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# Outcomes of Preoperative Transophthalmic Artery Embolization of Meningiomas: A Systematic Review with a Focus on Embolization Agent

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## ABSTRACT

**BACKGROUND:** Transophthalmic artery embolization of intracranial meningiomas is thought to be associated with a high complication risk.

**PURPOSE:** With advances in endovascular techniques, we systematically reviewed the current literature to improve our understanding of the safety and efficacy of transophthalmic artery embolization of intracranial meningiomas.

**DATA SOURCES:** We performed a systematic search using PubMed from inception until August 3, 2022.

**STUDY SELECTION:** Twelve studies with 28 patients with intracranial meningiomas embolized through the transophthalmic artery were included.

**DATA ANALYSIS:** Baseline and technical characteristics and clinical and safety outcomes were collected. No statistical analysis was conducted.

**DATA SYNTHESIS:** The average age of 27 patients was 49.5 (SD, 13) years. Eighteen (69%) meningiomas were located in the anterior cranial fossa, and 8 (31%), in the sphenoid ridge/wing. Polyvinyl alcohol particles were most commonly ( $n = 8$ , 31%) used to preoperatively embolize meningiomas, followed by *n*-BCA in 6 (23%), Onyx in 6 (23%), Gelfoam in 5 (19%), and coils in 1 patient (4%). Complete embolization of the target meningioma feeders was reported in 8 (47%) of 17 patients; partial embolization, in 6 (32%); and suboptimal embolization, in 3 (18%). The endovascular complication rate was 16% (4 of 25), which included visual impairment in 3 (12%) patients.

**LIMITATIONS:** Selection and publication biases were limitations.

**CONCLUSIONS:** Transophthalmic artery embolization of intracranial meningiomas is feasible but is associated with a non-negligible complication rate.

**ABBREVIATIONS:** OPH = ophthalmic artery; PVA = polyvinyl alcohol

Intracranial meningiomas are often highly vascular tumors, accounting for 13%–26% of primary intracranial neoplasms.<sup>1</sup> Intracranial meningiomas can be associated with seizures, headaches, vision loss, or focal neurologic deficits.<sup>2</sup> Surgical resection is the primary technique of treatment, which may result in

serious blood loss.<sup>1</sup> Increased blood loss is linked to worse patient outcomes.<sup>3</sup> Transarterial embolization of the tumor is an effective strategy to reduce intraoperative blood loss and facilitate the removal of meningiomas by shortening the operation time and increasing the likelihood of complete resection.<sup>4</sup>

Blood supply to meningiomas commonly arises from dural branches of the external and internal carotid and vertebral arteries, as well as from pial sources.<sup>5</sup> However, some meningiomas, specifically those located in the anterior and middle skull base, may be supplied by dural branches of the ophthalmic

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artery, such as the ethmoid, recurrent meningeal, and deep recurrent meningeal arteries.<sup>5,6</sup> Embolization via the ophthalmic artery (OPH) route poses a risk of retinal ischemia and visual deficits.<sup>6</sup> Given this hazard, preoperative embolization of OPH is rarely performed.

To better understand the efficacy and safety profile of trans-ophthalmic artery embolization of intracranial meningiomas, we reviewed the published literature regarding the type and location of meningiomas embolized, the type of embolic material used, and the type and frequency of procedural complications associated with OPH embolization of meningiomas.

## MATERIALS AND METHODS

### Search Strategy

A medical librarian searched the medical literature according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>12</sup> Search strategies used a combination of keywords and standardized index terms that included [("embolization, therapeutic" OR "embolism" OR "embolization" OR "embolisation" OR "embolotherap") AND ("meningioma" OR "meningeal Neoplasms" OR "meningeal tumor" OR "meningeal tumor" OR "meningeal cancer" OR "meningeal neoplasm")]. Searches were run on August 3, 2022, in the PubMed (MEDLINE) data base. Included articles met all inclusion criteria (published in English, reported data for a consecutive series of patients with meningiomas receiving embolization through the ophthalmic artery, a branch of the ICA, before surgical resection with an identifiable report of primary outcomes). Reviews, guidelines, technical notes, comments, conference abstracts, animal studies, and editorials were excluded.

