Surgical outcomes after reoperation for recurrent non–skull base meningiomas

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OBJECTIVE Recurrent meningiomas are primarily managed with radiation therapy or repeat resection. Surgical morbidity after reoperation for recurrent meningiomas is poorly understood. Thus, the objective of this study was to report surgical outcomes after reoperation for recurrent non–skull base meningiomas.

METHODS A retrospective review of patients was performed. Inclusion criteria were patients with recurrent meningioma who had prior resection and supratentorial non–skull base location. Univariate and multivariate logistic regression and recursive partitioning analysis were used to identify risk factors for surgical complications.

RESULTS The authors identified 67 patients who underwent 111 reoperations for recurrent supratentorial non–skull base meningiomas. The median age was 53 years, 49% were female, and the median follow-up was 9.8 years. The most common presenting symptoms were headache, weakness, and seizure. The WHO grade after the last reoperation was grade I in 22% of cases, grade II in 51%, and grade III in 27%. The tumor grade increased at reoperation in 22% of cases. Tumors were located on the convexity (52%), parasagittal (33%), falx (31%), and multifocal (19%) locations. Tumors involved the middle third of the sagittal plane in 52% of cases. In the 111 reoperations, 48 complications occurred in 32 patients (48%). There were 26 (54%) complications requiring surgical intervention. There was no perioperative mortality. Complications included neurological deficits (14% total, 8% permanent), wound dehiscence/infection (14%), and CSF leak/pseudomeningocele/hydrocephalus (9%). Tumors that involved the middle third of the sagittal plane (OR 6.97, 95% CI 1.5–32.0, $p = 0.006$) and presentation with cognitive changes (OR 20.7, 95% CI 2.3–182.7, $p = 0.001$) were significantly associated with complication occurrence on multivariate analysis. The median survival after the first reoperation was 11.5 years, and the 2-, 5-, and 10-year Kaplan-Meier survival rates were 91.0%, 68.8%, and 50.0%, respectively.

CONCLUSIONS Reoperation for recurrent supratentorial non–skull base meningioma is associated with a high rate of complications. Patients with cognitive changes and tumors that overlap the middle third of the sagittal plane are at increased risk of complications. Nevertheless, excellent long-term survival can be achieved without perioperative mortality.

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KEYWORDS recurrent; meningioma; complications; convexity; parasagittal; falx; morbidity; supratentorial; skull base

MENINGIOMAS are the most common primary intracranial tumors,⁵ representing approximately 34% of all primary intracranial neoplasms.²⁶ Surgery and/or radiation are the standard of care for primary meningiomas, and gross-total resection (GTR) provides long-term control for WHO grade I meningiomas.²⁶ Extent of resection is strongly associated with recurrence, with GTR being associated with longer recurrence-free survival.^{6,9,29} Nevertheless, recurrence can occur after both

GTR and subtotal resection (STR), particularly in cases of WHO grade II or III meningiomas.^{1,2,6,19,28,29} Published rates of recurrence following GTR in historical series not stratified by WHO grade range from 7%–23% at 5 years to 24%–60% at 15 years.²⁶ Rates of recurrence following STR are higher and have been reported at over 70% at 15 years.²⁶ With 25-year follow-up, recurrence rates for parasagittal meningiomas range from 38% (after Simpson grade 1 resection) to 69% (after Simpson grade 4 resec-

ABBREVIATIONS GTR = gross-total resection; STR = subtotal resection.

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tion).²² Thus, even after optimal resection, with enough time, many meningiomas will recur. Once a meningioma recurs, there is an increased risk of disease progression, with shorter overall survival and increased need for continued reoperations and radiotherapy.^{6,18,19} Adjuvant radiation therapy provides longer progression-free survival and overall survival in patients with recurrent meningiomas as compared to surgery alone.^{18,32} The best management of recurrent meningiomas remains unclear and a source of debate.²⁶

When considering repeat surgery as an option for management of a recurrence, it is important to consider the complication profile associated with reoperation. While the complication profile of primary non-skull base meningiomas has been previously described,^{4,5} there is limited data in the literature on the morbidity associated with reoperation for recurrent non-skull base meningiomas.¹⁴ Thus, we reviewed our institutional experience to report surgical morbidity after reoperation for non-skull base meningiomas and to identify risk factors for complications.

