Turk Neurosurg 34(2):331-342, 2024

Original Investigation

DOI: 10.5137/1019-5149.JTN.46067-23.1

Received: 11.12.2023
Accepted: 15.01.2024

Published Online: 13.02.2024

Effect of Resection and Surgical Experience on Survival in Patients with Craniopharyngiomas: Endoscopic Transsphenoidal Surgery in Series of 31 Cases

Buruc ERKAN[1,2], Ozan BARUT[1], Ebubekir AKPINAR[1], Mehmet Sait CIL[1], Suat DEMIR[1], Yusuf KILIC[1], Osman TANRIVERDI[1,2], Esra Suheda HATIPOGLU[2,3], Omur GUNALDI[1,2]

[1]University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Neurosurgery Clinic, Istanbul, Türkiye
[2]University of Health Sciences Pituitary Diseases Practice and Research Center (PDPRC), Istanbul, Türkiye
[3]University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Endocrinology and Metabolism Clinic, Istanbul, Türkiye

Corresponding author: Buruc ERKAN ✉ burucerkan@hotmail.com

ABSTRACT

AIM: To share the surgical outcomes of 31 patients who underwent endoscopic endonasal transsphenoidal surgery (EETS) at a single center.

MATERIAL and METHODS: This retrospective analysis of 31 craniopharyngioma cases (2013–2022) with a minimum 6-month follow-up included demographic data, preoperative findings, postoperative resection volumes, recurrence rates, pathological diagnoses, and complications.

RESULTS: Herein, 34 EETS surgeries were performed on 31 patients (12 males, 19 females). The presenting symptoms included visual loss (58%), hypopituitarism (54.8%), and diabetes insipidus (25.8%). Gross total resection was achieved in 87% of the patients, with 64.5% total and 22.5% near-total resection. Total resection prevented recurrences, contrasting with 75% recurrence in the subtotal resection patients (p=0.000). The primary patients showed 73.1% total resection, while only 20% of the recurrent patients achieved it (p=0.049). When comparing the first 16 cases with the last 15 cases in terms of surgical experience, the rates of resection (p=0.040) and recurrence-free survival (p=0.020) in the last 15 cases were statistically significant. Patients with preoperative visual loss demonstrated 94.4% improvement or stability postoperatively. Postoperative complications included hypopituitarism (71.4%), permanent diabetes insipidus (60.8%), worsening vision (6.5%), cerebrospinal fluid leakage (9.7%), meningitis (6.5%), and a 3.2% perioperative mortality rate.

CONCLUSION: This study underscores the role of surgical resection in craniopharyngiomas, emphasizing the impact of surgical experience on recurrence-free survival. Primary surgery, with minimal complications and maximal resection, is crucial in managing recurrence challenges. Endoscopic endonasal transsphenoidal surgery, particularly in experienced centers, offers advantages such as panoramic vision and access to the third ventricle base, facilitating total and near-total resection and extending recurrence-free survival.

KEYWORDS: Craniopharyngioma, Endonasal, Extended endoscopic approach, Recurrence, Third ventricle invasion

ABBREVIATIONS: CSF: Cerebrospinal fluid, **EETS:** Endoscopic endonasal transsphenoidal surgery, **DI:** Diabetes insipidus, **MRI:** Magnetic resonance imaging, **MT:** Microscopic transcranial

Buruc ERKAN : 0000-0001-8586-0613
Ozan BARUT : 0000-0001-6572-9589
Ebubekir AKPINAR : 0000-0002-4069-0021
Mehmet Sait CIL : 0009-0008-3507-2289
Suat DEMIR : 0000-0001-8344-4210
Yusuf KILIC : 0000-0001-5329-7117
Osman TANRIVERDI : 0000-0002-4846-4213
Esra Suheda HATIPOGLU : 0000-0001-8361-8866
Omur GUNALDI : 0000-0001-5071-1319

INTRODUCTION

Craniopharyngiomas, despite their benign histology, are locally invasive tumors that extend into the lateral or third ventricle, invade the infundibulum or hypothalamus, and have a close relationship with cerebral arteries and the optic chiasm. This proximity results in serious complications such as hypopituitarism, visual impairment, obesity, and cognitive disorders, ultimately affecting daily life activities (34).

Treatment options for craniopharyngiomas include surgical resection, adjuvant radiotherapy, and medical approaches, with surgical resection being the primary method (1,3,31,35). The primary goal in craniopharyngioma surgery is to achieve gross total resection, which determines tumor control and survival, aiming to prevent recurrence (1,3,9,12,17,22,29,31,35). Despite technological advancements, the choice of the surgical treatment method for achieving tumor control remains controversial (12,29). In this study, the clinical profiles, radiological classifications, resection amounts, complication rates, and long-term follow-up results of this series of 31 craniopharyngioma patients treated with the endoscopic endonasal transsphenoidal (EETS) approach is discussed, aiming to contribute to the literature by highlighting the relationship between recurrence and achieving total and near-total resection.

MATERIAL and METHODS

Patient Population

The study was conducted retrospectively following the principles of the Helsinki Declaration after obtaining approval from our local Ethics Committee (Approval No: KAEK/2022.06.191). Data from 33 patients diagnosed with craniopharyngioma and operated on using the EETS method between 2013 and 2022, with a minimum follow-up of 6 months, were retrospectively evaluated. Two patients who did not continue the follow-up after surgery were excluded from the study.

