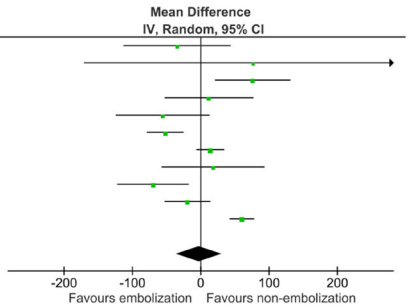
Heterogeneity: Tau² = 18028.94; Chi² = 25.61, df = 7 (P = 0.0006); I² = 73%
Test for overall effect: Z = 0.24 (P = 0.81)



b

Study or Subgroup	Embolized Mean	SD	Total	Non-embolized Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Dean et al. 1994	302.8	138	18	337.5	100	18	7.4%	-34.70 [-113.43, 44.03]	1994
Oka et al. 1998	780	298	12	703	262	8	1.6%	77.00 [-170.77, 324.77]	1998
Bendzus et al. 2000	310	129	30	234	84.6	30	9.4%	76.00 [20.80, 131.20]	2000
Lee et al. 2006	283	90	13	271	105	23	8.5%	12.00 [-53.08, 77.08]	2006
Wu et al. 2009	371	126	55	426.7	173.8	32	8.2%	-55.70 [-124.51, 13.11]	2009
Nania et al. 2013	204	33.7	28	256.1	51.76	18	11.8%	-52.10 [-79.07, -25.13]	2013
Raper et al. 2014	233	97.3	174	219	129.7	307	12.2%	14.00 [-6.48, 34.48]	2014
Ali et al. 2015	309.1	168	52	291	186	37	7.7%	18.10 [-57.25, 93.45]	2015
Fang et al. 2016	477	129.6	95	547	182.2	62	9.7%	-70.00 [-122.31, -17.69]	2016
Iacobucci et al. 2016	207.4	79.5	64	226.9	117.6	70	11.3%	-19.50 [-53.24, 14.24]	2016
Wirsching et al. 2018	270	128.3	337	210	119.2	404	12.3%	60.00 [42.04, 77.96]	2018
Total (95% CI)			**878**			**1009**	**100.0%**	**-2.39 [-35.54, 30.76]**	

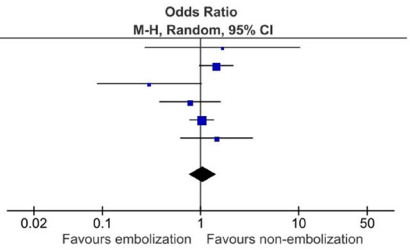
Heterogeneity: Tau² = 2243.97; Chi² = 72.43, df = 10 (P < 0.00001); I² = 86%
Test for overall effect: Z = 0.14 (P = 0.89)



c

Study or Subgroup	Non-embolized Events	Total	Embolized Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Oka et al. 1998	5	8	6	12	2.9%	1.67 [0.27, 10.33]	1998
Raper et al. 2014	228	307	116	174	28.6%	1.44 [0.96, 2.17]	2014
Ishihara et al. 2015	39	49	52	56	6.0%	0.30 [0.09, 1.03]	2015
Fang et al. 2016	44	62	72	95	14.4%	0.78 [0.38, 1.61]	2016
Wirsching et al. 2018	210	404	173	337	37.0%	1.03 [0.77, 1.37]	2018
Przybylowski et al. 2020	39	52	35	52	11.1%	1.46 [0.62, 3.42]	2020
Total (95% CI)		**882**		**726**	**100.0%**	**1.07 [0.77, 1.47]**	
Total events	565		454				

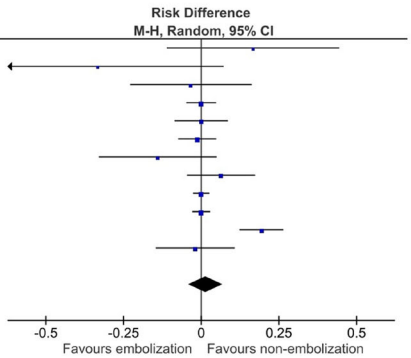
Heterogeneity: Tau² = 0.05; Chi² = 7.69, df = 5 (P = 0.17); I² = 35%
Test for overall effect: Z = 0.39 (P = 0.70)



