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Journal
Journal of Neurological Surgery Part B Skull Base, 83(Suppl 2)

ISSN
1526-8012

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Publication Date
2022-06-01

DOI
10.1055/s-0041-1735559

Peer reviewed

Comparison of Outcomes following Primary and Repeat Resection of Craniopharyngioma

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J Neurol Surg B Skull Base 2022;83(suppl S2):e545–e554.

Abstract

Introduction The management of recurrent craniopharyngioma is complex with limited data to guide decision-making. Some reports suggest reoperation should be avoided due to an increased complication profile, while others have demonstrated that safe reoperation can be performed. For other types of skull base lesions, maximal safe resection followed by adjuvant therapy has replaced radical gross total resection due to the favorable morbidity profiles.

Methods Seventy-one patients underwent resection over a 9-year period for craniopharyngioma and were retrospectively reviewed. Patients were separated into primary resection and reoperation cohorts and stratified by surgical approach (endonasal vs. cranial) and survival analyses were performed based on cohort and surgical approach.

Results Fifty patients underwent primary resection, while 21 underwent reoperation for recurrence. Fifty endonasal transsphenoidal surgeries and 21 craniotomies were performed. Surgical approaches were similarly distributed across cohorts. Subtotal resection was achieved in 83% of all cases. There were no differences in extent of resection, visual outcomes, subsequent neuroendocrine function, and complications across cohorts and surgical approaches. The median time to recurrence was 87 months overall, and there were no differences by cohort and approach. The 5-year survival rate was 81.1% after reoperation versus 93.2% after primary resection.

Conclusion Compared with primary resection, reoperation for craniopharyngioma recurrence is associated with similar functional and survival outcomes in light of individualized surgical approaches. Maximal safe resection followed by adjuvant radiotherapy for residual tumor likely preserves vision and endocrine function without sacrificing overall patient survival.

Keywords
- craniopharyngioma
- reoperation
- endonasal
- transcranial
- maximal safe resection

Introduction

Although craniopharyngiomas are histologically benign neoplasms, their location and predilection for local recurrence present substantial treatment challenges. The mortality and morbidity associated with this tumor is due to its close approximation to, and often involvement of, the visual apparatus, third ventricle, hypothalamus, and pituitary stalk

received
May 6, 2021
accepted after revision
July 25, 2021
published online
September 10, 2021

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Rüdigerstraße 14,
70469 Stuttgart, Germany

DOI https://doi.org/10.1055/s-0041-1735559.
ISSN 2193-6331.

which are critical for maintaining homeostatic processes such as thirst, appetite, thermoregulation, blood pressure, and endogenous hormones.[1–3] The tumor's positioning near intracranial vasculature, optic pathways, infundibular stalk, and the hypothalamus makes gross total resection of craniopharyngiomas technically challenging without significant operative morbidity.[4–7] Growing discussion in the literature has disputed the notion of a single optimal surgical approach and the necessity of achieving gross total resection, with some authors advocating for maximal safe subtotal resection (STR) followed by radiotherapy, similar to the management of vestibular schwannomas.[8–10]

Perhaps even more challenging is the management of recurrent craniopharyngioma, with some reports showing that 63% of patients with a gross total resection initially still experience recurrence.[11–13] Earlier studies have argued that repeat resection is associated with increased morbidity and mortality due to poor tissue planes, suggesting that reoperation should be avoided in favor of noninvasive approaches.[14,15] However, emerging evidence argues that successful reoperation can be achieved with adequate relief of symptoms and a comparable complication and survival profile to that of primary resection.[16–18] In this study, we wish to address this controversy by demonstrating that repeat surgical intervention for craniopharyngioma recurrence is comparable to primary resection in terms of functional neurologic and survival outcomes.