Endocrinological and Neuroophthalmological Assessment

All of the patients included in the study were evaluated from an endocrinological perspective by expert endocrinologists. Neuroophthalmological evaluation was performed by a single neuroophthalmologist, assessing visual field, visual acuity, and optical coherence tomography for all cases. All of the patients were followed-up in the early postoperative period, at 1, 3, and 6 months, and subsequently at 6-month intervals, both endocrinologically and neuroophthalmologically.

Neuroradiological Evaluation

For the neuroradiological assessment, all of the patients underwent preoperative evaluation and postoperative follow-ups with 3.0 and 1.5 Tesla magnetic resonance imaging (MRI). In the MRI, contrast-free T1-weighted, T2-weighted, and contrast-enhanced T1-weighted images were obtained in the sagittal and coronal planes.

According to the preoperative MRI, all of the patients were classified based on the tumor's location (sellar, suprasellar, sellar-suprasellar), its relationship with the third ventricle (no relationship, compressing the third ventricle wall, invading the third ventricle), and its consistency (cystic, solid, cystic-solid).

After the operation, tumor resection rates were determined by comparing the intraoperative recorded images with the preoperative MRIs and postoperative MRIs obtained within the first 48 h. Accordingly, total resection included patients in whom all solid, cystic, and capsular parts of the tumor were completely excised (Figure 1, 2); near-total resection involved patients in whom both solid and cystic portions of the tumor were completely excised, but invasive portions of the capsule could not be excised (Figure 3); subtotal resection classified patients in whom the solid or cystic portion could not be completely excised along with the tumor capsule. Patients undergoing total and near-total resection, where both solid and cystic portions were completely excised, and either the entire capsule was excised or the invasive portions were left, were considered to have undergone gross total resection.

The recurrence status after gross total resections was defined as the formation of new tumors or an increase in the volume of residual tumors. Recurrence status was determined by comparing the MRIs obtained in the postoperative period at 3, 6 months, and subsequent 6-month intervals with the MRI obtained in the first 48 h postoperatively. Recurrences within 6 months were considered early recurrences, and those occurring after 6 months were considered late recurrences.

Surgical Procedure

The surgical procedure involved pure EETS surgery guided by neuronavigation (Medtronic StealthStation S7 and S8, Minneapolis, Minnesota, USA) and was performed by a single surgical team for all of the patients. Classical EETS surgical procedures, as detailed in previous studies, were implemented (10,11,16). After debulking the cystic and solid components within the tumor, the tumor capsule was dissected and separated from the optic nerves, chiasm, and vascular system. Preservation of the pituitary stalk was attempted in our surgical procedure. A multi-layer closure of the skull base defect was performed using subcutaneous fat tissue, fascia lata, fibrin tissue adhesive, and a pedicled nasoseptal flap. After closing the defect, an intrasphenoidal balloon tamponade was used for 3–5 days to support the layers. All of the patients were followed-up postoperatively with either lumbar drainage or an external ventricular drainage system.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics for Windows 24.0 (IBM Corp., Armonk, NY, USA). The normal distribution of numerical data was assessed with the Kolmogorov–Smirnov test. Descriptive statistics for numerical data were expressed as the mean and standard deviation, while the categorical variables were presented as numbers and percentages. The comparison of categorical variables between two or more groups was done using the chi-squared test or Fisher's exact test. Results were evaluated at a 95% confidence interval, and $p<0.05$ was considered statistically significant.