### Study Selection Process

Title, abstract, and full-text screenings were conducted by 2 (M.Z. and K.M.P.) authors using EndNote ([https://support.clarivate.com/Endnote/s/article/Download-EndNote?language=en\\_US](https://support.clarivate.com/Endnote/s/article/Download-EndNote?language=en_US)). Conflicts were resolved by a senior author (M.A.E. or D.J.A.).

### Data Extraction and Outcome Measures

Baseline patient and tumor characteristics and technical information about the embolization procedure were extracted from each article. Outcomes were analyzed for embolization material, the reported postembolization devascularization rate, complications, postoperative surgical resection grades, and complications and clinical outcomes. Clinical outcomes were classified as favorable, disability (permanent neurologic complication), or death.

### Statistical Analysis and Risk of Bias Assessment

The continuous variables were summarized using means (SDs), and categorical variables were summarized using frequencies and proportions. No statistical comparisons were performed. The data analyses were performed using Excel 365 software (Microsoft).

The risk of bias among included studies was assessed using the Joanna Briggs Institute Critical Appraisal Tool for case reports ([https://www.researchgate.net/figure/The-Joanna-Briggs-Institute-JBI-critical-appraisal-checklist-for-studies-reporting\\_fig2\\_322317583](https://www.researchgate.net/figure/The-Joanna-Briggs-Institute-JBI-critical-appraisal-checklist-for-studies-reporting_fig2_322317583)). In addition, the risk of bias within this systematic review was performed using the ROBIS tool (<https://abstracts.cochrane.org/introduction-robis-tool-assess-risk-bias-systematic-review>).

## RESULTS

### Study Selection and Baseline Characteristics and Risk of Bias

After the initial review of 472 references collected from the PubMed library search, 12 studies with 28 patients (Online Supplemental Data) were included in this systematic review.<sup>1,5-15</sup> A flow chart of the screening process is illustrated in the Online Supplemental Data. The risk of bias was low in 10 and high in 2 studies (Online Supplemental Data). Publication bias and heterogeneity among studies were not evaluated due to the nature of the included studies, which were case reports, and due to the very small sample size. The risk of bias within this systematic review was medium. The risk of bias within the synthesis and findings was unclear because no statistical evaluation of publication bias and heterogeneity was performed due to the reasons mentioned earlier (Online Supplemental Data).

The average age of 27 patients was 49.5 (SD, 13) years, with 13 (48%) women (Online Supplemental Data). The most common symptom on presentation was visual disturbance (50%; 7 of 14), followed by organic psychological disorder/dementia (36%), headache (29%), hemiparesis (21%), anosmia (14%), and apathy (14%) (Online Supplemental Data).

Eighteen (69%) meningiomas were located in the anterior cranial fossa, and 8 (31%), in the sphenoid ridge/wing. Eleven (42%) meningiomas were fed by a single arterial feeder. The ethmoidal arteries were the most commonly embolized ophthalmic branches (60%), followed by other meningeal branches (40%, recurrent, accessory, or anterior arteries) (Online Supplemental Data).

### Technical Characteristics

Polyvinyl alcohol (PVA) particles overall ( $n = 8$ , four without coils and 4 with coils) were the most commonly (31%) used material to preoperatively embolize meningiomas, followed by  $n$ -BCA in 6 (23%), Onyx (Covidien) in 6 (23%) patients, Gelfoam (Pfizer) in 5 (19%), and primary coil embolization in 1 patient (4%) (Online Supplemental Data). Among 8 patients receiving PVA particles, the particle size was reported in 3 patients, including 90–180  $\mu\text{m}$  and 150–300  $\mu\text{m}$  in 2 meningiomas embolized via PVA particles alone and 1 meningioma embolized with a combination of 120- to 250- $\mu\text{m}$  PVA particles and coils. Microcatheters included Tracker 18 (Target Therapeutics) in 7 (54%) patients and Marathon (Covidien) in 6 (46%). Seven studies with 15 patients did not report the type of microcatheter used.