Materials and Methods

Study Inclusion and Preoperative Assessments

In this retrospective review, we analyzed 73 consecutive patients who underwent operative evaluation for craniopharyngioma at the University of California San Francisco. Seventy-one underwent resection between 2010 and 2018, while two patients who underwent biopsy only were excluded from the analysis. Patients were included in this study regardless of the chosen surgical approach (endonasal vs. cranial) which was decided by the attending surgeon based on preoperative imaging. Indications for craniotomy were tumors with significant lateral extension, purely intraventricular tumors, tumors with large solid suprasellar components, and tumors extending into the middle or posterior fossa. Indications for endonasal approaches were intrasellar lesions (with or without cystic suprasellar extension), interpeduncular tumors, and tumors in the infra-/retrochiasmatic space. The surgical goal was to perform maximal safe resection. This study was approved by the institutional review board (IRB no.: 19–29097) and all patients provided informed consent to participate.

The electronic medical record was retrospectively reviewed to determine the presenting symptom(s), surgical history, clinical examination, body mass index (BMI), basic laboratory and endocrine studies, Karnofsky's performance status (KPS) and magnetic resonance imaging (MRI) qualities of the tumor. Imaging characteristics included the anatomic location of the lesion, tumor dimensions, presence of optic chiasm compression, invasion into the cavernous sinus, extension into the third ventricle, and hydrocephalus. Tumor volumes were calculated using Brainlab SmartBrush version 2.5 using the pre- and postoperative T1 postgadolinium–enhanced sequences. All relevant tissue samples were sent to pathology for a final diagnosis and genetic profiling. Estimated blood loss, intraoperative complications, postoperative neurologic and endocrine deficits, and length of stay were recorded. Patients typically received follow-up with neurosurgery and/or neuroendocrinology at 1 month, 3 and 6 months postoperatively, and annually thereafter. Mortality was confirmed via records in the medical record and the U.S. Social Security Death Index.

Statistical Analysis

Analysis was performed using R version 3.6.2. The comparison of interest subsequently specified in each table is whether differences in preoperative features and postoperative outcomes exist between patients who underwent primary resection and reoperation. Each comparison is limited to the same approach (i.e., primary endonasal resection vs. repeat endonasal resection). Categorical data are reported as counts and proportions and comparisons were made using Fisher's exact test. Post hoc pairwise comparisons between subcategories were performed if the parent variable achieved a significance level of $p < 0.05$. Continuous data were treated as nonparametric and compared using the Wilcoxon's rank sum test for unpaired samples. Comparisons in time-to-event data were computed using the nonparametric log-rank test with the most recent date of surgery for the reoperation cohort serving as time = 0. Logistic regression was performed using generalized linear models for binomially distributed response variables.

Results

Demographics and Clinical History

Patient demographics and clinical history are summarized in ►**Table 1**. Of 71 patients, 50 underwent primary resection (33 endonasal and 17 cranial) while 21 underwent reoperation for recurrence (17 endonasal and 4 cranial). Among the reoperation cohort, 12 patients underwent an approach that was concordant with their initial approach (four repeat craniotomy and eight repeat endonasal), while nine underwent a discordant approach. Of note, all nine discordant patients initially underwent craniotomy and then repeat resection via endonasal approaches. There were no significant differences in sex, age, or BMI at presentation between cohorts for either operative approaches. Both adult and pediatric patients were included in this study (mean age = 35.43 and range: 2–76 years). The mean age was 35.4 years (95% confidence interval [CI]: 6.2) in the primary resection cohort and 35.6 years (95% CI: 10.4) in the reoperation cohort which was not statistically significant ($p = 0.97$). Overall, the most common symptoms at initial consultation were vision changes (49%), headache (42%), and fatigue (8%). There were no significant differences in neurological complaints between cohorts. Patients undergoing reoperation were more likely to be asymptomatic at surgical consultation (38 vs. 0%,