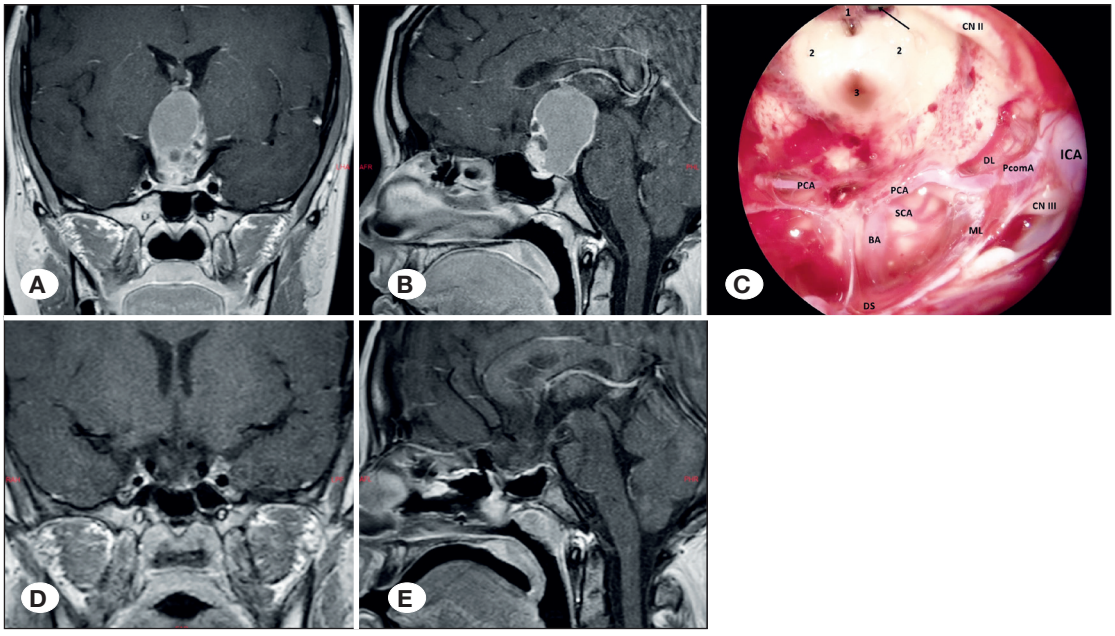

Figure 1: A 13-year-old female with Craniopharyngioma **A, B)** Preoperative T1-weighted contrast-enhanced coronal and sagittal magnetic resonance imaging (MRI) showing a well-defined solid-cystic mass with mild lobulated contours measuring 34 × 35 × 24 mm. The lesion originates from the posterior clinoid-clivus upper surface, extends posteriorly, and exerts pressure on the interthalamic region, demonstrating peripheral contrast enhancement. **C)** Intraoperative view after total resection of the mass using an endoscopic transnasal transsphenoidal approach. Key structures are labeled, including ICA (left internal carotid artery - supraclinoid), PcomA (left posterior communican artery), PCA (posterior cerebral artery), SCA (left superior cerebellar artery), BA (basilar artery), CN (cranial nerve), DS (diaphragma sella), ML (mesencephalic leaf), DL (diaphragmatic leaf), (1) choroid plexus, (2) thalamus, (3) cerebral aqueduct, and (arrow) left foramen of Monro. **D, E)** Postoperative second year, T1-weighted contrast-enhanced coronal and sagittal MRI, showing total removal of the mass without recurrence.

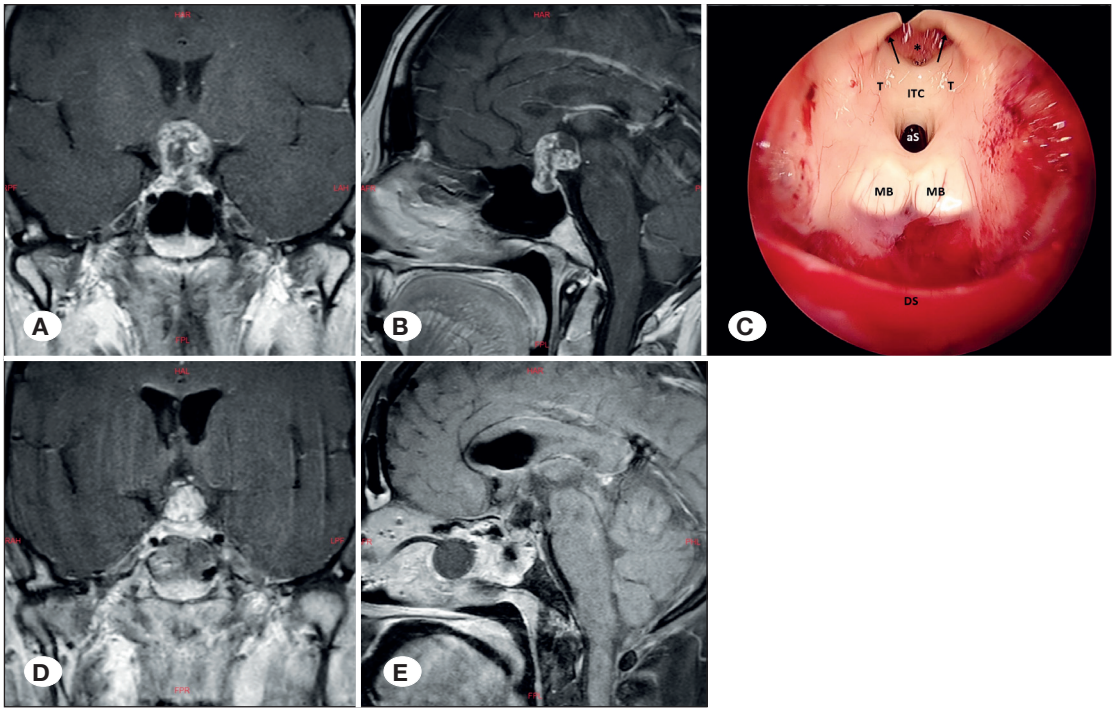

Figure 2: A 42-year-old female with Craniopharyngioma **A, B)** Preoperative T1-weighted contrast-enhanced coronal and sagittal MRI displaying a mass with heterogeneous contrast enhancement and areas of cystic degeneration measuring 23 × 21 × 22 mm in the suprasellar region. **C)** Intraoperative view after total resection of the mass using an endoscopic transnasal transsphenoidal approach. Key structures are labeled, including T (thalamus), ITC (interthalamic commissure), aS (aqueduct of Sylvius), MB (mammillary body), DS (diaphragma sella), * (choroid plexus), and (arrow) foramen of Monro. **D)** Postoperative twenty-four hours, T1-weighted contrast-enhanced coronal MRI showing total resection of the mass and the appearance of fat grafts used for reconstruction. **E)** Postoperative twenty-four hours, fat-suppressed sequence sagittal MRI, displaying total resection of the mass.

