The debate concerning preoperative embolization of meningiomas continues 4 decades after the procedure was first described by Manelfe et al. Despite some data suggesting benefits such as decreased blood loss and "softening of the tumor" during subsequent resection, the overall outcomes remain controversial. The pros of preoperative embolization, including less intraoperative blood loss and facilitation of surgery, have to be carefully weighed against the cons of an additional intervention, with its inherent risks and potential complications such as hemorrhage and stroke.

At this time, the choice to pursue preoperative embolization seems to be a personal preference of the operating surgeon, and only a portion of all patients with meningioma undergo tumor embolization. In light of the fact that the overall benefits of preoperative embolization of meningiomas are uncertain, it is important to realize that endovascular embolization has inherent risks.

In this article, we reviewed our experience with preoperative embolization of meningiomas and we reviewed the literature to analyze the indications, embolizing agents, timing, and complications.
Methods

The medical records of patients who had undergone preoperative meningioma embolization over the previous 6 years (March 2007–March 2013) were retrospectively reviewed. Approval was obtained from the State University of New York Upstate Medical University Institutional Review Board. The data collected included patients’ demographic data; characteristics of meningioma (location, size, associated edema); details of embolization procedure such as target arterial supply; details of embolizing agent used; timing between the endovascular embolization and surgery; details of the outcomes; results of pathological investigations; and any reported complications that relate both to endovascular embolization and resection.

We also performed a MEDLINE search using a combination of terms (“meningioma,” “preoperative,” and “embolization”) for the literature review. The last literature search was performed in July 2013. We limited our search to only original research articles in the English-language literature. Articles in which preoperative embolization was used during meningioma management were included in the study. Case reports and small case series with fewer than 25 patients were excluded. The papers that did not mention the complications related to preoperative meningioma embolization were also excluded. All articles were cross-referenced. The articles were screened for indications for preoperative embolization, embolization material used, time interval between embolization and surgery, outcomes after embolization, and complications associated with the embolization procedure.

Results

Patient Population

In our retrospective review, 18 cases (female/male ratio 12:6) were identified in which endovascular embolization was used prior to resection of an intracranial meningioma. Seventeen of these patients underwent subsequent craniotomy and resection of the tumor at our hospital, and 1 patient elected to undergo surgery at another facility in his home state.

Patient Presentation

The mean age of the patients in our series was 56 years. Eight patients (44%) presented with headaches and memory difficulties, 9 patients (50%) were identified during workup for a new-onset seizure, and 1 patient (6%) was found incidentally. Initial examination revealed no neurological deficit or mental status changes in 9 patients. Meningiomas were convexity-based or parafalcine in 9 cases, skull base in 7 cases, and infratentorial in 2 cases. The mean maximal diameter of the meningioma at its greatest dimension was 56.4 mm.

Indications for Preoperative Embolization

Analyzing the indications for preoperative meningioma embolization in our own institution, the surgeon’s own preference and experience appear to be the predominant factor when referring a patient for preoperative embolization. However, the review of tumor characteristics in our patient population does reveal that all referred cases were characterized by a large tumor size.

Details of Endovascular Embolization

In all patients, endovascular evaluation and embolization of the feeding vessels was performed in a single session. Feeding pedicles originating from the middle meningeal artery were the most common target (13 cases). Other targets included the occipital artery feeder (4 cases) and the internal maxillary artery feeder (1 case). Microcatheterization of more than one major feeding vessel was performed in 3 cases. The choice of microcatheter used was affected by the size of the feeding vessel as well as the surgeon’s preference and familiarity with the device. In most cases (12 of 18), embolization was performed using 100–300 μm Embospheres (trisacryl gelatin microspheres; Embospheres, Biosphere Medical). Polyvinyl alcohol (PVA) particles with Onyx-18 were used in 3 cases, Embozene microspheres (poly[bis(trifluorooethoxy)phosphazene]; Celonova BioSciences) were used in 2 cases, and Onyx-34 was used as the sole embolizing agent in 1 case. Routine postembolization CT scanning was performed to assess for immediate hemorrhage or change in mass effect in 6 cases per the attending neurosurgeon’s orders. In the remaining cases additional imaging was performed as part of presurgical planning for intraoperative neuronavigation.

Surgical Details

Craniotomy for tumor resection was performed within 4 days after endovascular embolization in all cases, with an average time to surgery of 1.9 days. The average surgical time was 4 hours and 18 minutes, and the average blood loss was 574 ml, with a range of 300–1000 ml. Simpson Grade I or II resection was achieved in 11 cases, Simpson Grade III resection was achieved in 4, and Grade IV resection was achieved in 2 cases. One patient was treated at another facility. No residual tumor was seen on follow-up imaging in 15 cases. Recurrence of tumor was seen in 1 case with incomplete resection (Simpson III).