Table 1 Demographics and clinical history

Characteristic	Primary resection ($n = 33$)	Endonasal Reoperation ($n = 17$)	*p*-Value	Primary resection ($n = 17$)	Craniotomy Reoperation ($n = 4$)	*p*-Value
Female sex	17 (52%)	9 (53%)	1.00	6 (35%)	1 (25%)	1.00
Mean age (y)	28.67 ± 7.57	36.18 ± 11.61	0.243	48.35 ± 8.84	33.00 ± 43.71	0.226
Mean BMI (kg.m^2)	26.21 ± 3.60	26.82 ± 5.26	0.921	30.10 ± 4.47	33.29 ± 21.08	0.494
Symptoms						
Neurologic						
Vision changes	16 (48%)	9 (53%)	1.00	7 (41%)	1 (25%)	1.00
Vertigo	2 (6%)	0	0.542	2 (3%)	1 (25%)	0.489
Fecal/urinary incontinence	1 (3%)	0	1.00	1	0	1.00
Focal weakness	2	0	0.542	0	0	–
Neuropsychiatric						
Headache	18 (55%)	3 (18%)	0.0164	8 (47%)	1 (25%)	0.603
Fatigue	4 (12%)	0	0.286	4 (24%)	0	0.546
Memory Changes	0	2 (12%)	0.111	4	0	0.546
Neuroendocrine						
Weight gain	1	0	1.00	3	0	1.00
Growth delay	4	0	0.286	0	0	–
Decreased libido	1	0	1.00	0	0	–
Galactorrhea	1	0	1.00	0	0	–
Gynecomastia	1	0	1.00	0	0	–
Amenorrhea	1	0	1.00	0	0	–
Polydipsia	0	0	–	1	0	1.00
Cold intolerance	0	0	–	1	0	1.00
None	0	7	0.0002	0	1	0.191
Prior radiotherapy	0	6	0.0008	0	2	0.029
Pathology						
Adamantinomatous	27	12		10	4	
Papillary	6	4		6	0	

Note: *p*-Values provide summary comparisons between primary resection and reoperation within each approach.

$p = 0.0002$) and to have received prior radiotherapy (38 vs. 0%, $p = 0.0002$). Patients undergoing primary endonasal resection were more likely to report neuropsychiatric symptoms such as headaches (55 vs. 18%, $p = 0.016$). Neuroendocrine symptoms were not significantly different between cohorts.

Preoperative and Operative Summary

The operative approaches implemented for each cohort are summarized in ►**Table 2**. Ten patients underwent a transcortical, transventricular approach, four pterional, four supraorbital, two interhemispheric transcallosal, and one retrosigmoidal. Fifteen patients underwent endoscopic endonasal resection, 11 microscopic transsphenoidal, and 24 combined transsphenoidal microscopic resections with endoscopic assist. Of those 50 patients, 17 underwent extended transsphenoidal approaches. The proportion of cases that were performed via craniotomy at primary resection (34%) did not differ from the proportion at repeat resection (19%, $p = 0.263$).

Preoperative examinations of patients undergoing primary resection versus reoperation stratified by surgical approach are summarized in ►**Table 3**. Visual field deficits were similarly distributed across both cohorts, with the most common being bitemporal hemianopsia. Patients undergoing endonasal reoperation were more likely to have panhypopituitarism at presentation (47 vs. 12%, $p = 0.012$). There were no significant differences in the presence of other endocrine derangements including hypogonadism, hypothyroidism, hypocortisolism, growth hormone deficiency, or diabetes insipidus at presentation for either surgical approach. The distributions of KPS scores were similar across cohorts for both approaches ($p = 0.1181$ for endonasal and $p = 0.107$ for cranial).

Table 2 Operative approach summary

Variable	Primary resection ($n = 50$)	Reoperation ($n = 21$)	*p*-Value	Total ($n = 71$)
Operative approach			0.263	
Craniotomy	17	4		21
Transcortical, transventricular	8	2		10
Pterional	4	0		4
Supraorbital	3	1		4
Interhemispheric, transcallosal	2	0		2
Retrosigmoidal	0	1		1
Endonasal	33	17		50
Endoscopic	8	7		15
Microscopic	6	5		11
Microscopic with Endoscopic assist	19	5		24

Preoperative imaging characteristics stratified by approach are summarized in ►**Table 4**.