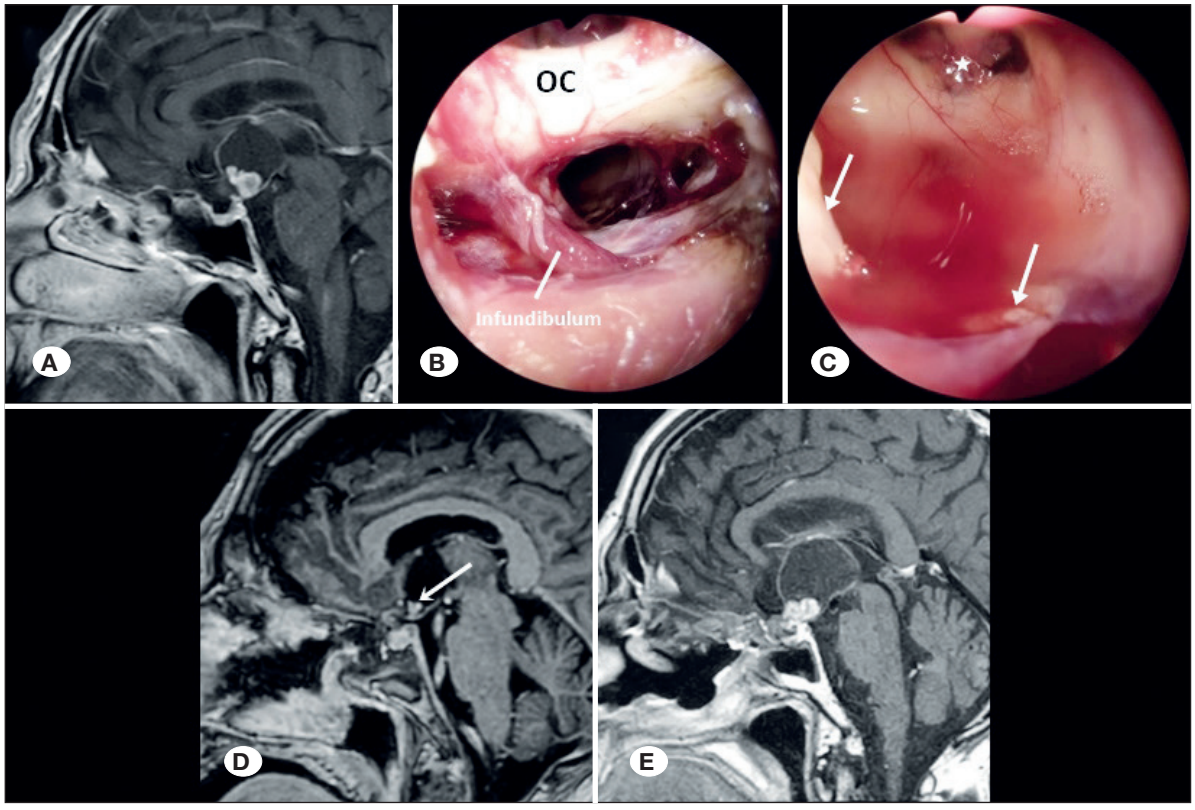

Figure 3: A 66-year-old male with Craniopharyngioma **A)** Preoperative T1-weighted contrast-enhanced sagittal MRI revealing a mass measuring 32 × 25 × 27 mm in the suprasellar region with a cystic component and an approximately 12 mm diffuse contrast-enhanced solid component. **B, C)** In intraoperative images obtained through endonasal transnasal transsphenoidal approach, a deviation of the pituitary stalk to the right was observed and preserved. The tumor capsule was visualized posterior-inferior to the optic chiasm. Following near-total resection, the walls of the third ventricle were intact, and both foramina of Monro were open. Residual capsule fragments adhered to surrounding structures are observed (arrows). OC, Optic Chiasm; Stlk, Pituitary Stalk; *, choroid plexus. **D)** Postoperative twenty-four hours, T1-weighted contrast-enhanced sagittal MRI showing residual tumor fragments (arrow) after near-total resection. **E)** Postoperative fourth month, T1-weighted contrast-enhanced sagittal MRI displaying a recurrent mass measuring 30 × 20 × 25 mm in the suprasellar region.

RESULTS

A total of 34 surgical procedures were conducted on 31 craniopharyngioma patients using the EETS method. The 31 patients, aged between 6 and 66 years (mean 36.8), were followed-up for an average of 34.6 months, with a minimum of 6 months and a maximum of 119 months. One patient underwent reoperation due to recurrence, and another patient underwent two reoperations. The time that elapsed between the reoperations was more than 12 months. Data regarding the patients' surgical histories are summarized in Table I.

The demographic characteristics as well as clinical and radiological findings of the patients are presented in Table II.

The most common presentations among the patients were headache (67.7%), visual loss (58%), and hypopituitarism (54.8%). Additionally, in one recurrent patient (3.2%), a rare symptom of left abducens paralysis was detected.

Among the 18 patients with preoperative visual loss, 17 (94.4%) either showed improvement or remained unchanged postoperatively. In one patient without preoperative visual

Table I: Surgical Histories of Patients

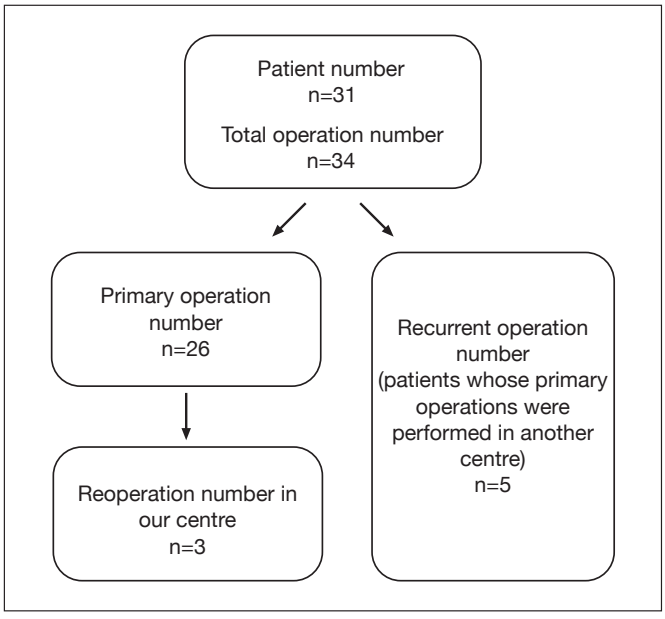

Table II: Demographic Information and Clinical, Radiological, and Pathological Findings of the Patients

