

Pre- and Post-operative Parameters among Patients Undergoing Pre-operative Embolization of Meningioma: a Tertiary Referral Center Experience

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ABSTRACT

Background and Objective. Meningiomas represent the most prevalent benign intracranial tumors, comprising 13-26% of primary intracranial neoplasms. These tumors derive their blood supply from both extracranial and intracranial circulation. Over recent decades, pre-operative embolization (POE) has emerged as a potential adjunctive therapy to surgery, aiming to reduce tumor vascularity. Our study seeks to explore the potential correlation between the extent of devascularization following POE of meningiomas and intraoperative blood loss.

Methods. This cross-sectional study involved nine meningioma patients at a tertiary hospital, involving chart review of patients across four years. These patients were referred for POE due to angiographic evidence of a hypervascular mass between January 2018 and January 2022. We collected demographic data, tumor characteristics (including location, size, and vascular supply), and intraoperative variables such as total operative time and blood loss. Statistical analyses aimed to uncover correlations between vascularization degree and various factors.

Results. Our population consists predominantly of females (53.68%), with a mean age of 45.85 ± 13.65 years. Only one mortality was recorded (7.7%). Pre-operative embolization achieved devascularization in the majority (69.2%) of cases, with approximately two-thirds (66.7%) experiencing complete devascularization. Mean total operative time stood at 336.11 ± 301.88 minutes, with a mean post-operative blood loss of 985.56 ± 1013.72 milliliters. Additionally, for those with recorded recovery times, the mean recovery time was 14.32 ± 13.51 hours.

Mortality rates showed no association with sex, devascularization status, or number of feeding vessel zones. Furthermore, the extent of devascularization did not correlate with age, sex, number of feeding vessel zones, post-operative blood loss, total operative time, or recovery time ($p > 0.05$).

Conclusion. In summary, this study represents a significant endeavor to elucidate factors influencing meningioma outcomes following pre-operative embolization. Despite limitations regarding patient numbers, our study offers valuable insights into operative parameters and embolization considerations for future analyses in our tertiary center.

Keywords: meningioma, embolization, interventional radiology

INTRODUCTION

Meningiomas are the most common benign intracranial neoplasms, accounting for 13-26% of all primary intracranial tumors.¹ These types of tumors are highly vascularized and arise from the arachnoid cap cells, which cover the brain and spinal cord.² Although generally benign, meningiomas are associated with other sequelae such as seizures, vision loss, and neurologic deficits, based on their location. Roughly 25%-40% of patients with seizures, and roughly one-third of patients have visual changes.³ These types of neoplasms parasitize its vascular supply from both extracranial and intracranial circulation.

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Interventional neuroradiology has been a valuable asset for diagnosing, evaluating, and treating intracranial and extracranial vascular neoplasms. In mapping out the vascular supply of tumors, the interventional radiologist is able to aid the surgeon in surgical planning. At the same time, the interventional radiologist is able to perform minimally-invasive procedures such as transarterial embolization prior to surgery to make way for a safer surgical procedure. In embolizing certain tumors, the interventional radiologist can aid in reducing intraoperative morbidities of greatest concern, one of which is blood loss. Both vascular extracranial and intracranial neoplasms may be treated with embolization prior to surgery to decrease tumor vascularity.⁴

In light of this, the role of POE in the management of meningioma is constantly evolving with modest scientific evidence but substantial differences in opinion on when and how the technique should be used for clinical workup or treatment decisions. Over the last four decades, pre-operative embolization (POE) of highly vascularized neoplasms has emerged as a potential adjunct to surgery.² Since the procedure was first described, there has been remarkable improvement in the technique employed, particularly regarding the development of microcatheters and embolic agents, together with growing experience of operators. Embolization leads to devascularization of the lesion, which lead to necrosis and facilitate resection through tumor softening. This is done ideally 24-72 hours prior to surgical resection to (1) allow maximal thrombosis of occluded vessels, (2) prevent recanalization of the occluded arteries or formation of collateral vessels, and (3) avoid significant progression of arteriovenous malformations at follow-up, possibly due to stimulation from hypoxia.⁵

Pre-operative embolization may provide an opportunity to preemptively reduce blood loss, allowing for a decrease in the overall blood product utilization of these patients, diminished expenditures on both patient and institution side, and better allocation of blood products for other more emergent cases. However, the role of POE in improving surgical outcomes have yet to be fully elucidated. Therefore, in this study, we investigated 1) the demographics of patients undergoing POE of meningiomas, 2) the perioperative parameters of meningioma patients, and 3) the correlation between the degree of devascularization after POE of meningiomas and perioperative parameters.