There were no significant differences in lesion location between primary resection and reoperation cohorts for either surgical approach. Craniotomy was not implemented in any patients with purely sellar lesions (0 vs. 52%, $p = 0.0005$).

The presence of optic pathway compression, cavernous sinus invasion, ventricular invasion, and hydrocephalus were similar between cohorts. Patients undergoing primary endonasal resection were more likely to have larger preoperative tumor volumes (11.94 vs. 3.38 mL, $p = 0.005$), though there were no differences in volumes for patients who underwent craniotomy.

Operative Outcomes

Operative outcomes are summarized in ►**Table 5**. For all patients, the goal of surgery was maximal safe resection. As previously described, radiographic evidence of extent of resection (EOR) was stratified by a neuroradiologist as partial (10–50%), subtotal (51–90%), near-total (>90% but less than 100%), or gross total resections (GTR; 100%).[19] In total, 4 patients received GTR, 3 patients near-total, 59 patients subtotal, and 3 patients partial resection. One patient was lost to follow-up and another was too medically unstable for postoperative imaging and thus their extents of resection could not be determined. There were no differences in extent of resection between primary resection and reoperation for either surgical approaches ($p = 0.275$ for endonasal and $p = 0.228$ for cranial). Estimated blood losses were similarly distributed across cohorts.

Adamantinomatous histology was demonstrated in a total of 53 patients (53/71, 74.6%), papillary in 12 (12/71,

Table 3 Preoperative assessments

Variable	Primary resection ($n = 33$)	Endonasal reoperation ($n = 17$)	*p*-Value	Primary resection ($n = 17$)	Craniotomy reoperation $n = 4$)	*p*-Value
Visual Deficits			0.878			0.657
Bitemporal hemianopsia	8	5		1	1	
Monocular blindness	2	2		1	0	
Homonymous hemianopsia	1	0		1	0	
Quadrantanopia	2	0		2	0	
Endocrine deficits						
Panhypopituitarism	4	8	0.012	2	2	0.148
Hypogonadism	6	1	0.398	3	0	1.00
Hypothyroidism	4	3	0.677	5	1	1.00
Hypocortisolism	1	0	1.00	1	0	1.00
Growth hormone deficiency	3	2	1.00	0	0	
Diabetes insipidus	4	3	0.677	1	1	0.352
Karnofsky's performance status			0.181			0.107
100	0	1		0	0	
90	7	5		1	1	
80	14	3		5	0	
70	11	6		6	2	
60	1	2		5	0	
30	0	0		0	1	

Note: *p*-Values provide summary comparisons between primary resection and reoperation within each approach.

Table 4 Preoperative imaging characteristics

Variable	Primary resection ($n = 33$)	Endonasal reoperation ($n = 17$)	*p*-Value	Primary resection ($n = 17$)	Craniotomy reoperation ($n = 4$)	*p*-Value
Predominant location			0.503			0.532
Suprasellar	15	8		12	4	
Sellar	18	8		0	0	
Third ventricle	0	0		5	0	
Sphenoid sinus	0	1		0	0	
Optic pathway compression	26	13	0.681	16	2	0.284
Cavernous sinus invasion	17	6	0.353	12	3	0.540
Ventricular invasion	8	2	0.455	13	2	1.00
Hydrocephalus	6	2	0.694	10	1	0.566
Mean tumor volume (mL)	11.94 ± 7.90	3.38 ± 1.33	0.005	14.64 ± 6.12	11.79 ± 27.66	0.690
Mean tumor dimensions (cm)						
Craniocaudal	2.70 ± 0.37	1.81 ± 0.39	0.001	3.10 ± 0.58	2.93 ± 3.98	0.695
Anteroposterior	2.53 ± 0.53	2.09 ± 0.47	0.334	2.96 ± 0.51	2.83 ± 3.37	0.404
Mediolateral	2.38 ± 0.34	1.99 ± 0.39	0.214	2.95 ± 0.36	3.20 ± 2.37	0.859

Note: *p*-Values provide summary comparisons between primary resection and reoperation within each approach.