Characteristics			n (%)	N
Mean age			36.8	31
Age, years	<18		6 (19.4)	31
	>18		25 (80.6)	
Sex	Male		12 (38.7)	31
	Female		19 (61.3)	
Clinical presentation	Headache		21 (67.7)	31
	Vision loss		18 (58.0)	
	Hypopituitarism		17 (54.8)	
	Diabetes insipidus		8 (25.8)	
	Hypogonadism		10 (32.2)	
	Menstrual irregularity		5 (16.1)	
Surgical history	Primary		26 (83.9)	31
	Recurrence		5 (16.1)	
Localization of tumour	Sellar		3 (9.7)	31
	Suprasellar		17 (54.8)	
	Sellar-suprasellar		11 (35.5)	
Relationship between tumour and the third ventricle	No relationship		8 (25.8)	31
	Compressing ventricle wall		5 (16.1)	
	Extension to ventricle and invasion		18 (58.0)	
Consistency of tumour	Solid		3 (9.6)	31
	Cystic		2 (6.5)	
	Solid-cystic		26 (83.9)	
Resection amount	Total (gross total)		20 (64.5)	31
	Near-total (gross total)		7 (22.5)	
	Subtotal		4 (13.0)	
Pathological subtyping	Adamantinomatous		24 (77.4)	31
	Papillary		7 (22.6)	
Recurrence status	No recurrence		22 (73.3)	30
	Late recurrence (>6 months)		3 (10.0)	
	Early recurrence (<6 months)		5 (16.6)	
Complications	New hypopituitarism		10 (71.4)	14
	New diabetes insipidus	Temporary	6 (26.1)	23
		Permanent	14 (60.8)	
	Vision loss		2 (6.5)	31
	CSF leak		3 (9.7)	
	Meningitis		2 (6.5)	
	Death	<1 month	1 (3.2)	
		>12 months	3 (9.7)	

loss, temporary visual loss started in the third month postoperatively, thought to be related to optic nerve edema and resolved with a short course of steroid treatment. In one patient with a tumor involving the third ventricle and preoperative visual loss, a slight deterioration in vision was observed in the postoperative period. Regarding complications, two patients had postoperative early cerebrospinal fluid (CSF) leakage, which was managed with surgical repair and simultaneous lumbar drainage. In the current series, four patients had a fatal course during an average follow-up period of 34.6 months. One patient experienced acute pancreatitis-related mortality in the perioperative period (<1 month). Two patients had complications related to the tumor, and one patient had long-term mortality due to respiratory causes after 12 months of follow-up (Table II).

The classifications of the tumor, surgical history, pathological subtypes, rates of newly developed diabetes insipidus (DI) and hypopituitarism, as well as the extent of resection and recurrence rates, were compared based on the preoperative MRI findings and are presented in Table III.

When comparing the resection status with recurrence, it was observed that the recurrence rate decreased from subtotal resection to total resection, and the progression-free period increased. It was found that the absence of recurrence in patients undergoing total resection was statistically significantly higher than in those undergoing near-total and subtotal resection. The incidence of late recurrence in patients undergoing near-total resection was statistically significantly higher than in those undergoing total and subtotal resection. In the patients who underwent subtotal resection, the incidence of early recurrence was statistically significantly higher than in those who underwent total and near-total resection (p=0.000) (Table III).

In the 26 (83.9%) primary patients, gross total resection was achieved in 92.3% (73.1% total resection + 19.2% near-total), while in the 5 (16.1%) recurrent patients, gross total resection decreased to 60% (20% total resection + 40% near-total), and this was statistically significant (p=0.049) (Table III).

When comparing the relationship of the tumor with the third ventricle with resection and recurrence, tumors without a

Table III: Comparisons of Pre- and Postoperative Findings Regarding Resection Amount and Recurrence Status