Pathological Findings

Intraoperative analysis of frozen and permanent tumor specimens was performed in all cases. Final results revealed WHO Grade I meningioma in 14 cases, in 3 cases the tumor grade was WHO II, and in 1 patient surgery was performed at another facility and the pathology report was unavailable. Signs of necrosis were explicitly noted by the pathologist in 12 cases.

Complications Attributed to Endovascular Therapy

Complications following endovascular therapy were identified in 3 (16.7%) of 18 cases. One patient had a transient right-sided pronator drift following embolization of a left frontoparietal convexity meningioma. Left middle meningeal artery feeders were embolized with PVA particles (150–250 μm) in combination with Onyx-18. No postembolization imaging was available in this case because the patient was transferred to a different facility for surgery.
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A second patient had headache and vomiting shortly after the embolization of a posterior fossa meningioma. A left occipital artery feeder was embolized with 100–300 μm Embospheres. A CT scan obtained approximately 20 hours after embolization, when the patient was reporting worsening headaches and vomiting, revealed increased compression of the fourth ventricle from tumor swelling and associated enlargement of lateral ventricles, for which ventriculostomy was performed. Hydrocephalus resolved following resection of the tumor.

In the third case, in which a planum sphenoidale meningioma was diagnosed, the patient was found to have a new-onset left-sided hemiparesis subsequently to resection. In this case, the craniotomy was performed within hours after preoperative embolization, and no postembolization imaging was obtained. A postoperative MRI study, however, revealed multiple areas of restricted diffusion within the right parietal and occipital lobes that were attributed to the embolization procedure. Patient symptoms improved slowly over the next 6 months with physical therapy.

No cases of death related to embolization occurred in our series. One patient died following a complication related to tumor resection. He was found to have a large epidural hematoma following craniotomy that necessitated an additional surgery. This was later complicated by infection with intracranial involvement, and the patient died of diffuse cerebral edema.

Literature Review

Our literature review performed based on our inclusion and exclusion criteria returned 15 articles. Most studies were retrospective or prospective case series. The 2 prospective studies found were comparative studies. A retrospective comparative case series that was found had 18 patients in both embolized and nonembolized groups and was excluded from the table. No randomized controlled trials were found. The details of the embolization material used, time interval between embolization and surgery, outcomes after embolization, and complications are presented in Table 1.

In the literature, the indications for preoperative embolization of meningiomas are unclear and the overall benefits remain uncertain. On reviewing the literature, no consensus was found regarding the specific indications for preoperative embolization. However, the surgeons’ own preferences and institutional practices have been cited as a common factor. In general, several characteristics of the tumor itself did play a role in patient selection for preoperative embolization. These include large meningioma size, high tumor vascularity, arterial supply that is difficult to reach intraoperatively, such as in skull base lesions, and significant external carotid artery–derived arterial supply. Only several authors provided a specific algorithm for patient selection that explicitly incorporated these factors. In addition, Walron et al. introduced several exclusion criteria such as significant peripheral vascular disease and a history of stroke that can significantly impact the risk-benefit ratio of embolization. Latchaw has defined 5 instances in which preoperative embolization of meningioma can play a significant role. These include skull base meningiomas, which often have a difficult vascular supply; large tumors with significant edema in which the surgical plane may be obscured; tumor involvement of dural sinuses; involvement of scalp and calvaria; and tumors in proximity to eloquent cortex.

Embolization has been shown to offer benefits such as decreased operative blood loss, easier resection, and shortened surgical time. The risks include hemorrhage, ischemic complications, cranial nerve deficits, tumoral and/or peritumoral edema, and those related to the interventional procedure itself such as groin hematoma, femoral pseudoaneurysm formation, and vascular dissection. In this review article we analyzed the literature for outcomes, embolizing agents, incidence of complications, and potentially modifiable factors that can reduce these risks.

Posttreatment Outcomes

A number of studies suggested a beneficial effect of preoperative meningioma embolization. In a retrospective comparative case series, Macpherson comparing 28 embolized and 24 nonembolized meningiomas and Dean et al. (comparing 18 embolized and 18 nonembolized meningiomas) reported decreased blood loss, a reduced need for transfusions, and fewer surgical complications in embolized cases. There were no major complications or adverse long-term effects caused by the embolization procedure. Bendszus et al. prospectively compared embolized and nonembolized meningiomas and reported that only complete tumor devascularization resulted in significant reduction in blood loss. In another recent retrospective case series, Waldron et al. reported good outcomes with preoperative embolization of skull base meningiomas fed by the internal carotid artery circulation, with a low rate of complications. Quiñones-Hinojosa et al. also reported beneficial effects of preoperative embolization during resection of giant intracranial meningiomas (≥ 5 cm).

