Association of Morbidity with Extent of Resection and Cavernous Sinus Invasion in Sphenoid Wing Meningiomas*

Michael E. Ivan, M.D.¹ Jason S. Cheng, M.D.¹ Gurvinder Kaur, B.S.¹ Michael E. Sughrue, M.D.¹
 Aaron Clark, M.D., Ph.D.¹ Ari J. Kane, M.D.¹ Derick Aranda, M.D.¹ Michael McDermott, M.D.¹
 Igor J. Barani, M.D.¹ Andrew T. Parsa, M.D., Ph.D.¹

¹Department of Neurological Surgery, University of California, San Francisco, California.

Address for correspondence and reprint requests Andrew T. Parsa, M.D., Ph.D., 505 Parnassus Avenue, Box 0112, San Francisco, CA 94143-0112 (e-mail: parsaa@neurosurg.ucsf.edu).

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Abstract

Sphenoid wing meningiomas (SWMs) typically are histologically benign, insidious lesions, but the propensity of these tumors for local invasion makes disease control very challenging. In this review, we assess whether the degree of resection and extent of cavernous sinus invasion affects morbidity, mortality, and recurrence in patients with SWM. A comprehensive search of the English-language literature was performed. Patients were stratified according to extent of resection and extent of cavernous sinus invasion, and tumor recurrence rate, morbidity, and mortality were analyzed. A total of 23 studies and 131 patients were included. Overall recurrence and surgical mortality rate were 11% and 2%, respectively (average follow-up = 65 months). Cranial nerve III palsy was significantly associated with incompletely versus completely resected SWMs (7 to 0%) as well as meningiomas with cavernous sinus invasion versus no sinus invasion (14 vs. 0%). No significant difference in tumor recurrence rate was noted between these groups. In conclusion, complete excision of SWMs is always recommended whenever possible, but surgeons should acknowledge that there is nonetheless a chance of recurrence and should weigh this against the risk of causing cranial nerve injuries.

Keywords

- sphenoid
- meningioma
- tumor control
- prognosis
- morbidity
- sphenoid meningiomas

Cranial meningiomas occur on the sphenoid wing in 15 to 20% of all cases.^{1,2} The first surgical experience with sphenoid wing meningiomas (SWM) was reported by Cushing and Eisenhardt³ in 1938. They divided SWMs into four categories based on the following location: (1) tumors of the deep or clinoidal third, (2) middle-ridge tumors, (3) en-plaque pterional tumors, and (4) global pterional tumors. Although this system of nomenclature has to be slightly modified to account for contemporary multiplanar imaging and advances in microsurgical techniques, it remains for the most part accurate. Unfortunately, this classification system has not been widely used in the literature.

Sphenoid wing meningiomas can involve the dura of the greater and lesser wings of the sphenoid, the anterior clinoid process, the spheno-orbital bone, and the middle cranial fossa. Moreover, the cavernous sinus, the orbital apex and superior and lateral orbital region, the sellar-suprasellar region, the pterygopalatine, temporal, and infratemporal fossae may also be infiltrated in more invasive cases.⁴ Consequently, the complex extension of these tumors, in addition to their proximity to vital neuronal and vascular structures, has always made them challenging for neurosurgeons.^{5–8} In spite of all the progress made in recent decades in the diagnosis and operative technique for wide removal of skull base lesions, various opinions^{9–14} in the literature indicate that a range of methods exists for treating SWMs.

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There is currently a large collection of published data on treatment outcomes for SWM, highlighting the effect of different treatment modalities on morbidity, mortality, and recurrence rates. Still, significant variability exists between surgeons because an overwhelming majority of these studies are either case studies or of small to moderate size possessing individual or institutional bias and, therefore, lacking sufficient statistical power to reliably guide clinicians in their management of SWM patients. For this reason, we reviewed the English-language literature to determine the recurrence rate and surgical morbidity of SWM, while placing special emphasis on the extent of resection and cavernous sinus involvement.

Methodology

Article Selection

PubMed searches were performed with keywords “sphenoid ridge meningioma” and “sphenoid wing meningioma” alone and in combination with “treatment,” “morbidity,” and “mortality.”

Articles were included if: (1) follow-up data for patients treated for sphenoid ridge meningioma were presented in a usable format; (2) disaggregated individual patient data (age, sex, treatment modality, and follow-up survival data) were present for each patient; and (3) Simpson grade and cavernous sinus invasion were identified following surgical resection, or a description of the surgical resection and boundaries was provided. After reviewing these articles, all referenced sources were also reviewed.