		Resection amount (N=31)				Recurrence status (N=30)			
		Total (n=20)	Near-total (n=7)	Subtotal (n=4)	p-value	None (n=22)	Late (n=3)	Early (n=5)	p-value
Localization of tumour	Sellar	2 (66.7)	0 (0.0)	1 (33.3)		2 (66.7)	1 (33.3)	0 (0.0)	
	Suprasellar	10 (58.8)	5 (29.4)	2 (11.8)	0.656	12 (75.0)	1 (6.3)	3 (18.8)	0.654
	Sellar-suprasellar	8 (72.7)	2 (18.2)	1 (9.1)		8 (72.7)	1 (9.1)	2 (18.2)	
Relationship between tumour and the third ventricle	No relationship	6 (75.0)	1 (12.5)	1 (12.5)		7 (87.5)	1 (12.5)	0 (0.0)	
	Compressing ventricle wall	4 (80.0)	1 (20.0)	0 (0.0)	0.739	4 (80.0)	0 (0.0)	1 (20.0)	0.580
	Invading ventricle	10 (55.6)	5 (27.8)	3 (16.7)		11 (64.7)	2 (11.8)	4 (23.5)	
Consistency of tumour	Solid	1 (33.3)	1 (33.3)	1 (33.3)		1 (33.3)	1 (33.3)	1 (33.3)	
	Cystic	1 (50.0)	1 (50.0)	0 (0.0)	0.588	1 (100.0)	0 (0.0)	0 (0.0)	0.499
	Solid-cystic	18 (69.2)	5 (19.2)	3 (11.5)		20 (76.9)	2 (7.7)	4 (15.4)	
Patient's surgical history	Primary	19 (73.1)	5 (19.2)	2 (7.7)		20 (80.0)	2 (8.0)	3 (12.0)	
	Recurrence	1 (20.0)	2 (40.0)	2 (40.0)	**0.049***	2 (40.0)	1 (20.0)	2 (40.0)	0.176
Surgical team's experience	First 16 cases	8 (50.0)	4 (25.0)	4 (25.0)		8 (50.0)	3 (18.75)	5 (31.25)	
	Last 15 cases	12 (80.0)	3 (20.0)	0 (0.0)	**0.040***	14 (100.0)	0 (0.0)	0 (0.0)	**0.020***
Pathological subtyping	Adamantinomatous	17 (70.8)	3 (12.5)	4 (16.7)		17 (73.9)	3 (13.0)	3 (13.0)	
	Papillary	3 (42.9)	4 (57.1)	0 (0.0)	**0.037***	5 (71.4)	0 (0.0)	2 (28.6)	0.429
Resection amount	Total					20 (100.0)	0 (0.0)	0 (0.0)	
	Near-total					2 (33.3)	2 (33.3)	2 (33.3)	**0.000***
	Subtotal					0 (0.0)	1 (25.0)	3 (75.0)	

**<0.05 was considered significant.*

relationship with the third ventricle showed higher resection (p=0.739) and fewer recurrence rates compared to tumors compressing the third ventricle wall and invading the third ventricle (p=0.580). However, no statistically significant difference was observed (Table III).

The first 16 patients (1st group) and the last 15 patients (2nd group) of this craniopharyngioma surgical series were evaluated in terms of surgical experience, resection, and recurrence. In the 2nd group, it was found that the rate of total resection was statistically significantly higher than that of near-total and subtotal resection (p=0.040), and the rates of recurrence-free survival were statistically significantly different than the rates of late and early recurrence (p=0.020) (Table III).

Twenty-four patients (77.4%) were reported as having adamantinomatous type craniopharyngioma, and seven (22.6%) had papillary type craniopharyngioma, with significantly higher resection observed in the adamantinomatous type (p=0.037) (Table III).

DISCUSSION

Surgical methods for craniopharyngiomas encompass EETS surgery, microscopic transcranial (MT) surgery, endoscopic intraventricular surgery, and combined EETS with MT surgeries. EETS surgery has gained prominence in recent times, exhibiting increased rates of gross total resection and decreased complication rates compared to MT surgery. EETS surgery provides direct access to the pituitary stalk, infundibulum, hypothalamus, and the base of the third ventricle, offering advantages with its panoramic view, which has led to its more predominant use compared to MT surgery (2,3,12,14,22,30,35). Studies have suggested that the broad visualization provided by the endoscopic perspective offers extensive surgical control over the corridor extending from the anterior skull base to the base of the third ventricle. In this clinical series, it was our belief that surgical experience, radical resection, recurrence-free follow-up, and reasonable clinical outcomes demonstrated the effectiveness of EETS surgery.

Resection Rates and Impact on Recurrence

The gross total resection rates in EETS surgery series have been reported to range from 28.5% to 95.5% (4,5,7–9,12,15,17,18,22,23,27,28,33,40) (Table IV). Recurrence, a crucial factor determining survival, has been associated with gross total resection in EETS series. In these series, the recurrence rates ranged from 0% to 25% in cases of gross total resection, but when subtotal resection was performed, this rate significantly increased, ranging from 25% to 100% (9,22,27,28,33,36). In the current study, while recurrence was observed in 73.3% of the patients, early recurrence occurred in 16.6% within the first 6 months, and late recurrence occurred in 10% after the 6th month. Independent of volumetric resection, gross total resection was distinguished based on the resection of invasive capsule portions of the tumor, categorizing it as total and near-total resection. The gross total resection rate was 87.5%, with 62.5% classified as total resection and 25% as near-total. This differentiation allowed us to observe that patients with total resection did not experience recurrence, while many patients with near-total resection showed late recurrence.

Adjuvant radiotherapy is recommended in studies for cases with subtotal resection following EETS surgery (25,41). There are also publications reporting similar therapeutic outcomes in patients who underwent gross total resection and those who underwent subtotal resection with the addition of adjuvant radiotherapy (32,37). However, radiation therapy for craniopharyngiomas includes important morbidities associated with surgical resection, such as hypothalamic-pituitary dysfunction, and radiation-specific complications such as cognitive impairment, memory loss, optic neuropathy, vascular damage, radiation necrosis, and secondary neoplasms. After radiotherapy, more than two-thirds of children develop growth hormone deficiency or hypothyroidism. Therefore, especially in children under the age of 4 (including subtotal resection), it is preferable to delay radiotherapy until evidence of recurrence or tumor progression, considering the significantly increased cognitive risks of radiotherapy (20). In the present study, although tumor control was achieved in all of the patients with total resection and in more than half of the patients with near-total resection, tumor control could not be achieved in 3 of the 4 patients with subtotal resection despite the administration of adjuvant radiotherapy.