Choice of Embolizing Material

Over the past few decades, various embolizing agents have been used for the preoperative embolization of meningiomas. Embolizing materials can be broadly defined by their physical form as particulate or liquid agents, and by the duration of their effects into temporary or permanent categories. Particulate embolizing agents include PVA particles; microspheres (such as trisacryl gelatin microspheres [Embospheres], Biosphere Medical; or Embozene microspheres [poly[bis(trifluoroethoxy)phosphazene]), Celonova BioSciences); and cellulose beads. Liquid agents include NBCA (N-butyl cyanoacrylate), Onyx (ethylene vinyl alcohol copolymer dissolved in dimethyl sulfoxide) and fibrin glue. Comparative studies are lacking in the literature.

A majority of reports in the literature involve embolization with the use of PVA particles or microspheres. The only large series (128 patients) in which cellulose beads (200 μm) were used for preoperative embolization reported total to significant devascularization in 72% of patients.
<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Type of Publication</th>
<th>No. of Pts who Underwent Embolo</th>
<th>Systemic Heparinization</th>
<th>Mean Age in Yrs</th>
<th>No. of Pts w/ Major Complications (%)</th>
<th>No. of Pts w/ Minor Neurological Complications (%)</th>
<th>Death Attributed to Embolo (%)</th>
<th>Additional Nonneurological Sequelae</th>
<th>Embolizing Agent Used in Series, w/ Size in μm Where Appropriate</th>
</tr>
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<tbody>
<tr>
<td>Bendzus et al., 2005</td>
<td>retro case series</td>
<td>185 yes</td>
<td>63</td>
<td>12 (6.5)</td>
<td>0</td>
<td>1 (0.5)</td>
<td>0</td>
<td>Embospheres 40–120 (n = 12), Embospheres 100–300 (n = 165), BeadBlock 100–300 (n = 8)</td>
<td></td>
</tr>
<tr>
<td>Carli et al., 2010</td>
<td>retro case series</td>
<td>198 no</td>
<td>54.4</td>
<td>11 (5.6)</td>
<td>0</td>
<td>1 (0.5)</td>
<td>0</td>
<td>PVA 45–150 (n = 108) or 150–250 (n = 93)</td>
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<tr>
<td>Gruber et al., 2000</td>
<td>retro case series</td>
<td>63 NR</td>
<td>56.6</td>
<td>2 (3.2)</td>
<td>0</td>
<td>1 (1.6)</td>
<td>0</td>
<td>fibrin, “LA mixture,” PVA, or IBPA</td>
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<tr>
<td>Rosen et al., 2002</td>
<td>retro case series</td>
<td>167 NR</td>
<td>50.5</td>
<td>15 (9.0)</td>
<td>21 (12.6)</td>
<td>0</td>
<td>5: groin hematoma (n = 3), bradycardia (n = 1), Fourier gangrene (n = 1)</td>
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<td>Waldron et al., 2011</td>
<td>retro case series</td>
<td>199 yes</td>
<td>NR</td>
<td>4 (2.0)</td>
<td>0</td>
<td>0</td>
<td>1: femoral artery AVF</td>
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<tr>
<td>Law-ye et al., 2013</td>
<td>retro case series</td>
<td>137 NR</td>
<td>52.9</td>
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<td>0</td>
<td>0</td>
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<tr>
<td>Bendzus et al., 2000</td>
<td>prospective comparative</td>
<td>30 NR</td>
<td>55.7</td>
<td>1 (3.3)</td>
<td>0</td>
<td>0</td>
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<td>Borg et al., 2013</td>
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<td>107 yes</td>
<td>NR</td>
<td>3 (2.8)</td>
<td>0</td>
<td>0</td>
<td>1: scalp necrosis postop</td>
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<td>Kai et al., 2006</td>
<td>retro case series</td>
<td>128 yes</td>
<td>NR</td>
<td>2 (1.6)</td>
<td>0</td>
<td>0</td>
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<td>34 yes</td>
<td>60</td>
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<td>15 (44.1)</td>
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<td>Kai et al., 2002</td>
<td>retro case series</td>
<td>42 NR</td>
<td>54.4</td>
<td>2 (4.8)</td>
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<td>0</td>
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<td>Macpherson, 1991</td>
<td>study design NR</td>
<td>28 NR</td>
<td>54</td>
<td>1 (3.6)</td>
<td>4 (14.3)</td>
<td>0</td>
<td>3: systemic artery embo, scalp necrosis, scalp &amp; ear cyanosis</td>
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<tr>
<td>Richter &amp; Schachenmayr, 1983</td>
<td>study design NR</td>
<td>30 NR</td>
<td>NR</td>
<td>1 (3.3)</td>
<td>3 (10.0)</td>
<td>0</td>
<td>1: thrombopenia</td>
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<td>Quiñones-Hinojosa et al., 2009</td>
<td>retro case series</td>
<td>45 NR</td>
<td>NR</td>
<td>1 (2.2)</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</table>