Methods

Study Design, Setting, Participants, and Inclusion Criteria

This is a retrospective cohort study. Patients who underwent resection of meningiomas between 1985 and 2016 at our institution were identified. Clinical data on 2120 patients were screened to identify patients who underwent reoperation for recurrent supratentorial non-skull base meningiomas. Inclusion criteria were: 1) age older than 18 years, 2) supratentorial non-skull base location, 3) prior resection at the site of recurrence, 4) reoperation for recurrent disease, and 5) adequate information in the electronic medical record, including pathology reports, operative reports, and admission/discharge information. The Committee on Human Research at our institution approved this study.

Data Sources, Variables, and Bias

Data were collected from the electronic medical records, radiological archives, and pathology archives. Clinical variables included sex, age, date of diagnosis, presenting symptoms, tumor grade at diagnosis, tumor location, tumor size, smoking history, treatment history (including radiation therapy and resection), timing of surgery for recurrent disease, perioperative course, complications, and mortality. Tumor location and size were measured on the preoperative postcontrast T1-weighted MR images. The largest tumor dimension was used as a surrogate for tumor size. Tumor location was classified as convexity, parasagittal, falx, or multifocal. Some tumors involved multiple locations (i.e., convexity and parasagittal, or parasagittal and falx). In parallel, we categorized tumors based on whether part of the tumor overlapped and involved the middle third of the sagittal plane from the glabella to the tocalar herophili, corresponding to the middle third of the superior sagittal sinus. This is easily done for falx/parasagittal tumors that are adjacent to the sinus. For convexity tumors, the corresponding area of the cortex was divided into thirds in the sagittal plane and tumors were classified as to whether they involved the middle third or were

only in the anterior or posterior thirds. Tumor grade was from the pathology report and reflects the WHO grading system at time of resection. Regrading of each tumor according to current WHO grading criteria was beyond the scope of this study.¹³ Mortality data were collected from the Social Security Death Index, the medical record, and publicly searchable obituaries. Only information recorded in the medical record could be reviewed. Thus, as with all retrospective studies, this study is limited by observer and recall bias.

Statistical Analysis

All descriptive and statistical analyses were performed using IBM SPSS 24.0 (IBM Corp.). The Kaplan-Meier method was used to calculate survival. Subjects were censored based on last recorded follow-up or death. Univariate analysis was performed using Pearson chi-square tests to test for the association of complications with sex, age at recurrence, tumor grade, tumor location, tumor size at recurrence, interval radiotherapy, presenting symptoms, and time to recurrence. Recursive partitioning was used in order to partition tumors based on size most associated with perioperative complications. Number of partitions was based on k-fold cross-validation with the greatest R^2 value. The primary outcome of interest was any complication following resection of recurrent disease. Multivariate analysis of risk factors associated with complications was performed using binary logistic regression. The criterion for inclusion into multivariate analysis was association with complications in univariate analysis at the $p < 0.2$ level. Following backward selection, only covariates significant at the $p < 0.1$ level were included in the final multivariate analysis.

Results

Demographics, Tumor Characteristics, and Treatment Information

Of the 2120 patients who underwent surgical treatment of meningiomas at our institution during the study period, 67 (3.2%) underwent at least 1 reoperation for a recurrent supratentorial non-skull base meningioma. The patients' median age at the first reoperation for recurrent disease was 53.2 years (range 20–83 years), and 49% were female. The presenting symptoms at time of initial diagnosis are listed in Table 1. The median duration of follow-up from the time of initial diagnosis was 9.8 years (range 1.5–36 years). Tumor grade after the final resection, tumor location, and size are reported in Table 2. The majority of the recurrent tumors were WHO grades II (50.7%) or III (26.9%), and 15 tumors (22.4%) had an increase in WHO grade at the time of recurrence compared to grade at the previous resection. Smoking history was available for 47 patients; 31 (66.0%) had ever smoked, and 9 (19.1%) were active smokers at the time of reoperation.