Meningiomas embolized with PVA particles were predominantly located in the anterior cranial fossa and were of the meningotheial histopathologic type. A higher prevalence of fibroblastic meningiomas was reported among the  $n$ -BCA and Onyx groups (Online Supplemental Data).

### Outcomes

Embolization outcomes were not reported in 9 patients. Eight (47%) of 17 patients received complete embolization of target meningioma feeders, 6 (32%) had partial embolization, and 3 (18%) were suboptimally embolized (Online Supplemental Data).

Complications were not reported in 3 patients from 2 studies. The overall endovascular complication rate was 16% (4 of 25 cases), which included visual impairment in 3 (12%, quadrantanopsia or hemianopsia in 2, and total vision loss in 1) and peritumoral hemorrhage/oculomotor nerve palsy in 1 (4%) (Online Supplemental Data). In addition, loss of retinal blush occurred in 1 (4%) patient but without clinical sequelae.

Surgical outcomes were reported among 15 cases. Postoperative complete meningioma excision was descriptively reported in 14 (93%). Simpson scale grades were reported by only 2 studies with 5 patients, including 1 (20%) meningioma with grade I, 3 (60%) with grade II, and 1 (20%) with grade IV (Online Supplemental Data). On the postoperative histopathologic evaluation of resected meningiomas, 4 (50%) of 8 meningiomas were a meningothelial type, 2 (25%) were fibroblastic, one (13%) was transitional, and one (13%) was atypical (Online Supplemental Data).

Clinical outcomes were reported among only 9 patients. Postoperative clinical outcomes were favorable or improved in 8 of 9 (89%) patients, and one (11%) died due to progressive brain edema. No long-term follow-up was reported among any patients in the included studies.

### Outcomes by Embolization Agent

Among 4 patients with meningiomas embolized with PVA, 2 showed suboptimal embolization outcomes, defined as delayed opacification of the occluded vessel (Online Supplemental Data). Varying results of PVA  $\pm$  coils and *n*-BCA were reported among the studies included. Complete or partial embolization of the feeders was reported after Onyx and *n*-BCA embolization of 5 and 3 meningiomas, respectively. One (17%, of 6 receiving Onyx) patient experienced total vision loss after Onyx, and another patient had a loss of retinal blush on an angiogram after Onyx embolization with a microcatheter positioned distal to the origin of the central retinal artery but without visual sequelae. One patient with a sphenoid wing meningioma was embolized using Onyx and experienced total vision loss after the procedure. Two (40%) patients with meningiomas embolized via Gelfoam experienced partial visual impairment after the procedure. The first patient with an olfactory groove meningioma embolized through the posterior ethmoidal artery experienced postprocedural quadrantanopsia. The second patient with a sphenoid wing meningioma embolized through both the posterior ethmoid and anterior choroidal arteries and ICA perforators using Gelfoam powder developed hemianopsia, which the authors attributed to anterior choroidal artery embolization. Complete tumor resection was achieved in most cases with different embolization materials. However, only 1 patient with a 5.5-cm sphenoid wing meningioma embolized using coils alone had a postsurgical Simpson grade of IV. No difference in clinical outcomes and mortality by embolization material was reported except for 1 mortality event of a patient with sphenoid wing meningioma embolized using *n*-BCA who died after surgical resection because of brain edema.

## DISCUSSION

To date, few case reports of patients with meningiomas undergoing OPH embolization have been reported. To the best of our knowledge, this systematic review is the first to comprehensively

summarize the available literature evidence on the outcomes of OPH embolization of skull base meningiomas, with a vision loss of 12%.