*Embo = embolization; IBPA = isobutyl cyanoacrylate; LA = a mixture of denatured microfibrillar collagen, PVA particles, and 30% ethanol as defined by Gruber et al.; NR = not reported; pts = patients; retro = retrospective.
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Use of PVA Particles Versus Microspheres

Sluzewski et al.27 reported better outcomes with the use of large (400-μm) calibrated microspheres (Embozene microspheres) compared with smaller PVA particles of 45–150 μm. There was no difference in complication rates between the use of 400-μm calibrated microspheres and larger PVA particles of 150–250 μm. However, the efficacy in decreasing blood loss or providing ease of surgery was not reported, which limits the comparison.

In another comparative study, trisacryl gelatin microspheres (100–300 μm) were shown to achieve more distal penetration and subsequently resulted in greater devascularization and less blood loss than any size of PVA particles (45–150 or 150–250 μm). This was attributed to the fact that their uniform shape and deformable nature cause less clumping/aggregation and subsequent obstruction of the vessel.1

Size of PVA Particles

Small PVA particles (45–150 μm) have been shown to be more effective in preoperative devascularization than larger particles (150–250 μm) due to more distal penetration of smaller particles into the capillaries feeding the tumor.29 Although smaller particles can achieve greater and more distal penetration of the tumor, they have been criticized due to the higher risk of complications such as cranial nerve palsies and postprocedural hemorrhage. Cranial nerve palsies can occur due to occlusion of the vasa nervorum of cranial nerves.19 Carli et al.6 reported that the use of small PVA particles (45–150 μm) proved to be a significant risk factor for serious hemorrhagic complications in their large series of approximately 200 patients. The higher risk of complications associated with the use of smaller particles also includes occlusion of the venous outflow, leading to backpressure and hemorrhage or microvascular friability from occlusion, inflammation, and subsequent hemorrhage.

Therefore, some authors generally do not recommend the use of particles smaller than 100 mm, especially whenever there is a risk for potentially dangerous anastomoses or loss of vascular supply to the cranial nerves.5,21,29

The review based on retrospective case series suggests that although the small particles are more efficacious than larger ones, whether PVA or microspheres, they are associated with a significantly higher rate of complications and should be used with caution.

Larger particles are not reported to be risk free either. Bendzus et al.5 reported a neurological complication rate of 6.5% with the use of both the small (40–120 μm) or larger (100–300 μm) embospheres. Kallmes et al.19 reported that the use of particles in the 150–300 μm size is safe, but not risk free.

The literature on the efficacy of larger particles in preoperative meningioma embolization is limited to PVA particles. Larger PVA particles (> 400 μm) are associated with fewer complications, but simultaneously result in less effective devascularization because they cause occlusion of larger vessels, which can result in revascularization through the collateral blood supply.4,10,29 The data on the use of larger microsphere particles is currently unavailable. Sluzewski et al.27 reported fewer complications with the use of 400-μm calibrated microspheres compared with small PVA particles (45–150 μm), but did not report the comparative effect on devascularization.

Liquid Embolizing Agents

The literature on the use of liquid embolizing agents (NBCA, fibrin glue, and Onyx) in preoperative embolization of meningiomas is also lacking. Kominami et al.14 reported more than 50% devascularization in 29 of 31 meningiomas embolized with NBCA. The use of Onyx as the embolizing agent has been reported only in small case series or case reports, and it is difficult to draw any significant conclusions.9,28 Fibrin glue has also been reported in only a single large case series, and the authors concluded that the use of this material is safe and technically easy.22

Timing of Surgery After Embolization

The adequate time interval between tumor embolization and surgery has been another area of debate, without any strong recommendations for either early or delayed surgery after embolization. Time to surgery after embolization was not consistently reported across the articles and hence could not be included in the table. Surgery after approximately 1 week has been suggested for reasons including greater softening of the tumor and relative ease of resection, less edema, and less blood loss. The greatest degree of meningioma softening is achieved approximately 1 week after embolization, underlining the importance of nonabsorbable embolizing agents.12 Chun et al.7 reported significantly less blood loss if the surgery was performed more than 24 hours after the embolization procedure. Shi et al.26 reported less edema if the surgery was delayed more than 10 days after embolization in their series of 3 patients treated with preoperative embolization with Onyx.