Interval treatments between each surgery and follow-up for each surgery are in shown in Table 3. Prior to the first reoperation, 38.8% of patients had received either fractionated radiotherapy or stereotactic radiosurgery. Patients who had not received radiotherapy and went directly to reoperation had recurrences that were not amenable to

TABLE 1. Demographic and clinical characteristics

Characteristic	Value
No. of patients	67
No. of ops	111
Median age at 1st reop, yrs (range)	53.2 (20–83)
Median follow-up after Dx, yrs (range)	9.8 (1.5–36)
Female sex	49%
Initial presenting Sx, n (%)	
Headache	23 (34.3%)
Weakness	16 (23.9%)
Seizure	15 (22.4%)
Personality/cognitive changes	9 (13.4%)
Gait abnormalities	5 (7.5%)
Speech disturbance	3 (4.5%)

Dx = diagnosis; Sx = symptoms.

radiotherapy or refused radiotherapy, or the multidisciplinary tumor board at our institution recommended surgical debulking prior to radiotherapy. All patients who were treated with interstitial brachytherapy at the time of reoperation had already received prior treatment with fractionated radiotherapy (Table 3).

Survival Outcomes Following Resection of Recurrent Supratentorial Meningiomas

Kaplan-Meier survival analysis was performed (Fig. 1). A total of 23 deaths occurred during the study follow-up period. Using the available data in the electronic medical record, publically searchable obituaries and the Social Security Death Index, 4 patients were identified whose cause of death was attributable to their meningioma. The cause of death was not defined for the other 19 deaths. The median survival after initial diagnosis was 24.6 years, and the survival rates for 2, 5, and 10 years after initial diagnosis were 97.9%, 90.1%, and 82.8%, respectively. The median survival after the first reoperation was 11.5 years, and the 2-, 5-, and 10-year survival rates were 91.0%, 68.8%, and 50.0%, respectively. The median survival after the second reoperation was 7.8 years, and the 2-, 5-, and 10-year survival rates were 72.0%, 55.1%, and 45.9%. The median survival after the third reoperation was 4.6 years, and the 2-, 5-, and 10-year survival rates were 64.8%, 40.5%, and 0.0%.

Complications After Reoperation for Recurrent Supratentorial Meningiomas

A total of 48 complications were observed following 111 operations in 67 patients (Table 4). Overall, 32 patients (47.7%) experienced at least 1 complication after at least 1 operation (some patients experienced multiple complications or complications after multiple operations). A total of 26 (54.2%) complications occurred that required surgical intervention in 16 patients (some patients required surgery for multiple complications). The most common complications observed were wound infections (n = 10, of which 9 required reoperation); permanent new neurological defi-

TABLE 2. Tumor characteristics

Variable	Value
WHO grade at last reop	
I	15 (22.4%)
II	34 (50.7%)
III	18 (26.9%)
Change in WHO grade from primary op	15 (22.4%)
I to II	8 (11.9%)
II to III	6 (8.9%)
I to III	1 (1.5%)
Location	
Convexity	35 (52.2%)
Parasagittal	22 (32.8%)
Falx	21 (31.3%)
Multifocal	13 (19.4%)
Middle 3rd sagittal plane	
Yes	35 (52.2%)
No	32 (47.8%)
Largest tumor dimension	
1st reop (n = 67)	
Median, cm (range)	3.2 (1–9)
<3 cm, n (%)	16 (23.9%)
≥3 cm, n (%)	23 (34.3%)
Unknown, n (%)	28 (41.8%)
2nd reop (n = 27)	
Median, cm (range)	3.3 (1–7)
<3 cm, n (%)	4 (14.8%)
≥3 cm, n (%)	16 (59.3%)
Unknown, n (%)	7 (25.9%)
3rd reop (n = 13)	
Median, cm (range)	2.7 (1.5–5.6)
<3 cm, n (%)	4 (30.8%)
≥3 cm, n (%)	3 (23.1%)
Unknown, n (%)	6 (46.1%)
4th reop (n = 4)	
Median, cm (range)	4.6 (4.2–5)
<3 cm, n (%)	0 (0%)
≥3 cm, n (%)	3 (75%)
Unknown, n (%)	1 (25%)

Values are numbers of cases (%) unless otherwise indicated.

cit (9); transient new neurological deficit (7); and wound dehiscence requiring surgical revision (6). Permanent neurological deficits observed included weakness (7) and visual field deficits (2). Wound-related complications (surgical site infections and wound revisions) represented the majority of complications requiring return to the operating room. Wound infections occurred on a spectrum from superficial infections requiring local surgical debridement (6) to deep infections requiring bone flap removal (3). Similarly, wound-healing complications included a range from superficial wound revisions (3) to persistent bone de-