16.9%), and further unspecified in 6. A total of five patients (5/71, 7.04%) were identified to have known mutations associated with craniopharyngioma. Four patients had *BRAF* V600E mutations and one had a *CTNNB1* mutation. Of the patients with *BRAF* mutations, all had papillary tumor histology which is in line with prior reports of the strong linkage between the two.[3,15] The proportions adamantinomatous pathology were equally distributed across cohorts (74% in primary resection and 76% in reoperation, $p = 0.82$).

Clinical Outcomes

Comprehensive postoperative visual field examinations were available for 54 patients. Twenty patients experienced improvements in their visual field examinations, one patient had worsening, and 33 patients had no changes. Repeat operation, either via craniotomy or endoscopic endonasal resection, was not associated with worsening vision. Neuroendocrine outcomes were similar across cohorts when stratified by surgical approach. Furthermore, there were no significant differences in neurologic complications across cohorts. All cerebrospinal fluid (CSF) leaks (five) occurred in endonasal approaches and there was no significant difference in its occurrence between primary resection and reoperation (4/33 vs. 1/17, $p = 0.6623$).

Two patients suffered from pulmonary embolus and one from sepsis. There was one mortality in the cohort secondary to a pulmonary embolism following primary resection. The mean length of stay in the intensive care unit and in the hospital overall was 3.53 days and 6.38 days, respectively. There was no significant difference in length of stay based on whether a patient underwent primary resection versus reoperation for recurrence. However, craniotomy was associated with longer lengths of stay in the intensive care unit (7.40 vs. 1.77 days, $p = 1 \times 10^{-5}$) and in the hospital (10.23 vs. 4.73 days, $p = 3 \times 10^{-6}$) compared with endonasal resection. A majority of patients who underwent craniotomy received external ventricular drain placement (12/21, 57%).

Rates of adjuvant radiotherapy and chemotherapy were similarly distributed across primary resection and reoperation cohorts within each nested approach (►**Table 6**). Twenty-seven patients (38%) experienced recurrence during the follow-up period (mean follow-up = 35 months). There was no difference in median time to recurrence between primary resection and reoperation cohorts (87 vs. 80 months, $p = 0.8$; ►**Fig. 1A**). However, there was a tendency toward earlier recurrence among patients who underwent craniotomy (28 vs. 87 months, $p = 0.07$). A total of six patients expired during the 58.5-month follow-up period. Thus, the median survival time was not reached (►**Fig. 1B**). There were no differences in 5-year survival rates across primary resection and reoperation cohorts (93.2 vs. 81.1%, $p = 0.3$) and cranial and endonasal approaches (87.4 vs. 90.2%, $p = 0.9$).

Logistic Regression

Logistic regression was run to identify factors associated with greater log odds of recurrence including preoperative tumor volumes, extent of resection, and postoperative radiation therapy. None of these variables reached statistical significance on univariate analysis: tumor volume (odds ratio [OR] = 0.96, $p = 0.184$), extent of resection (OR = 0.61, pooled $p = 0.19$) and radiation therapy (OR = 0.55, $p = 0.26$). Therefore, we did not perform a multivariate analysis.