MATERIALS AND METHODS

Study design

This is a cross-sectional study encompassing four years in a tertiary hospital in Manila. Purposive sampling was utilized for this study. The records of patients with meningioma referred to the Vascular and Interventional Radiology Section of the Department of Radiology for POE with angiographic findings of a hypervascular mass from 2018 – 2022 were initially enrolled in the study (n = 77). The final inclusion

criteria included: 1) patients with meningioma of any age who underwent pre-operative embolization and were operated within 72 hours, and 2) the embolic agent used should be limited only to polyvinyl alcohol and gel foam. Patients were excluded if 1) the operation after embolization is more than 48 hours, and 2) patients with other tumor or vascular malformations. Out of the 77 enrolled patients initially, only 13 patients (16.9%) met the inclusion criteria, and these patients had their relevant chart data collected accordingly.

Data Collection

All POE angiography reports and intraoperative patient charts were reviewed. Three groups of data were obtained; 1) demographics, 2) pre-operative parameters [estimated POE devascularization (complete or extensive), tumor size, vascular supply], and 3) intraoperative parameters (blood loss, operative time). Among the 13 patient records, only nine patients (11.7%) had complete data eligible for statistical analysis.

Statistical Analysis

Paired sample t-test was done to determine the difference in mean between patient's angiographic and intraoperative findings. Logistic and ordinal regressions were used to determine the correlation between the degrees of devascularization and intraoperative blood loss and operating time. All statistical tests were run at an α value of 0.05 using STATA 13.1.

Ethical Considerations

This research proposal was submitted and approved (Study code: UPMREB 2021-0541-01) by the UP-Manila Research Ethics Board prior to the project implementation. The research team complied with the ethical guidelines in the conduct of health research as stated in the National Ethical Guidelines for Health Research handbook.

RESULTS

The mean age for our population is 45.85 ± 13.65 years, with females (53.68%, n = 7) outnumbering the males (46.2%, n = 6), in the study. Only one mortality was noted (7.7%).

Majority of the patients opted for a pre-operative embolization devascularization (69.2%, n = 9). Among those who have opted to have the procedure done, six of these patients had complete devascularization of the meningioma (66.7%), two of them had 70-80% devascularization (22.2%), while only one had 50-60% devascularization (11.1%). Among these patients, there was the preponderance of two zones of feeding vessels (44.4%, n = 4), although these locations vary individually. The mean total operative time was 336.11 ± 301.88 min, with a mean post-operative blood loss of 985.56 ± 1013.72 mL. For those who had recorded recovery times, the mean recovery time was 14.32 ± 13.51 hrs. A summary of the cases is shown in Table 1.