Articles were excluded if: (1) patients were diagnosed with combined sphenoid ridge meningiomas with clinoidal extension or other intracranial meningiomas; (2) patients were diagnosed with metastatic or multiple tumors; or (3) adequate follow-up or description was not provided.

Mortality was defined as death within 30 days of treatment. Morbidity was included if not resolved within 1 month of surgery.

Data Extraction

Data from individual and aggregated cases were extracted from each paper. These data were disaggregated and all references further scrutinized to avoid duplication of patients and ensure a complete review of the entire English-language literature.

The Simpson Criteria described by surgeon observation in each article were used for determining the following degree of excision of meningiomas¹⁵:

- Grade 1: Complete removal with excision of dural attachment
- Grade 2: Complete removal with endothermic coagulation of dural attachment
- Grade 3: Complete removal without resection or coagulation of dural attachment or its extradural extensions or involvement of bone and/or sinuses
- Grade 4: Partial removal leaving tumor in situ
- Grade 5: Simple decompression (or biopsy)

Incomplete surgical resection entailed partial, subtotal, or near-total resection or an inability to remove bone and/or dura (Simpson Grade II, III, and IV). Complete excision entailed complete removal of SWM along with involved bone, dura, and/or sinuses (Simpson Grade I). The term “recurrence” describes tumors that: (1) regrew after complete excision or (2) progressed after incomplete resection. Patients with cavernous sinus invasion were included if this was noted by preoperative imaging or intraoperative observation.

Data on recurrence, morbidity, and mortality were analyzed in total before stratification into subgroups by degree of resection of the SWM (complete excision versus incomplete resection) and degree of cavernous sinus invasion (invasion or no invasion). Morbidity data was only noted if the patient's deficit was worse than it was preoperatively.

Statistical Analysis

Differences in all demographic variables between treatment cohorts were compared using the Pearson's χ^2 test. Independent paired two-tailed *t*-test analysis was used for statistical evaluation and comparison of recurrence rate and morbidity rate in each subgroup. The recurrence/tumor progression rates were estimated by the Kaplan–Meier method and a log-rank test. The *p*-value was considered significant at less than 2% (<0.02) level after correcting for multiple comparisons. Statistical analysis was performed using SPSS version 17.0.

Results

Our search yielded 170 articles on the treatment of patients with sphenoid ridge meningioma. After using our inclusion and exclusion criteria, 23 articles^{16–38} from 1969 to 2010 with 131 associated patients were identified for this review. Univariate comparisons of demographic information between treatment cohorts noted no significant differences in gender or age distribution (►Table 1). The overall recurrence rate was 11% (14 patients) and surgical mortality rate was 2% (three patients). The overall follow-up was 65 months (range = 2 to 228 months) with an average time to recurrence of 65 months (range = 12 to 187 months). The rate of extraocular movement morbidity was 8% (10 patients), including cranial nerve III morbidity in 5% (six patients). Other morbidities included: epidural hemorrhage in 2% of patients; hemiparesis in 4%; and impaired vision in 5%.

Degree of Resection Versus Recurrence

Eighty-nine patients had their SWM incompletely removed (Simpson Grade II, III, and IV) and were followed up for a median period of 72 months, whereas the other 42 patients underwent complete excision (Simpson Grade I) and had a median follow-up time of 50 months. The recurrence rates for completely versus incompletely resected patients were 5 and 13% (*p* = 0.08), respectively, but this was not significant in our analysis (►Table 2). In the two patients that underwent complete resection, recurrence was noted at an average follow-up time of 72 months. In the 12 patients that