d

Study or Subgroup	Embolized Events	Total	Non-embolized Events	Total	Weight	Risk Difference M-H, Random, 95% CI	Year
Dean 1994	6	18	3	18	3.1%	0.17 [-0.11, 0.44]	1994
Oka et al. 1998	2	12	4	8	1.6%	-0.33 [-0.74, 0.07]	1998
Bendzus et al. 2000	5	30	6	30	5.0%	-0.03 [-0.23, 0.16]	2000
Wu et al. 2009	0	55	0	32	11.8%	0.00 [-0.05, 0.05]	2009
Nania et al. 2013	0	28	0	18	9.9%	0.00 [-0.09, 0.09]	2013
Raper et al. 2014	21	174	41	307	11.2%	-0.01 [-0.07, 0.05]	2014
Ali et al. 2015	11	52	13	37	5.2%	-0.14 [-0.33, 0.05]	2015
Ishihara et al. 2015	7	56	3	49	8.6%	0.06 [-0.05, 0.17]	2015
Fang et al. 2016	0	95	0	62	12.6%	0.00 [-0.03, 0.03]	2016
Iacobucci et al. 2016	0	64	0	70	12.6%	0.00 [-0.03, 0.03]	2016
Wirsching et al. 2018	192	337	152	404	10.7%	0.19 [0.12, 0.26]	2018
Przybylowski et al. 2020	6	52	7	52	7.7%	-0.02 [-0.15, 0.11]	2020
Total (95% CI)		**973**		**1087**	**100.0%**	**0.01 [-0.04, 0.07]**	
Total events	250		229				

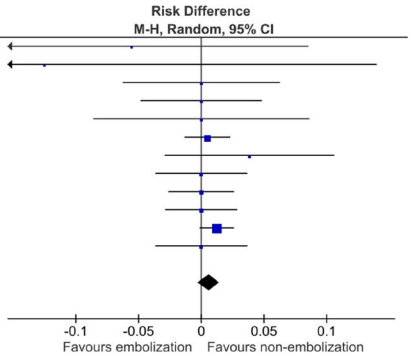
Heterogeneity: Tau² = 0.01; Chi² = 79.76, df = 11 (P < 0.00001); I² = 86%
Test for overall effect: Z = 0.50 (P = 0.62)



e

Study or Subgroup	Embolized Events	Total	Non-embolized Events	Total	Weight	Risk Difference M-H, Random, 95% CI	Year
Dean 1994	0	18	1	18	0.4%	-0.06 [-0.20, 0.09]	1994
Oka et al. 1998	0	12	1	8	0.1%	-0.13 [-0.39, 0.14]	1998
Bendzus et al. 2000	0	30	0	30	1.9%	0.00 [-0.06, 0.06]	2000
Wu et al. 2009	0	55	0	32	3.2%	0.00 [-0.05, 0.05]	2009
Nania et al. 2013	0	28	0	18	1.0%	0.00 [-0.09, 0.09]	2013
Raper et al. 2014	2	174	2	307	22.3%	0.00 [-0.01, 0.02]	2014
Ali et al. 2015	2	52	0	37	1.6%	0.04 [-0.03, 0.11]	2015
Ishihara et al. 2015	0	56	0	49	5.5%	0.00 [-0.04, 0.04]	2015
Fang et al. 2016	0	95	0	62	10.8%	0.00 [-0.03, 0.03]	2016
Iacobucci et al. 2016	0	64	0	70	8.9%	0.00 [-0.03, 0.03]	2016
Wirsching et al. 2018	5	337	1	404	38.9%	0.01 [-0.00, 0.03]	2018
Przybylowski et al. 2020	0	52	0	52	5.5%	0.00 [-0.04, 0.04]	2020
Total (95% CI)		**973**		**1087**	**100.0%**	**0.01 [-0.00, 0.01]**	
Total events	9		5				

Heterogeneity: Tau² = 0.00; Chi² = 4.13, df = 11 (P = 0.97); I² = 0%
Test for overall effect: Z = 1.41 (P = 0.16)



◀ **Fig. 2** Forest plots showing comparisons **a** estimated blood loss, **b** operative duration, **c** gross-total resection, **d** postoperative complications, and **e** postoperative mortality in embolized versus non-embolized treatment groups. The squares indicate means or the incidence of event from each study, with square sizes reflecting the statistical weight of the study. The black diamonds indicate the summary effect size. The horizontal lines indicate 95% confidence intervals. The vertical solid line indicates the line of no effect i.e. mean difference or risk difference of 0, or odds ratio of 1. These plots demonstrate that none of the parameters achieved a statistically significant difference in favor of embolization over surgical excision alone

Despite these successful reports, routine ICA feeder embolization cannot be fully justified due to the limited number of studies.

Limitations and future directions

This study is not limitation-free. The meta-analysis was based on data mostly from level III and level IV (retrospective cohort studies and case series) studies. Additionally, there is an inherent degree of heterogeneity in the patient populations (e.g., varying meningioma sizes and locations) and study designs, as well as selection bias as shown by the vague patient selection criteria. Nonetheless, the huge variation in the utilization of POE between institutions (3-70%) while yielding similar outcomes—as per our findings—is noteworthy. This calls for well-controlled studies that allow better identification of the patient populations most likely to benefit from embolization, thereby justifying the additional risk and cost associated with the procedure.