Table 1. Summary of Meningioma Cases that were Eligible for Data Collection

Diagnosis	Age/Sex	Mortality	Pre-op degree of devascularization (%)	Post-op blood loss (ml)	OR time (mins)	Recovery time (hours)	Angiographic Feeding Vessels
<i>Sagittal meningioma</i>	51/F	N	100	20	80 mins	10 hrs	<ul style="list-style-type: none"> • Middle meningeal, accessory meningeal, deep temporal and foramen rotundum branches of the right internal maxillary artery • Frontal and parietal branches of the right superficial temporal artery • Temporal branches of the right middle cerebral artery
<i>Sagittal meningioma</i>	33/M	N	100	50	80 mins	3 hrs	<ul style="list-style-type: none"> • Left middle meningeal artery • Frontal and parietal branches of the right superficial temporal artery
<i>Left middle third parasagittal meningioma</i>	53/M	N	100	900	271 mins	-	<ul style="list-style-type: none"> • Left middle meningeal artery
<i>Tumor recurrence, meningioma</i>	29/F	N	100	300	190 mins	22 hrs	<ul style="list-style-type: none"> • Middle meningeal, deep temporal, and sphenopalatine branches of the left internal maxillary artery • Frontal and parietal branches of the left superficial temporal artery (more frontally) • One (1) distal frontal branch from the right superficial temporal artery • One (1) distal frontal branch from the right middle meningeal artery
<i>Meningioma</i>	48/F	N	100	400	300 mins	-	<ul style="list-style-type: none"> • Right middle meningeal artery
<i>Recurrent frontotemporal meningioma</i>	18/F	N	80	2500	449 mins	34 hrs	<ul style="list-style-type: none"> • Middle meningeal, deep temporal, and sphenopalatine branches of the left internal maxillary artery • Frontal and parietal branches of the left superficial temporal artery (more frontally) • All branches of the left middle cerebral artery (not embolized) • Left internal carotid angiograms show suboptimal opacification of the left anterior cerebral artery, likely due to steal phenomenon secondary to the abovementioned mass
<i>Left falcine meningioma</i>	69/M	Y	60	1800	295 mins	2.6 hrs	<ul style="list-style-type: none"> • Middle meningeal, deep temporal, and sphenopalatine branches of the left internal maxillary artery • Cortical branches of the left middle cerebral artery
<i>Left tentorial meningioma</i>	46/F	N	100	400	280 mins	-	<ul style="list-style-type: none"> • Left middle meningeal artery • Left superficial temporal artery
<i>Right Petrotentorial meningioma</i>	57/M	N	80	2500	1080 mins	-	<ul style="list-style-type: none"> • Middle meningeal and deep temporal branches of the right internal maxillary artery • Cortical branches of the right middle cerebral artery
<i>Carotico-cavernous fistula</i>	38/M	N	No pre-op embolization data	No operation done	-	-	-
<i>Meningioma</i>	53/F	N	No pre-op embolization data	3700	440 mins	5.3 hrs	-
<i>Brain mass</i>	58/M	N	No pre-op embolization data	No operation done	-	-	-
<i>Sellar mass</i>	43/F	N	No pre-op embolization data	No operation done	-	-	-

*Gray rows indicate patients that were not included in the final statistical analysis.

Mortality rate was not associated with sex ($p = 0.261$), devascularization status ($p = 0.488$), and number of zones of feeding vessel ($p = 0.704$). Ordinal regression for degree of devascularization demonstrated no correlation ($p > 0.05$ for each covariate) with age, sex, number of zones of feeding vessels, post-operative blood loss volume, total operative time, or total recovery time.

DISCUSSION

In the past decades wherein meningioma surgery has been performed, pre-operative embolization (POE) has been a common practice performed prior to craniotomy in order to decrease intraoperative blood loss and total operative time.¹ Meningiomas have highly variable blood supplies, arising from either external or internal carotids, vertebral arteries, or any permutations of these vessels.² Intracranial surgery, regardless of whether for meningioma or any other neurological tumor, brings about a risk of intracranial hemorrhage as high as 50.0%.³ In cases where the meningioma is incompletely excised, there could still be residual hemorrhage that leads to hematoma formation in the post-operative period⁴; hematoma is a strong predictor of a poor neurologic outcome despite the tumor is surgically resected, with its presence accounting for almost a fourfold increase in brain injury⁴.

However, since the introduction of POE in the 1970s⁵, only a single randomized controlled trial has been performed to evaluate its efficiency and safety. Iacobucci et al. observed that between POE vs non-POE meningioma patients, there were no significant differences between the two groups in terms of intraoperative blood loss, blood transfusions required, or post-operative hemoglobin decrease, but there was a significant reduction in total operative time.⁶ Multiple studies have shown that there is a leaning trend towards reduction of blood loss during meningioma resection in embolized patients.⁷⁻¹⁵ A meta-analysis reports that POE may reduce intraoperative blood loss significantly, and does not increase postsurgical complications concomitantly.¹⁶

Our meningioma patients are predominantly female, although the difference in sex distribution may not be significant. This is similar to published data from our institution, which describes a female predominance in brain tumor patients.¹⁷ Nonetheless, meningiomas are observed to be hormonally responsive and there is a host of progesterone, estrogen, and other steroid hormones that may affect its growth.¹⁸⁻²¹ This becomes especially important in situations where hormone levels fluctuate or are consistently elevated, such as during puberty²², breastfeeding²³, exogenous use of hormones^{24,25}, and menarche²³.