Table 1 Clinical Characteristics

Clinical Characteristics: Complete vs. Incomplete Resection				
	Total	Complete Resection	Incomplete Resection	
	Number of Patients	Number of Patients (%)	Number of Patients (%)	p-value
Number of patients	131	42 (32)	89 (68)	0.38
Gender (male/female)	31/100	8/34	23/66	
Age $\pm$ standard deviation	53 $\pm$ 13	52 $\pm$ 11	54 $\pm$ 13	0.85
Simpson Grade	I–IV	I	II, III, IV	
Prior surgical treatment	13 (10)	6 (14)	7 (8)	0.16
Preoperative symptoms				
-Decreased acuity/blindness	61 (47)	9 (21)	52 (58)	<0.02
-Headache	46 (35)	11 (26)	35 (39)	0.10
-Seizure	21 (16)	2 (5)	19 (21)	<0.02
-Diplopia	15 (11)	5 (12)	10 (11)	0.76
-Exophthalmos	33 (25)	20 (48)	13 (15)	<0.02
-Facial pain	5 (4)	3 (7)	2 (2)	0.07
-Hemianopsia	3 (2)	1 (2)	3 (3)	0.48
-Confusion	16 (12)	2 (5)	14 (15)	0.03
Cavernous sinus invasion	43 (33)	5 (12)	38 (43)	<0.02
Average size (cm)	4.9 (n = 76)	3.9 (n = 8)	5.1 (n = 68)	0.65
Clinical Characteristics: No Cavernous Sinus Invasion vs. Cavernous Sinus Invasion				
	Total	No Cavernous Sinus Invasion	Cavernous Sinus Invasion	
	Number of Patients (%)	Number of Patients (%)	Number of Patients (%)	p-value
Number of patients	131	88 (67)	43 (33)	0.72
Gender (male/female)	31/100	20/68	11/32	
Age $\pm$ standard deviation	53 $\pm$ 13	53 $\pm$ 13	53 $\pm$ 13	1
Cavernous sinus invasion	43 (33)	88	43	
Simpson Grade				
I	42 (32)	37 (42)	5 (12)	<0.02
II	43 (33)	35 (40)	8 (19)	<0.02
III	12 (9)	2 (2)	10 (23)	<0.02
IV	34 (26)	14 (16)	20 (47)	<0.02
Prior surgical treatment	13 (10)	10 (11)	3 (7)	0.32
Preoperative symptoms				
-Decreased acuity/blindness	61 (47)	36 (41)	25 (58)	0.07
-Headache	46 (35)	26 (30)	20 (47)	0.03
-Seizure	21 (16)	12 (14)	9 (21)	0.18
-Diplopia	15 (11)	8 (9)	7 (16)	0.10
-Exophthalmos	33 (25)	29 (33)	4 (9)	<0.02
-Facial pain	5 (4)	3 (3)	2 (5)	0.48
-Hemianopsia	3 (2)	1 (1)	2 (5)	0.03
-Confusion	16 (12)	11 (13)	5 (12)	0.77
Average size (cm)	4.9 (n = 76)	2.5 (n = 47)	5.1 (n = 68)	0.28

Table 2 Outcomes

Outcomes: Complete vs. Incomplete Resection				
	Overall	Complete Resection	Incomplete Resection	
	Number of Patients (%)	Number of Patients (%)	Number of Patients (%)	p-value
Number of patients	131	42 (32)	89 (68)	0.08
Recurrence	14 (11)	2 (5)	12 (13)	
Average time to recurrence	52 mo $\pm$ 55	72 mo $\pm$ 34	49 mo $\pm$ 58	0.50
Average time of follow-up	65 mo $\pm$ 66	50 mo $\pm$ 47	72 mo $\pm$ 73	
Postoperative symptoms				0.04
-Decreased acuity/blindness	6 (5)	1 (2)	5 (6)	0.34
-Diplopia (cranial nerve III, IV, VI)	10 (8)	2 (5)	10 (11)	0.23
-Only cranial nerve III palsy	6 (5)	0 (0)	6 (7)	<0.02
-Hemiparesis	5 (4)	0 (0)	5 (5)	0.02
Epidural hematoma	3 (2)	2 (5)	1 (1)	0.30
Mortality	3 (2)	0 (0)	3 (3)	0.08
Outcomes: No Cavernous Sinus Invasion vs. Cavernous Sinus Invasion				
	Overall	No Cavernous Sinus Invasion	Cavernous Sinus Invasion	
	Number of patients (%)	Number of patients (%)	Number of patients (%)	p-value
Number of patients	131	88 (67)	43 (33)	0.72
Recurrence	14 (11)	10 (11)	4 (13)	
Average time to recurrence	52 mo $\pm$ 55	35 mo $\pm$ 25	95 mo $\pm$ 90	0.28
Average time of follow-up	65 mo $\pm$ 66	68 mos $\pm$ 64	57 mo $\pm$ 70	
Postoperative symptoms				0.47
-Decreased acuity/blindness	6 (5)	4 (5)	2 (5)	0.98
-Diplopia (cranial nerve III, IV, VI)	10 (8)	1 (1)	9 (20)	0.03
-Only cranial nerve III palsy	6 (5)	0 (0)	6 (14)	<0.02
-Hemiparesis	5 (4)	1 (1)	4 (9)	0.08
Epidural hematoma	3 (2)	1 (1)	2 (5)	0.31
Mortality	3 (2)	2 (2)	1 (2)	0.99

underwent incomplete resection, tumor progression was noted at an average follow-up time of 49 months. In addition, the Kaplan-Meier analysis did not show statistical difference in overall tumor progression survival ($p = 0.18$) (►Fig. 1A).