On the contrary, other authors have recommended shorter time intervals (1–7 days) between embolization and the surgery due to the potential for subsequent collateralization and revascularization of the tumor if the surgery is delayed.21,24 For the same reason, nonabsorbable embolizing agents have been recommended.

Posttreatment Complications

The complications from preoperative embolization of meningiomas can include hemorrhage, ischemic stroke, tumoral edema, and cranial nerve palsies.19,28,24 The overall complication rate reported in patients with preoperative meningioma embolization ranges from as high as 21% in some of the older literature29 to approximately 6% in recent literature detailing newer embolization techniques.26 In the literature review, we divided the complications that were reported into major complications such as hemiparesis, cranial nerve palsies, tumoral swelling, ischemia, or hemorrhage on the imaging studies. Minor neurological complications included headache, dizziness, and vomiting. Noneurological complications mainly include those related to the procedure, such as arteriovenous fistula (AVF), groin hematoma, and scalp necrosis (Table 1).
One of the recent articles reported a complication rate of 3.7% in a series of 107 patients treated with preoperative embolization (of the 117 patients included in this study, 10 cases were abandoned and did not receive preoperative embolization). Of the 4 complications (3.7%), 2 resulted in permanent neurological deficits (1 patient developed right hemianopia and 1 had sixth cranial nerve palsy). One patient had a peritumoral hemorrhage with no neurological deficits and another patient developed scalp necrosis after embolization of an intraosseous meningioma through a superficial temporal artery branch. Three were in the “cyanoacrylate glue only” group and one was from the “glue plus acrylic particle” group. There were no complications in the “particle only” group.

Hemorrhage in embolized meningiomas has been hypothesized to be related to the thin friable walls of the tumor vessels. Particles may pass from the arterial to the venous side via shunts, causing obstruction to the venous outflow and resulting in pressure gradients. Additionally, tumor ischemia and subsequent necrosis might convert intratumoral hemorrhage. The location of hemorrhage after meningioma embolization can be intratumoral, subarachnoid, or subdural in location. Carli et al reported an approximately 5% risk of hemorrhage with the use of smaller PVA particles in their series of 201 embolized meningiomas in 198 patients. Bendszus et al reported a 3.2% rate of hemorrhage in their 185 patients.

The risk factors for postprocedural hemorrhage include atypical kinds of meningioma and use of smaller particles. Graduated increases in particle size, with the use of smaller particles (45–150 μm) in the beginning and finishing with large particles (350–500 μm), has been suggested to offer protection to these friable distal vessels.

Ischemic complications can be either transient ischemic attacks or stroke causing permanent neurological deficits. They can occur due to thromboembolism or unintentional embolization of the parenchymal vessels. Risk factors that increase the chances of ischemic complications include an arterial-arterial anastomosis between dural and neuroparenchymal vessels, skull base meningiomas with feeding vessels from the internal carotid artery, and the use of smaller particles. The incidence of ischemic complications can be lowered through the use of relatively large particles, anticoagulation with heparin, thorough understanding of the arterial anatomy, provocative testing, and use of neuromonitoring in high-risk cases such as large skull base meningiomas. Likewise, appreciation of the anastomosis between the proximal middle meningeal artery branches with arteries supplying cranial nerves can lower the incidence of cranial nerve palsies.

Other rare major complications include tumoral and/or peritumoral swelling and blindness. Minor complications include headache, facial pain, scalp necrosis, and those related to the procedure itself such as groin hematoma, femoral pseudoaneurysm, or AVF formation.

Conclusions

The evidence in the literature supporting the use of preoperative meningioma embolization is mainly from case series and represents Level III evidence. Due to the lack of randomized controlled clinical trials, it is difficult to draw any significant conclusions on the overall usefulness of preoperative embolization during the management of meningiomas to consider it a standard practice.

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Author contributions to the study and manuscript preparation include the following. Conception and design: Singla. Acquisition of data: Singla, Melnyk, Tosheki, Choi. Analysis and interpretation of data: all authors. Drafting the article: Singla. Critically revising the article: Singla, Deshaies, Melnyk, Swarankar, Chin. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Singla.

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