Age-specific incidence for nonmalignant meningioma has been shown to significantly increase over time.²⁶ In this study, the age-specific incidence is closer to published data from our institution, with a mean age of 41.7 years for meningioma patients.¹⁷ Our reported mean age also falls

within the 35-44 years old group, which was reported to have the highest ratio of female:male meningioma patients.²⁶ Younger age seems to be more favorable for survival in meningioma patients, although current evidence needs more robust studies.^{22, 27-29}

Only a handful of papers describe how vessels originating and draining the meningioma affect operative parameters. A cohort of patients who underwent microsurgical operations demonstrated that meningiomas with the involvement of important blood vessels such as the internal carotid and the venous sinus are more likely to display higher blood losses.³⁰ It is generally thought that meningiomas with a blood supply originating from the internal carotid arteries are more dangerous, due to the possibility of acute take-offs that would increase the perforation hazard.^{31,32} External carotid artery branches seem to be more forgiving, and pre-operative embolization has been shown to decrease in efficiency in cases of interna carotid artery feeders.¹³ Fortunately, all our patients had vascular supplies coming from at least the middle meningeal artery, as understood from the distribution of meningiomas of the frontal convexity and falcine regions.^{33,34} The presence of the middle meningeal artery is a common occurrence in meningiomas, but the tumor can also involve other arteries or even invade the dura to establish neogenic blood supplies.³⁵ Nonetheless, the meningioma vascular supply heavily depends on the location of the tumor, with variations in anastomoses and terminal branches, and there is a paucity of literature as to exactly how vascularity predicts intra- and post-operative complications of meningioma resection. In a more recent imaging-focused study between nonembolized and embolized meningioma patients, it was observed that perioperative embolization provides better outcomes in meningiomas with (1) more than half of the vascular supply being accessible branches of the external carotid artery, (2) hypervascular meningiomas, and (3) surgically inaccessible vascular supply.³⁶

Single institutional studies on brain tumor surgery patients have demonstrated that there is no significant risk associated with a longer post-operative time. For instance, in a retrospective study of 581 consecutive patients who had craniotomy for meningioma resection, the observed rates for thromboembolic events were not associated with operative time, but rather with patient weight and a post-operative bedridden status.³⁷ Another retrospective cohort of 1148 patients undergoing craniotomy for brain tumors demonstrated non-significance of operative time in affecting the likelihood of thromboembolic events occurring post-operatively.³⁸ However, as these studies were single-center studies, a more standardized database would provide more cohesive evidence for the effect of operative time on meningioma outcomes. Indeed, when the National Surgical Quality Improvement Program (NSQIP) was utilized for a larger study, it was demonstrated that longer operative length is truly associated with a higher risk for thromboembolic events, such as venous thromboembolism, deep vein

thrombosis, and pulmonary embolism.³⁹ Some studies have provided data demonstrating that intraoperative blood loss and operative duration were significantly lower in embolized patients, especially when complete devascularization has been achieved.^{6,14,40,41} Our study however precludes any strong assessment of operative time, since there is a wide range of documented operative times for different patients. The longest operation took 1080 mins, but even then, there were no recorded complications arising from this patient's surgery.

There are several limitations to this study. We only had 13 patients in this study, which may poorly reflect the statistics of the general population. In recent global statistics, east Asia has the lowest age-standardized rates of central nervous system cancer; the Philippines even had a decrease in the incidence of these diseases.⁴² Nonetheless, by utilizing an ambispective study design, we attempted to capture as much of the meningioma patients as possible. Perhaps a longer time period in the retrospective cases would increase our yield of patients that can be analyzed for the study. Another limitation is the incomplete hospital records, especially those parameters that are operative in nature. Since primarily the benefits and risks of meningioma excision have been shown to mainly occur in the perioperative setting, it would have been better if these factors were complete in our records. We attempted to analyze the records that were obtained; however, the small sample size precludes us again from determining any deviation from the general population.

CONCLUSION

This is a landmark study to determine factors affecting meningioma outcomes after pre-operative embolization in our tertiary center. Although this study is limited by the number of patients analyzed for outcomes, we have provided data as to which of these operative parameters and embolization considerations may be identified and utilized for analysis of future studies. While there are no clear guidelines as to which population this intervention can be given exactly to, any additional studies will always be beneficial to the general pool of knowledge. Moreover, the low risks associated with pre-operative embolization and the leaning trend towards reduced blood loss can be argued for the utility of this procedure in our meningioma patients.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest.

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