TABLE 3. Reoperation and interval treatment data

Variable	1st Reop	2nd Reop	3rd Reop	4th Reop
No. of patients	67	27	13	4
Median age at op, yrs (range)	53.2 (20–83)	56.4 (21–78)	60.2 (38–79)	67.3 (42–77)
Median time since prior op, yrs (range)	4.5 (0.7–21)	2.9 (0.6–14)	1.4 (0.3–4.5)	5 (2.5–6)
Median postop follow-up, yrs (range)	3.5 (0–23)	3.1 (0–13)	2.7 (0–9)	1.4 (0.3–5)
Intraop brachytherapy, n (%)	7 (10.4%)	3 (11.1%)	5 (38.5%)	1 (25%)
Extent of resection				
GTR, n (%)	22 (32.8%)	16 (59.2%)	3 (23.1%)	0 (0%)
STR or NTR, n (%)	23 (34.3%)	9 (33.3%)	8 (61.5%)	4 (100%)
Unknown	22 (32.8%)	2 (7.4%)	2 (15.4%)	0 (0%)
Interval treatment since prior op				
Fractionated RT, n (%)	9 (13.4%)	3 (11.1%)	1 (7.7%)	0 (0%)
SRS, n (%)	17 (25.4%)	9 (33.3%)	6 (46.1%)	2 (50%)

NTR = near-total resection; RT = radiation therapy; SRS = stereotactic radiosurgery.

fects requiring cranioplasty or adjustment of hardware (2) and a complicated wound requiring a free flap with plastic surgery (1). Other complications included hydrocephalus (5 required ventriculoperitoneal shunt placement and 1 patient with a pre-existing shunt required shunt revision), subdural hematoma requiring surgical evacuation (1), CSF leaks or pseudomeningocele (4 total; 3 were managed surgically with wound revision and 1 required a shunt), and symptomatic pneumocephalus requiring high-flow O₂ (1). One patient with a pre-existing ventriculoperitoneal shunt developed low-pressure hydrocephalus postoperatively

that required a shunt valve change, and this is counted as the shunt revision in Table 4. Noted medical complications were new seizures (5), postoperative arrhythmia (1), and hyponatremia (1). Complications delineated by each reoperation are presented in Table 4.

In a univariate analysis, personality or cognitive changes at presentation ($p = 0.004$) and location involving the middle third of the sagittal plane ($p = 0.005$) were significantly associated with complications (Table 5). Sex, age at reoperation, smoking history, WHO grade, location, tumor dimension, radiotherapy prior to reoperation, time

FIG. 1. Kaplan-Meier survival curves. **A:** Overall survival from initial diagnosis. **B:** Survival after first reoperation. **C:** Survival after second reoperation. **D:** Survival after third reoperation. Figure is available in color online only.

TABLE 4. Complications

Variable	1st Reop	2nd Reop	3rd Reop	4th Reop	Total
No. of cases	67	27	13	4	111
Patients w/ comp, n (%)	22 (32.8%)	8 (29.6%)	3 (23.1%)	4 (100%)	32 (47.7%)*†
Total no. of comp	27	12	5	5	48
Comp req op, n (%)	9 (33.3%)	9 (75.0%)	5 (100%)	3 (60.0%)	26 (54.2%)†
Patients w/ comp req op, n (%)	8 (11.9%)	6 (22.2%)	3 (23.1%)	2 (50.0%)	16 (23.9%)*†
Surgical					
Permanent new neurol deficit	9 (13.4%)				9
Transient new neurol deficit	4 (6.0%)	1 (3.7%)		2 (50%)	7
Wound dehiscence	3 (4.5%)	1 (3.7%)	2 (15.4%)		6
Required op	3 (4.5%)	1 (3.7%)	2 (15.4%)		6
Wound infection	3 (4.5%)	4 (14.8%)	2 (15.4%)	1 (25%)	10
Required op	2 (3.0%)	4 (14.8%)	2 (15.4%)	1 (25%)	9
CSF leak/pseudomeningocele	2 (3.0%)	2 (7.4%)			4
Required op	2 (3.0%)	1 (3.7%)			3
Required shunt		1 (3.7%)			1
Hydrocephalus	1 (1.5%)	2 (7.4%)	1 (7.7%)	2 (50%)	6
Required shunt or shunt revision	1 (1.5%)	2 (7.4%)	1 (7.7%)	2 (50%)	6
Subdural hematoma	1 (1.5%)				1
Required op	1 (1.5%)				1
Pneumocephalus	1 (1.5%)				1
Medical					
Seizures	3 (4.5%)	2 (7.4%)			5
Arrhythmia	1 (3.0%)				1
Hyponatremia		1 (3.7%)			1

Comp = complication(s); neurol = neurological; req = requiring.