Surgical Experience

Ceylan et al. emphasized that surgical experience is a significant factor influencing resection rates. In their series of 84 patients, they reported a gross total resection rate of 48.5% in the first 33 patients and 86.3% in the subsequent 51 patients, highlighting surgical experience as a positive predictive factor for resection (12). In the current craniopharyngioma series, when comparing the first 16 patients with the last 15 patients, it was observed that with increasing surgical experience, the gross total resection rate increased from 75% (with a total resection rate of 50% in these patients) to 100% (with a total resection rate of 80% in these patients).

Craniopharyngiomas present greater challenges for tumor control in recurrent patients compared to primary patients, regardless of the surgical method employed (EETS or MTK). Adhesions secondary to previous surgery in recurrent patients make tumor control more difficult, highlighting the crucial role of achieving gross total resection in the initial surgery (13). In studies comparing primary and recurrent patients, the gross total resection rates ranged from 66% to 83.3% for primary patients and 27.8% to 62.1% for recurrent patients. These results indicate that achieving gross total resection is more feasible in the initial surgery for primary patients (9,12,22). In the present study, gross total resection was achieved in 92.3% of the primary patients (73.1% total resection + 19.2% near-total resection) and decreased to 60% in the recurrent patients (20% total resection + 40% near-total resection) (p=0.049). We also acknowledge the increased challenges of resection in recurrent patients due to invasion into surrounding tissues and the formation of adhesions. Therefore, we emphasize the importance of achieving gross total resection, or even total resection, if possible, in the initial surgery for recurrent patients.

Table IV: Previous Endoscopic Endonasal Surgery Series for Craniopharyngioma and This Study

Reference	Approach	Number of Patients	Follow-up (mo)	GTR 100% (%)	NTR >95% (%)	STR >80% (%)	PR <80% (%)	Adjuvant Therapy (%)	Recurrence (%)	Complication (%)
Gardner et al., 2008 (18)	EETS	16	34	50.0	18.75	6.25	25.0	31.25	25.0	CSF leak (58) New Permanent DI (8) New HP (18) Vascular injuries (6.25) Perioperative Mortality (0)
Jane et al., 2010 (23)	EETS	12	13	41.67	41.67	16.67	-	8.3	The follow-up duration is short	New DI (44) New HP (67) Meningitis (8.3) Hyponatremia (16.6)
Campbell et al., 2010 (7)	EETS	14	-	28.5	35.7	35.7	-	35.7	7.0	CSF leak (35.7) New DI (7) New HP (7) Vision worsening (7) Meningitis (14.2) Perioperative Mortality (7)
Leng et al., 2012 (28)	EETS	24	35	66.6	8.3	25.0	-	29.1	25.0	CSF leak (3.8) New DI (42) New HP (38) Meningitis (4) Perioperative Mortality (0)
Koutourousiou et al., 2013 (27)	EETS	64	38	37.5	34.4	21.9	6.2	15.6	34.4	CSF leak (23.4) New HP (58.3) New DI (46.7) Meningitis (7.8) Hydrocephalus (12.7) Temporary cranial nerve palsy (7.8) Perioperative Mortality (0)
Bosnjak et al., 2013 (5)	EETS	8	27	75.0	12.5	12.5	-	-	-	CSF leak (25) New HP (62.5) New DI (62.5) Vision worsening (12.5) Meningitis (25)
Cavallo et al., 2014 (9)	EETS	103	48	68.9	-	25.2	5.8	15.5	22.3	CSF leak (14.6) New DI (48) New HP (46) Meningitis (1) Hydrocephalus (1.9) Subdural hematoma (1.9) Vascular Injuries (1.9) Perioperative Mortality (1.9)
Yadav et al., 2015 (40)	EETS	44	19	59.0	-	25.0	16.0	22.7	13.6	CSF leak (9) New DI (14) New HP (9) Meningitis (2.2) Perioperative Mortality (2.2)

Table IV: Cont.

Fomichev et al., 2016 (17)	EETS	136	42	72.0	-	-	%10-20	52.0	20.0	CSF leak (8.8) New HP (42.6) New DI (42) Meningitis (16) Vision worsening (11) Mental disorder (12.5) Temporary neurological deficits (3.7) Perioperative Mortality (5.8)
Bal et al., 2016 (4)	EETS	25	56	80.0	-	20.0	-	-	-	CSF leak (12) New DI (50) New HP (80) Meningitis (0) Perioperative Mortality (0)
Park et al., 2017 (33)	EETS	116	35	46.0	39.0	15.0	-	15.5	15.5	CSF leak (11,2) New DI (25.5) New HP (47.4) Meningitis (6) Hydrocephalus (4) Hyponatremia (5) Carotid injury (1) Stroke (1) Perioperative Mortality (0)
Dho et al., 2018 (15)	EETS	68	30	91.1	-	8.9	-	1.5	2.9	CSF leak (2.9) New DI (52.4) New HP (47.1) Meningitis (17.6) Perioperative Mortality (0)
Ceylan et al., 2021 (12)	EETS	84	31	71.4	-	28.6	-	-	42.0	CSF leak (8.3) New DI (29.7) New HP (14.2) Hydrocephalus (4.7) Vision worsening (1.2) Perioperative Mortality (6)
Iranmerh et al., 2021 (22)	EETS	29	25	62.0	24.1	6.9	6.9	15.3	15.3	CSF leak (13.8) Meningitis (6.9) New DI (50) New HP (34,6) Vision worsening (7.7) Perioperative Mortality (6.9)
Cao et al., 2022 (8)	EETS	22	22	95.5	4.5	-	-	4.5	9.0	CSF leak (4.5) New DI (13.6) New HP (54.5) Meningitis (0) Vision worsening (9.1) Perioperative Mortality (0)
Current Series	EETS	31	34	64.5	22.5	13.0	-	9.7	26.6	CSF leak (9.7) New Permanent DI (60.8) New HP (71.4) Meningitis (6.5) Vision worsening (6.5) Perioperative Mortality (3.2)