The role of preoperative transarterial embolization for meningioma resection remains controversial. While it can improve resection rates and reduce intraoperative blood loss, the procedure comes with the risk of serious complications. A meta-analysis published in 2021 included 34 studies with 1782 preoperatively embolized meningiomas and found no significant difference in technical and safety outcomes of preoperative embolization versus nonembolization of meningiomas.<sup>16</sup> Akimoto et al,<sup>17</sup> in a recent retrospective propensity-matched analysis of 186 patients with World Health Organization grade 1 meningiomas, compared the outcomes of 42 patients receiving embolization with 42 patients who did not undergo embolization before the operation. The authors found that the embolization group had favorable recurrence-free survival (49.4 versus 24.1 months,  $P = .049$ ) and less intraoperative blood loss (mean 178 [SD, 203] mL versus 221 [SD, 165] mL,  $P = .009$ ) compared with the nonembolization group. However, they found no significant differences in Simpson IV resection (33.3% versus 28.6%,  $P = .637$ ) or overall perioperative complications (21.4% versus 11.9%,  $P = .241$ ). Notably, middle cranial fossa meningiomas supplied by the meningohipophyseal and inferolateral trunks have been safely embolized.<sup>18</sup>

Meningiomas with primary arterial supply from the ophthalmic artery are located in the skull base,<sup>12</sup> as we found in this study, which included meningiomas located in the olfactory groove and sphenoid wing. Meningiomas in these locations are large and highly vascularized, with multiple feeders from the ophthalmic artery such as ethmoidal arteries (most commonly) and other arteries.<sup>19,20</sup> Thus, surgical treatment of these lesions carries a high risk of complications. Transcranial surgical resection of these meningiomas comes with a higher potential risk than meningiomas primarily supplied by external carotid sources. The expanded transnasal endoscopic approach to treating anterior skull base meningiomas has increased in use during the past decade. While this technique is extremely useful in limiting brain retraction and its secondary consequences, the ability to control bleeding is technically more complex than traditional open surgical approaches. As a result, transarterial embolization may have a more valuable role when deciding to use endoscopic approaches for meningioma resection.

While ophthalmic artery feeder embolization comes with a clear and serious risk of vision loss, advances in microcatheters and microwires may make this approach safer and more feasible now compared with the past. Terada et al,<sup>5</sup> in 1996, reported a rate of posttreatment visual impairment of 25% among 4 meningiomas embolized with Gelfoam powder, PVA particles, and/or microcoils through the ophthalmic artery. Trivelatto et al<sup>6</sup> described promising safety outcomes of Onyx for the embolization of meningiomas fed by the ophthalmic artery, which they attributed to the nonadhesive characteristics and the low precipitation rate of Onyx, allowing more controlled injection.<sup>21,22</sup> The authors suggested that successful embolization of the OPH branches with a low risk of inadvertent central retinal artery occlusion can only be achieved when the microcatheter tip is positioned safely and Onyx injections are performed very slowly and intermittently to avoid excessive reflux.

On the other hand, other reports mentioned that preservation of central retinal artery occlusion could be better achieved when PVA particles of  $>300\text{ }\mu\text{m}$  are used, considering that the central retinal artery is narrower than  $300\text{ }\mu\text{m}$ .<sup>5,23</sup> Nevertheless, precautions were reported to be necessary because the PVA particles have a high potential to fragment into smaller pieces during the mixing process and occlude the central retinal artery with retrograde filling. Most included cases received PVA embolization with particles with sizes between 80 and  $300\text{ }\mu\text{m}$ . Furthermore, no visual impairment was reported among the patients who received PVA particles or *n*-BCA.