* Total is all individual patients who had a complication (some had multiple complications).

† Percentage represents the number of patients who had a complication divided by the total number of patients (n = 67).

to disease recurrence, and tumor dimensions were not significantly associated with complications. Prior radiotherapy was not associated with complications generally ($p = 0.286$), nor was it associated with wound-related complications (wound dehiscence, CSF leaks, or surgical site infections), which were evaluated in a separate analysis ($p = 0.544$). Similarly, smoking status was not associated with complications ($p = 0.946$). We performed recursive partitioning analysis to partition tumor size by the presence of any complication. Tumor size was dichotomized at 3.9 cm, and after binning tumors by size greater or less than 3.9 cm, there was no association with complications (categorical/binning: $p = 0.279$; continuous: $p = 0.895$).

On multivariate analysis of factors identified in the univariate analysis at $p < 0.2$ level (Table 6), cognitive or personality changes at presentation and middle cortex location were significantly associated with perioperative complications ($p = 0.001$ and $p = 0.006$, respectively). Sex was not significant ($p = 0.091$). We performed recursive partitioning using the same variables included in the multivariate analysis to identify patients at high risk for complications after the first reoperation (Fig. 2). Of the 7 patients with personality or cognitive changes at presentation, 2 patients experienced permanent neurological deficits postoperatively, 1 patient experienced seizures

postoperatively, 2 patients experienced wound-related complications (surgical site infection or CSF leak requiring repair), 1 patient developed a subdural hematoma, and 1 patient developed pneumocephalus postoperatively and low-pressure hydrocephalus necessitating shunt revision. Patients who presented with personality or cognitive changes were significantly older than those who presented without such changes (mean age 63.9 vs 52.5 years at time of recurrence, $p = 0.022$). The majority of patients ($n = 58$, 86.6%), however, did not have cognitive changes. The second split was based on whether the tumor involved the middle third of the sagittal plane. The complication rate after the first reoperation was much higher (40% vs 10.7%) for patients whose tumors involved the middle third of the sagittal plane compared to those whose tumors did not.

Discussion

Key Results

The objective of this study was to report surgical outcomes following reoperation for recurrent supratentorial non-skull base meningiomas and identify risk factors for complications. First, we found that there is significant morbidity associated with reoperation for recurrent meningioma. Second, we found that patients whose tumors

TABLE 5. Univariate analysis of risk factors for any complication after first reoperation

Variable	No Comp	Comp	p Value
Sex			0.123
Male	26 (57.8%)	8 (36.4%)	
Female	19 (42.2%)	14 (63.6%)	
Mean age at 1st reop in yrs	53.5 ± 14.6	55.0 ± 13.1	0.680
Smoking history			0.946
Never smoker	11 (35.5%)	5 (31.3%)	
Previous smoker	14 (45.2%)	8 (50.0%)	
Active smoker	6 (19.4%)	3 (18.8%)	
WHO grade			0.504
I	14 (31.1%)	4 (18.2%)	
II	21 (46.7%)	13 (59.1%)	
III	10 (22.2%)	5 (22.7%)	
Tumor location			0.637
Convexity	16 (35.6%)	8 (36.4%)	
Parasagittal	12 (26.7%)	5 (22.7%)	
Falx	7 (15.6%)	6 (27.3%)	
Multifocal	10 (22.2%)	3 (13.6%)	
Middle 3rd sagittal plane			0.005
No	27 (60.0%)	5 (22.7%)	
Yes	18 (40.0%)	17 (77.3%)	
RT before 1st reop			0.286
No RT	31 (68.9%)	12 (54.5%)	
Any RT	14 (31.1%)	10 (34.5%)	
Seizure at presentation			0.223
No	37 (82.2%)	15 (22.4%)	
Yes	8 (17.8%)	7 (46.7%)	
Weakness at presentation			0.070
No	37 (82.2%)	13 (59.1%)	
Yes	8 (17.8%)	9 (40.9%)	
Personality/cognitive changes at presentation			0.004
No	43 (95.6%)	15 (68.2%)	
Yes	2 (4.4%)	7 (31.8%)	
Headache at presentation			0.099
No	33 (73.3%)	11 (50.0%)	
Yes	12 (26.7%)	11 (50.0%)	
Mean time from Dx to 1st reop in yrs	5.6 ± 4.6	7.0 ± 5.4	0.307

Data are presented as number of patients (%) unless otherwise indicated. Mean values are presented with SDs. Boldface type indicates statistical significance.

overlapped the middle third of the sagittal plane had a markedly higher rate of perioperative complications, as did patients who presented with personality or cognitive changes.