Table 5 Operative outcomes

Variable	Endonasal primary resection ($n = 33$)	Reoperation ($n = 17$)	*p*-Value	Primary resection ($n = 17$)	Craniotomy reoperation ($n = 4$)	*p*-Value
Extent of resection			0.275			0.228
Gross total	3	1		0	0	
Near total	1	0		2	0	
Subtotal	28	14		14	3	
Partial	0	2		0	1	
Lost to follow-up	2	0		1	0	
Estimated blood loss (mL)	64 ± 35	74 ± 44	0.136	184 ± 144	367 ± 217	0.191
Visual field examination			0.135			0.005
Improved	14	4		2	0	0.750
Worsened	0	1		0	0	–
Unchanged	12	9		10	1	0.035
New neuroendocrine deficits						
Diabetes insipidus	15	10	0.551	7	2	1.00
Hypothyroidism	4	0	0.286	0	0	–
Hyponatremia	2	0	0.542	1	0	1.00
Panhypopituitarism	0	0	–	4	0	0.546
Growth hormone deficiency	1	0	1.00	0	0	–
Hypocortisolemia	1	0	1.00	0	0	–
Weight gain	0	0	–	1	0	1.00
Neurologic complications						
CSF leak	4	1	0.650	0	0	–
Hydrocephalus	0	0	–	2	0	1.00
Intracranial hemorrhage	0	0	–	2	0	1.00
Medical complications within same admission						
Pulmonary embolus	0	0	–	2	0	1.00
Sepsis	0	0	–	1	0	1.00
Mean length of stay (d)						
ICU	2.21 ± 0.77	1.00 ± 0.80	0.231	8.24 ± 6.45	2.67 ± 5.17	0.489
Total	4.97 ± 1.03	4.29 ± 1.51	0.007	10.94 ± 6.15	7.25 ± 6.67	0.367
Discharge medications						
Dexamethasone	18	8	0.767	10	3	1.00
Desmopressin	7	5	0.729	4	2	0.544
Levothyroxine	9	1	0.134	3	1	1.00
Levetiracetam	0	0	–	5	1	1.00
Somatotropin	0	1	0.34	0	0	–
30-day mortality	0	0	–	1	0	1.00

Abbreviations: CSF, cerebrospinal fluid; ICU, intensive care unit.
Note: *p*-Values provide summary comparisons between primary resection and reoperation within each approach.

Discussion

In this single-institution retrospective review, we demonstrated that reoperation for craniopharyngioma recurrence is comparable to primary resection in terms of EOR, visual outcomes, complications, tumor recurrence, and overall survival. These results were achieved in light of (1) individualized surgical approaches tailored to preoperative imaging

Table 6 Follow-up therapies, recurrence, and survival

Variable	Primary resection ($n = 33$)	Endonasal reoperation ($n = 17$)	*p*-Value	Primary resection ($n = 17$)	Craniotomy reoperation ($n = 4$)	*p*-Value
Postoperative radiotherapy	15	5	0.365	7	0	0.255
Postoperative chemotherapy	3	0	0.542	1	1	0.352
Recurrence			0.200			0.100
Events	14	5		5	3	
Median time (months, from most recent resection)	39	80		Not reached	36.5	
Death			0.700			0.09
Events	1	1		2	2	
Median time (months, from most recent resection)	Not reached	Not reached		Not reached	50	
5-year survival OR (CI)	96.6% (90.1–100%)	90.9% (75.4–100%)		87.5% (72.7–100%)	37.5% (8.39–100%)	

Abbreviations: CI, confidence interval; OR, odds ratio.
Note: *p*-Values provide summary comparisons between primary resection and reoperation within each approach.