In order to overcome previously mentioned limitations, future studies may consider cohort matching in their methodology. Przybylowski et al. compared the clinical outcomes of POE in two cohorts (56 patients each) matched by age, tumor size, location, laterality, and invasion into dural sinuses. They found no difference in intraoperative blood loss, gross-total resection, perioperative complications, or postoperative modified Rankin Scores between the two groups. Embolization did, however, lead to greater clinical improvement compared to surgical resection alone [28]. Matching allows for the use of smaller sample sizes while helping to eliminate important confounders such as tumor size, tumor location, patient age, and embolization technique.

Conclusions

The current meta-analysis showed no direct benefit of embolizing meningiomas preoperatively. There are currently no randomized clinical trials or large comparative studies that can solidly establish POE as a routine component in the treatment of meningiomas. At the time being, the decision to embolize a meningioma preoperatively must be tailored to each individual patient based on the anticipated degree of blood loss and the difficulty

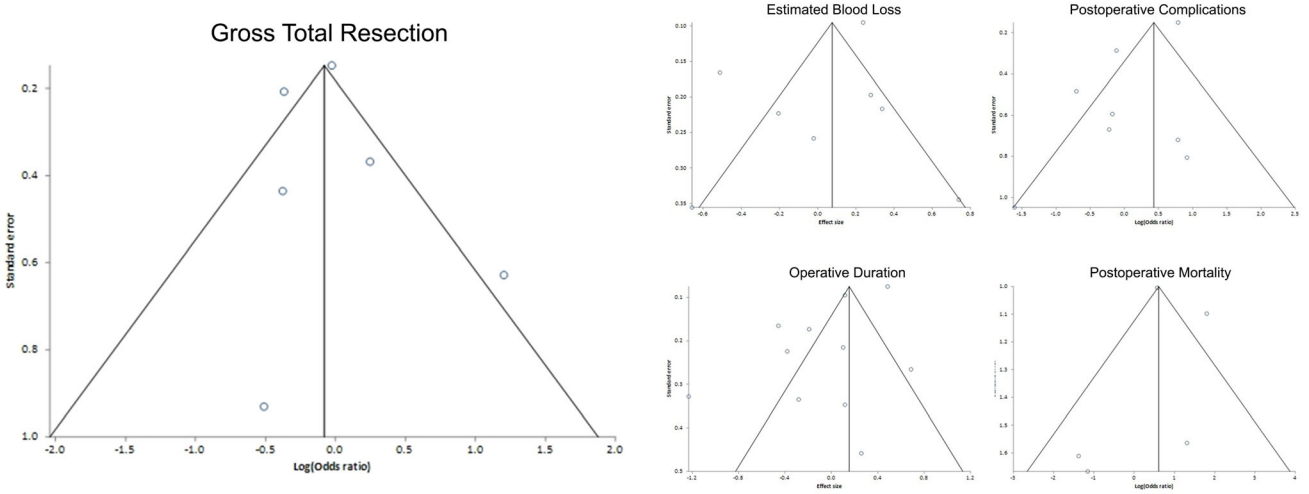


Fig. 3 Funnel plots. The funnel plot on the left was generated using the 6 studies that reported gross-total resection (outcome with lowest heterogeneity, I^2 = 35%). No signs of publication bias are observed [Begg-Mazumdar: Kendall's 0.2, p = 0.72; Egger: bias = 0.55 (95% CI = −2.35 to 3.44) p = 0.63; Harbord-Egger: bias = 0.55 (92.5% CI = −2.06 to 3.15), p = 0.6417]. Although the remaining funnel plots had higher degrees of heterogeneity (I^2 = 69-88%), they show minimal signs of publication bias

in securing the vascular supply intraoperatively. Until further evidence from clinical trials emerges, we recommend the use of matched control groups in future studies where the benefits and risks of embolization can be more accurately assessed.

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Code availability Not applicable.

Author contribution • Conception of design and work: Nimer Adeeb, Fareed Jumah, Bharath Raju, Anan Abu Rmilah.
• Data collection: Fareed Jumah, Anan AbuRmilah, Suhaib Jaber.
• Data analysis and interpretation: Fareed Jumah, Anan AbuRmilah.
• Drafting the article: Fareed Jumah, Anan AbuRmilah, Bharath Raju, Suhaib Jaber, Nimer Adeeb, Vinayak Narayan, Hai Sun, Hugo Cuellar, Gaurav Gupta, Anil Nanda.
• Critical revision of the article: Fareed Jumah, Anan AbuRmilah, Bharath Raju, Suhaib Jaber, Nimer Adeeb, Vinayak Narayan, Hai Sun, Hugo Cuellar, Gaurav Gupta, Anil Nanda.
• Final approval of the version to be published: Fareed Jumah, Anan AbuRmilah, Bharath Raju, Suhaib Jaber, Nimer Adeeb, Vinayak Narayan, Hai Sun, Hugo Cuellar, Gaurav Gupta, Anil Nanda.

Data Availability Data used for this meta-analysis is available in the manuscript and supplementary material.

Declarations

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

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