Interpretation

Morbidity associated with reoperation for recurrent

TABLE 6. Multivariate analysis of risk factors for any complication at first reoperation

Variable	OR for Any Comp	95% CI	p Value
Personality or cognitive change at presentation	20.70	2.34–182.69	0.001
Middle 3rd location	6.97	1.52–32.00	0.006
Female sex	3.16	0.80–12.44	0.091
Headache at presentation	1.86	0.49–7.06	0.360
Weakness at presentation	1.38	0.33–5.84	0.664

Boldface type indicates statistical significance.

non-skull base meningiomas is high, with 47.7% patients having at least 1 complication at some point. These complications are significant, with more than half of the affected patients requiring additional surgery to manage the complication. Furthermore, the complication rate after reoperation is significantly higher than the published complication rates associated with primary resection of convexity meningiomas (10%, 16 complications/141 patients),²⁷ and parasagittal or falx meningiomas (19%, 30 complications/135 surgeries).³¹ Interestingly, the complication rate was higher for recurrent non-skull base meningiomas (48% of patients had a complication, 24% had a complication requiring surgery) than for recurrent skull base meningiomas. In our series of 78 patients undergoing 100 reoperations for recurrent skull base meningiomas, 30% of patients experienced at least 1 complication and one-third of the complications required additional surgery.¹⁴ One potential factor influencing this could be the inherent biology of the tumors. Recurrent non-skull base tumors were more often grade II (51% vs 22%) or grade III (27% vs 6%) compared to recurrent skull base meningiomas. Furthermore, 22% of the recurrent non-skull base tumors increased in grade from the primary resection, suggesting increasingly aggressive and invasive behavior of these meningiomas.

A significant portion of the complications were impaired wound healing/infection and pseudomeningocele. Intuitively, it is not surprising that repeat surgery had higher rates of wound healing impairment, but we were surprised that neither smoking nor diabetes was associated with complications. However, the prevalence of diabetes (4.5%) and the proportion of patients who were active smokers (13.4%) were very low in this study. Prior radiation therapy has also been implicated in impaired wound healing and wound-related complications;¹⁰ however, in this series prior radiation therapy was not associated with wound-related complications or overall complications. Of note, only 38.8% of patients underwent adjuvant radiation therapy prior to their first reoperation for recurrent disease, although 67.1% presented with a WHO grade II or III meningioma. This is most likely due to referral patterns and patients who had their initial surgery elsewhere and were lost to follow-up prior to presenting/being referred to our institution and may limit the generalizability of our findings. Despite the morbidity, there was no perioperative mortality. Perioperative mortality for parasagittal and falx meningiomas was recently reported to be as high as 4.6%

FIG. 2. Recursive partition of variables included in multivariate analysis of patients at high risk for complication. The number of partitions (2) was based on the k-fold cross-validation with the highest R^2 value. Comp. = complication(s).

in 87 patients in one series,²⁰ and 1.5% in 110 patients with parasagittal meningiomas in another.²⁴ While there was a high rate of complications associated with reoperation in our series, there were no deaths, and the median survival after the first reoperation was 11.5 years, thus providing patients with excellent survival after recurrence.

The strongest predictors of complication occurrence were cognitive changes at presentation and tumors that overlapped the middle third of the sagittal plane, this included falx and parasagittal meningiomas that were adjacent to the superior sagittal sinus, as well as middle-third convexity tumors. This association likely reflects the abundance of large draining veins found in this region.²⁵ Furthermore, the close proximity to the motor strip bilaterally and language areas in the dominant hemisphere leads these tumors to be more symptomatic preoperatively. Resection is challenging in patients who have undergone prior surgery and radiation treatment due to arachnoiditis and scarring. Thus, any adherence or invasion by the tumor, or damage to venous outflow, can increase the risk of postoperative neurological deficits.^{4,16,24} Indeed, we found that a significant portion of the complications observed following the first reoperation occurred in patients whose tumor involved the middle third of the sagittal plane, where there are numerous large draining veins into the superior sagittal sinus, reinforcing the high-risk nature of resecting tumors in this location.