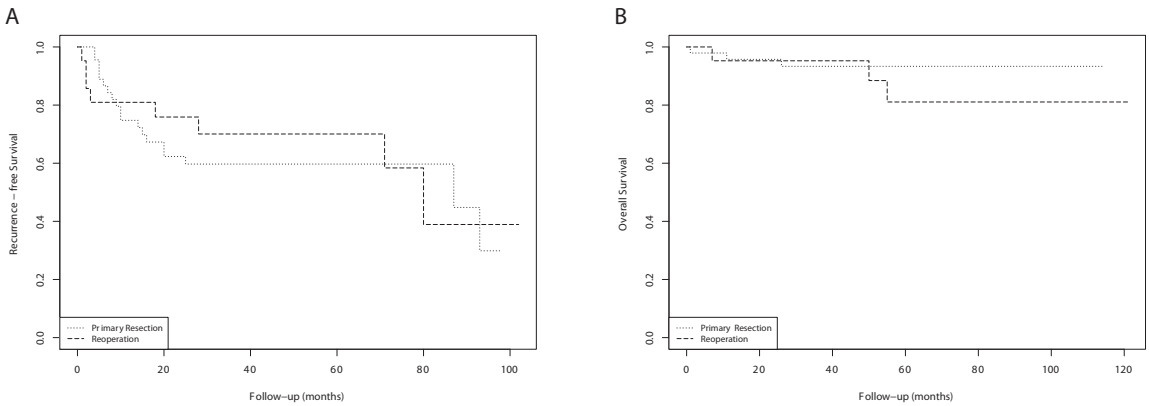

Fig. 1 Kaplan–Meier curves estimating recurrence-free survival (**A**) and overall survival (**B**), stratified by cohort (i.e., primary resection versus reoperation). No significant differences were observed in either recurrence-free or overall survival across cohorts ($p > 0.05$, log-rank test). Median survival was not reached in either cohort by the end of the 120-month follow-up period.

characteristics and (2) a goal of maximal safe resection as opposed to radical resection. While the endonasal approach played an important role in the removal of purely sellar and retrochiasmatic lesions, cranial approaches were safe and effective for patients with larger supra- and parasellar extensions. Furthermore, endonasal approaches were successfully implemented to control recurrent disease among patients who initially underwent craniotomy and developed postoperative scarring.[17] Coupled with adjuvant radiation therapy, excellent disease control can be achieved following reoperation even in the absence of an aggressive GTR.[20,21]

More recent reports have argued that endonasal resection can be implemented regardless of tumor size or location with superior safety profiles, and thus may be the preferred approach for initial craniopharyngioma resection.[22–24] However, experience varies across institutions and taking a "one size fits all" approach may lead to suboptimal approaches for an individual tumor.[25,26] In our series, rates of endocrine, neurologic, and medical complications after craniotomy were similar to that of endonasal resection, despite higher preoperative tumor volumes in craniotomy. Importantly, we did not find higher rates of diabetes insipidus after transsphenoidal surgery.[17] Similarly, rates of CSF leaks were low following endonasal approaches, suggesting that with advances in skull base reconstruction techniques this challenging complication can be limited.[27] A recent meta-analysis that pooled 3,079 cases provides further support for this notion by demonstrating no differences in endocrine outcomes and recurrence between the two approaches among patients with similar baseline characteristics, and we find

that this remains the case for recurrent craniopharyngiomas as well.[28] In terms of the open craniotomy approaches used to safely access the pathology in each patient, we also recommend a personalized strategy. In our series, the selected approach was a function of surgeon comfort/experience, cosmetic goals, and the critical neurovascular structures that were expected to be encountered prior to debulking, as no one approach has been found to be universally associated with better outcomes in cranipharyngioma.

Prior reports in the literature have demonstrated that reoperation for craniopharyngioma recurrence is associated with higher rates of neurologic complications and endocrine dysfunction.[29] As a result, some authors argue that radiotherapy may need to be a primary consideration in the management of recurrence.[30,31] One review of seven independent series, in particular, found that the mortality rate for reoperation was significantly, and universally, higher compared with primary resection.[32] Notably, we did not find significant differences in rates of 5-year and overall survival from the time of reoperation in our series compared with patients who underwent primary resection. Furthermore, in terms of absolute numbers, our 5-year survival rate of 81.1% after reoperation is in the higher range of the 54 to 96% reported in the literature after primary resection.[33]