Degree of Resection Versus Morbidity and Mortality

Incidence of cranial nerve III deficits was significantly greater in patients with incomplete resection (7%) than those with complete resection (0%) ($p < 0.02$) (►Table 2). Similarly, hemiparesis occurred in 5% of incompletely resected patients compared with 0% of completely resected patients ($p = 0.02$). There were no significant differences in the rates of the other postoperative morbidities, including change in vision, diplopia, and epidural hematoma. Finally, the mortality rate was not significantly different between groups, although the

complete-resection group had no mortality while the incomplete-resection group had three deaths (►Fig. 1A).

Degree of Cavernous Sinus Invasion Versus Recurrence

Forty-three patients had documented cavernous sinus invasion preoperatively and were followed up at a median time of 57 months, whereas the other 88 patients had no cavernous sinus invasion and had a median follow-up time of 68 months. There was no statistical difference in recurrence rate between patients with cavernous sinus invasion (13%) and those without (11%) ($p = 0.72$) (►Table 2). The four patients that had cavernous sinus invasion were found to have tumor recurrence or progression at an average follow-up time of 95 months, compared with 35 months in the 10 patients that had no cavernous sinus invasion. In

Figure 1 (A) Kaplan–Meier analysis of overall tumor progression–free survival in patients with complete resection compared with incomplete resection. The differences between the two groups are not significant ($p = 0.18$). (B) Kaplan–Meier analysis of overall tumor progression–free survival in patients with cavernous sinus invasion compared with no cavernous sinus invasion. The differences between the two groups are not significant ($p = 0.96$).

addition, the Kaplan–Meier analysis did not show statistical difference in overall tumor progression survival ($p = 0.96$) (→Fig. 1B).

Degree of Cavernous Sinus Invasions Versus Morbidity and Mortality

A higher incidence of cranial nerve III deficits occurred in patients with cavernous sinus invasion (14%) than those without (0%). Likewise, the rates of hemiparesis and diplopia were higher in patients with cavernous sinus invasion than those without (1 vs. 9%; $p = 0.08$ and 1 vs. 20%; $p = 0.03$, respectively). Other postoperative morbidities, including change in vision and epidural hematoma showed no increased disposition to either group. Finally, an equal mortality rate of 2% was observed in both groups.

Discussion

The management of patients with SWMs has evolved over the past decades, resulting in minimal morbidity and a satisfactory surgical mortality rate of ~4%.³⁹ After gross total resection, almost all of the larger series with a minimum 5-year follow-up report a 5 to 10% recurrence rate. Subtotal resection, however, has at times been reported to increase the recurrence rate to as high as 60%, while in other cases it has appeared to facilitate growth arrest of the tumor.^{12,40,41} Our review found an overall mortality rate of 2% and recurrence rates of 13 and 5% for patients undergoing partial versus complete resection, respectively. Additionally, we found that the recurrence rate in Simpson Grade IV patients was 24% (8 of 34 patients). Interestingly, although we noted an increase in recurrence rate in incompletely versus completely resected SWMs, it was not statistically significant. This leads to the

question: Does the benefit of completely resecting the remaining tumor outweigh the risk? Initially, we anticipated that a greater extent of resection would be associated with higher morbidity. However, we found this to be untrue. Patients undergoing incomplete resection (Simpson Grade II, III, IV) actually have a higher rate of morbidity than those whose tumors were completely removed (Simpson Grade I).