The association of cognitive changes with complications may be an epiphenomenon ultimately reflecting a combination of tumor factors, such as size and reduced functional reserve of patients with increased age or comorbid conditions. Patients who presented with cognitive changes were older, and increased age has been associated with increased risk of postoperative neurological deficits, pneumonia, and other complications following meningioma resection.^{15,21,23,33} Interestingly, age was not significantly associated with complications in our series, which may reflect the variability inherent in age-associated changes

or the fact that recurrent tumors tend to occur in younger patients (the median age at first reoperation was 53 years), or our sample size may simply have been too small to allow us to identify an age cutoff that was associated with complications. Other potential contributing factors not captured in our data set include baseline frailty and the presence of other comorbid conditions, which has also been associated with an increased rate of perioperative complications and which may increase patient susceptibility to nonspecific changes in cognitive function.^{3,11,17,30}

The increased incidence of complications in patients with cognitive symptoms may also reflect an increased risk of complications in symptomatic patients. Prior series have demonstrated that the clinical course of symptomatic meningiomas is distinct from that of asymptomatic meningiomas, and symptomatic meningiomas have been associated with an increased risk of complications.³³ In a series of 513 meningioma patients, Zeng et al. reported a complication rate of 21.7% in symptomatic patients, in comparison to a 13.6% rate of complications in asymptomatic patients.³³

Finally, the most important question is when to operate when a meningioma recurs. The answer is complex and must be individualized to each patient and tumor. Adjuvant radiation therapy is our first option for appropriately sized recurrent meningiomas and subtotally resected high-grade meningiomas.^{7,8,12} Surgery is considered when patients are symptomatic from their tumor, although our findings argue for the importance of counseling patients on the high risk of complications, particularly patients presenting with cognitive changes such as confusion. Surgery for asymptomatic patients is reserved for large recurrences or based on patient preference after the case is discussed with our multidisciplinary tumor board, which includes neuro-oncologists and radiation oncologists. A final interesting observation is that 22% of meningiomas were found to have increased in grade at the time of recurrence, including 13% of grade I meningiomas that had increased to grades

II or III. This increase in grade has significant prognostic implications and would be missed if a patient undergoes radiotherapy alone at recurrence. While molecularly targeted therapies for meningioma are currently limited to clinical trials, in the future we may need pathology from the recurrent tumor to guide therapeutic choices.

Limitations

Given the retrospective nature of this study, there is selection and information bias present in the study. Our findings are dependent on the availability of patient data in the electronic medical record. Some patients in this series had undergone prior surgical treatment and/or radiation therapy at outside institutions; data regarding these interventions were not available for review and may result in underreporting of interval radiation treatment. Medical complications are also likely underreported due to suboptimal documentation.

Generalizability

These results are those of a specialized neurosurgical team at a large referral center with considerable experience. Our results should be generalizable to other similar centers, but may not apply to low-volume centers. Furthermore, this series contained a high proportion of recurrent grade II and grade III meningiomas, which should be taken into account when generalizing these findings to other situations.

Conclusions

Reoperation for recurrent supratentorial non-skull base meningioma is associated with a high rate of complications. Patients with cognitive or personality changes and tumors located in the middle third of the sagittal plane were at an increased risk of complications. Nevertheless, excellent long-term survival can be achieved without perioperative mortality. Given the morbidity, laboratory studies must be supported to develop molecular therapeutic options for recurrent meningiomas to improve care for future patients.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Conception and design: Magill, Raleigh, Aghi, Theodosopoulos, McDermott. Acquisition of data: Magill, Diaz, Jalili, Aghi, Theodosopoulos, McDermott. Analysis and interpretation of data: Magill, Dalle Ore, Diaz, Jalili, Raleigh, McDermott. Drafting the article: Magill, Dalle Ore, Raleigh, McDermott. Critically revising the article: Magill, Dalle Ore, Raleigh, McDermott. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Magill. Statistical analysis: Magill, Dalle Ore. Study supervision: Magill, Raleigh, Aghi, Theodosopoulos, McDermott.

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