In our series, patients who underwent reoperation had lower tumor volumes at baseline and were more likely to be asymptomatic which may have skewed outcomes. However, this discrepancy may be generalizable to the population of patients presenting with recurrence at large, as they are more likely to undergo surveillance imaging and radiotherapy prior to reoperation. This notion is further supported by the significantly higher proportion of asymptomatic patients in our reoperation cohort. Taken together, our data argue that reoperation for recurrence is an acceptable method of local tumor control provided that care is taken to keep surrounding structures intact and radiotherapy is offered if residual tumor persists postoperatively.

The variability in outcomes reported in the literature subsequent to reoperation may be in part due to underlying differences in goals of surgery between studies. While radical resection traditionally offered favorable outcomes, this strategy may be associated with excess mortality when implemented in reoperation.[34] In this series, GTR was only pursued and achieved in a minority of cases whereas STR $\pm$ adjuvant radiotherapy comprised the majority. In primary resection, this strategy has been previously associated with a more favorable progression-free survival outcome than GTR alone (82 vs. 29% at 10 years).[35] Recent studies further dispute the benefit of radical resection in terms of recurrence and mortality.[10,36] One study of 122 patients, in particular, demonstrated higher rates of neuroendocrine complications after GTR without any improvements in recurrence or survival compared with conservative surgery followed by radiation.[37] In terms of neurological morbidity, a systematic review of over 100 studies found that STR did not lead to new postoperative neurological impairment, whereas GTR carried several-fold increases in the risk of panhypopituitarism and diabetes insipidus. A separate systematic review similarly reported a substantially increased risk of endocrine morbidity in patients who underwent GTR.[38] It is important to note, however, that maximal safe resection does not necessarily rule out GTR, as the term implies that any tumor that can be safely removed should be removed.

Finally, we maintain that the treatment modalities offered in the setting of recurrence should be individualized to each patient and based on a combination of their stated goals, as well as a thorough evaluation of the strengths and weaknesses of each therapy. At our institution, we implemented a multidisciplinary conference consisting of board-certified (pediatric) neurosurgeons, neurooncologists, neuroradiologists, and radiation oncologists to determine the safest and most efficacious strategy for each patient. For instance, in the present series, only 38% of patients who underwent reoperation had previously received radiotherapy, signifying that there is no "default" treatment modality on recurrence. Indeed, especially among younger patients who are more susceptible to the deleterious long-term effects of radiotherapy,[39–41] surgery was frequently offered as the only therapy to manage recurrence when the lesions were associated with a new neurological deficit, easily accessible, large and cystic, and discernable tissue planes were present on preoperative imaging.

Limitations

Our conclusion is limited by the retrospective nature of this study and inability to randomize patients to a given approach or management algorithm. The cases in this study were also performed by different surgeons which may add an extra element of confounding secondary to surgeon experience and preference. In terms of outcomes, only 53 patients had comprehensive postoperative visual field examinations, so our visual outcomes may not be representative of our entire cohort. Our conclusion regarding the efficacy of radiotherapy in preventing recurrence and mortality is somewhat limited by the variability in modalities (i.e., external beam radiation vs. stereotactic radiosurgery). Furthermore, because our institution is a tertiary-level referral center serving a large geographic region, our conclusion may also be limited by attrition in patients who opted to receive adjuvant therapy at local facilities. Such patients were retained to bolster the study's external validity and statistical power, using public records and interoperable electronic medical record queries wherever possible. Future investigations with larger cohorts may allow for separation and more precise comparisons of the varied approaches implemented in this study.

Conclusion

In our retrospective series, we demonstrated that repeat, maximal safe resection for craniopharyngioma recurrence is efficacious in providing local tumor control without increased neuroendocrine morbidity compared with primary resection. The surgical approach should be tailored to each patient's surgical history and imaging characteristics.

Funding
None.

Conflict of Interest
None declared.

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