The microcatheter used to deliver the embolization material plays a crucial role in safely completing the embolization procedure. Half of the included patients had details reported of the microcatheter used, including Tracker 18 in 7 (54%) patients and Marathon in the rest. Among 3 patients with severe visual complications, 2 had meningiomas embolized with Gelfoam delivered by a Tracker 18 microcatheter and 1 had a meningioma embolized with Onyx, but the microcatheter used was not reported. The Tracker 18 microcatheter is an old microcatheter with a relatively large inner diameter (0.024 inch). Injury to the central retinal artery can be caused by accidental embolization due to improper catheter position or excessive reflux to the point of origin of the central retinal artery. Superselective microcatheter injection, with a detailed analysis of the vascular anatomy, is essential for understanding the safe position of the embolic injection and preventing this potential complication.

A second cause of injury to the central retinal artery can be the inadvertent dissection of the OPH secondary to vascular access or the formation of a clot around the microcatheter. Injection of vasodilators such as verapamil and administration of a heparin bolus may help to reduce the risk of inadvertent vascular injury during access to the OPH. Preoperative embolization of skull base meningiomas through the OPH can be much more feasible and safer with the recently introduced microcatheters (eg, Headway Duo microcatheter; MicroVention). Finally, some investigators mentioned that provocative tests before embolization might be beneficial for embolization decisions;<sup>5</sup> nevertheless, other reports of false-negative or -positive tests are available.<sup>5,13</sup>

Investigation of the effect of OPH embolization on the postoperative surgical outcomes of skull base meningiomas through this systematic review is difficult due to the small sample size, a serious amount of missing data, high heterogeneity, and lack of postoperative outcome reports by included studies. In this study, the postoperative complete resection rate was 93% among 15 cases, which is higher than or similar to reported gross total removal rates after transcranial resection of skull base meningiomas with no preoperative embolization (69%–100%).<sup>24–26</sup> Furthermore, the surgical treatment resulted in good clinical outcomes, with only 1 death due to brain edema. However, this comparison is invalid due to the limitations mentioned earlier. Furthermore, other operative outcomes, such as surgical complications and intraoperative blood loss, were not reported. Thus, evaluation of the benefits of embolization on those outcomes is impossible. Further studies on endovascular and surgical nuances of OPH embolization of skull base meningiomas are required to evaluate these effects.

In conclusion, caution must be exercised before the embolization of OPH branches, considering the advantages and disadvantages of the embolization procedure. This can be achieved through preprocedural casewise evaluation of the need for the meningioma embolization based on factors such as tumor size, location, vascularity, and anatomic variations of the OPH (origin and proximity of the tumor to the central retinal artery) to facilitate surgical resection and decrease intraoperative complications. Furthermore, an initial provocative test can be used to assess the tolerance of OPH branch occlusion and subsequently make the final decision about embolization. However, published studies have inconclusive results based on a limited number of cases, and the outcomes of embolization attempts of meningiomas fed by the OPH may have gone unreported. Therefore, the literature evidence needs to be more robust to give recommendations.

### Limitations

This systematic review includes only the reported cases in the literature, which may lead to selection bias and may not be an accurate representation of the procedure-related complications or outcomes. Furthermore, a considerable amount of heterogeneity is present due to several factors, including tumor-related (size, location, vascularity), anatomic (origin and branches of the ophthalmic artery), and technical factors (microcatheter used, embolization agents).

### CONCLUSIONS

OPH embolization of meningiomas is feasible and efficient. However, its safety remains a matter of concern. Advances in embolization techniques and materials are expected to facilitate and improve the outcomes of this procedure. Although not generalizable due to this limited, very small sample of the study, embolization materials such as PVA are safely deployable and have relatively fewer complications than liquid agents, which have better technical outcomes. Finally, most included studies were case reports published before 2015. Thus, further studies investigating the outcomes of the preoperative embolization of meningiomas through the ophthalmic artery in the current endovascular era are warranted.

**Disclosure forms** provided by the authors are available with the full text and PDF of this article at [www.ajnr.org](http://www.ajnr.org).

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