We hypothesized that tumor location and invasion, rather than extent of resection, caused increase risk of morbidity. Unfortunately, because SWM location and World Health Organization categorization were insufficiently reported, we were unable to fully analyze this hypothesis. In support of our hypothesis, invasion of cavernous sinus when noted in the literature and has been widely associated with high postoperative morbidity. In our view, this is an adequate approximation of overall tumor invasiveness. Upon review and analysis, we noted a significant elevation in cranial nerve III palsy (from 0 to 14%) in patients with cavernous sinus invasion compared with those without. There was also a notable increase in postoperative diplopia, although it did not meet our threshold for statistical significance. These results are no doubt due to the anatomical proximity of cranial nerves III, IV, and VI within the walls of substance of the cavernous sinus. These nerves are likely to already be compromised prior to surgery, and, with cavernous sinus invasion, require minimal disruption to cause marked postoperative morbidity. Therefore, patients with cavernous sinus invasions should be counseled about this risk associated with surgery, irrespective of the surgeon's preference for complete or incomplete tumor resection. There were no changes in visual acuity in patients with or without cavernous sinus invasion.

In the subgroups (cavernous sinus invasion versus no invasion), there was an unequal distribution of Simpson Grade resections. The distribution showed higher rate of Grade I and II resection without cavernous sinus invasion and a higher rate of Grade III and IV resection with cavernous sinus invasion. This result is not unexpected, due to the known operative difficulty of tumor resection within the cavernous sinus. In the studies reviewed, there was limited data available on the value of radiation therapy as an adjuvant treatment. Future studies should explore the role of postoperative radiation therapy in controlling recurrence.

The observation that the deficits increase in patients who have cavernous sinus invasion can also be attributed to the likelihood that these patients are usually patients with advanced disease. Tumor size, although not statistically significant, is increased in both incompletely resected patients and patients with cavernous sinus invasions. We did not attempt to classify the extent of cavernous sinus involvement by compartment or volume, and this may be a limit of our review. The difficulty with removing tumor from the lateral wall is much different than removing tumor from the contents of the sinus between nerves and the carotid artery. On the other hand, large tumors of the sphenoid wing with diffuse attachments are much more difficult to manipulate surgically and even more difficult to achieve complete re-

moval. The difficulty of the surgical maneuvers required for these tumors is reflected in our series in that it does confirm that cranial nerve deficits continue to be the leading surgical morbidity among patients surgically treated for sphenoid ridge meningiomas.

Consequently, the recent trend in the management of these patients has targeted near complete excision of the tumor with conservation of cranial nerve function, reserving reoperation or adjuvant treatments with radiotherapy or radiosurgery for recurrence. Based on our data, we can argue that preservation of cranial function is more important for satisfactory patient outcomes, as extent of resection is not as strongly correlated to recurrence as previously thought. In addition, the finding of cavernous sinus invasion should be considered a risk to postoperatively ocular motor morbidity, independent of the intention of extent of resection. Consideration of ocular motor morbidity must always be a priority when treating these patients surgically because even in cases where surgical intervention has been contraindicated (e.g., due to advance age), these patients survive for a rather lengthy period of time, from 5 to 22 years, but a major disability is the loss of normal eye movement.¹⁸

There are several studies in the literature that focus on visual acuity outcome of patients undergoing surgical intervention for sphenoid ridge meningioma, and surgical measures taken to avoid this significant morbidity. For instance, one study done by Lee et al⁴² demonstrated that extradural bony decompression of the superior orbital fissure, optic canal and anterior followed by sectioning of the falciform ligament, all before tumor resection produced an improvement in preoperative vision in 75% of the patients. Another study conducted by Russell et al³⁰ adds that although minimizing the indirect compression of optic nerve by releasing it from against the falciform ligament during tumor resection attributes to good visual outcome, but careful surgical manipulation and strict preservation of all vessels feeding the optic structures is equally if not more germane to positive visual outcome. An investigation into decompression and minimizing disruption of the cavernous sinus and the ocular motor cranial nerves would be as useful information as those stated above, which focus primarily on the optic nerve manipulation.

Conclusion

In conclusion, complete excision of sphenoid ridge meningiomas is always recommended whenever possible although tumor progression and/or recurrence rates and morbidity may not be as strongly correlated to the extent of resection as initially thought. In ideal patients without tumor invasion of the cavernous sinus, morbidity risks are lower and therefore more aggressive attempt at resection may be warranted. However, there is only a moderate increase in tumor control rates in patients who underwent complete versus incomplete resection or with patients who had cavernous sinus invasion or not. The differences were not significantly different. Cranial nerve morbidity was highly correlated with cavernous sinus invasion despite extent of resection. Therefore,

preoperative disclosure of these morbidities should be discussed with the patient prior to surgical resection.

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