CSF: *Cerebrospinal fluid,* ***DI:*** *Diabetes insipidus,* ***EETS:*** *Endoscopic endonasal transsphenoidal surgery,* ***GTR:*** *Gross total resection,* ***HP:*** *Hypopituitarism,* ***NTR:*** *Near total resection,* ***PR:*** *Parsiyel removal,* ***STR:*** *Subtotal resection.*

Tumor localization, especially due to the infiltration of craniopharyngiomas into surrounding structures, can pose challenges during surgical intervention. This may lead to damage to neighboring structures and a high risk of morbidity/mortality after radical resection. In the current study, a total excision rate of 75% was observed in tumors without a relationship with the third ventricle, while in cases associated with the third ventricle, this rate was found to be lower at 60.8%. However, it was not statistically significant.

Craniopharyngiomas are histologically categorized as adamantinomatous and papillary subtypes. The adamantinomatous type, linked to a younger age and more cystic components than the papillary type, has a higher recurrence risk (6,24,39). The present study found no significant associations between the pathological subtypes and age, gender, preoperative radiological tumor classifications, or recurrence rates.

Craniopharyngiomas are frequently associated with visual impairment due to their common origin from the infundibulum, extension into the third ventricle, and compression of the optic chiasm (19,26,38). In the current series, one of the most prevalent findings was visual impairment in 18 patients (58%). Among these 18 patients with visual impairment, 12 (66.6%) exhibited extension into the third ventricle, establishing a close relationship between visual impairment and extension into the third ventricle, consistent with the literature. Fomichev et al. (17) reported a visual improvement rate of 52% in their series of 136 patients, presenting the lowest visual improvement rate in the literature, whereas other series reported rates ranging from 72% to 94% (4,9,22,27). In the present study, preoperative and postoperative visual field defects were evaluated by optical coherence tomography. Among patients with preoperative visual field defects, 94.4% showed either improvement or remained unchanged postoperatively. EETS surgery has been demonstrated to provide a better visual field compared to other surgical methods, resulting in fewer visual complications (30). In one patient without preoperative visual impairment, transient visual loss occurred at the postoperative 3rd month, which resolved with short-term steroid treatment. We hypothesize that this may be attributed to the inferior displacement of the optic chiasm following craniopharyngioma resection. Another patient with a tumor involving the third ventricle had a total resection, and no recurrence was observed during the 2-year follow-up. However, permanent worsening of visual acuity, with the right eye perceiving light and the left eye being non-functional, was noted in the postoperative period.

Endocrinopathies represent one of the most common clinical presentations of craniopharyngiomas, as reported in varying numbers in the literature (24). Due to the presence of hypothalamic, infundibular, and pituitary adhesions, the postoperative development of hypopituitarism and DI stands out as a major concern, although cases in the literature are limited (12,21). The incidence of new-onset hypopituitarism after EETS series ranges from 18% to 80%, with the largest series by Fomichev et al. (17) reporting a rate of 42.6%, and Cavallo et al. (9) reporting a rate of 46%. Detailed studies on hormone deficiency are limited (12,21,22). In the series herein, 54.8% of the patients had preoperative hypopituitarism, and there was no improvement in hypopituitarism symptoms postoperatively. Moreover, among the 14 patients without preoperative hypopituitarism, 71.4% developed new-onset hypopituitarism after EETS surgery.

Although DI is less frequent than other symptoms preoperatively, the development of new-onset DI postoperatively is a significant problem, especially closely related to the preservation of the infundibulum (21). Particularly in lesions with suprasellar extension and transinfundibular lesions where the infundibulum cannot be preserved, DI is more frequently observed (29). Different case series have reported incidences of new-onset DI ranging from 7% to 62% (5,7,9,12,15,17,18,21,33). In the present study, preoperative DI was present in 25.8% of patients, and among the 23 patients without preoperative DI, 60.8% developed new-onset permanent DI postoperatively. Additionally, postoperative transient DI, which is less discussed in the literature, occurred in 26.1% of the 23 patients.

CSF leakage is considered one of the most significant advantages of EETS surgery over other surgical approaches and is one of the most common and challenging complications post-EETS surgery. However, the use of pedicled nasoseptal flaps and multilayer grafts in EETS surgery significantly reduces the incidence of CSF leakage (2,14,22). The literature reports a CSF leakage incidence between 0% and 25%, with Fomichev et al. reporting 8.8% (17), and Cavallo et al. reporting 14.6% in their large series (9). In the present study, CSF leakage occurred in 9.7% of patients, and these patients required skull base repair and lumbar drainage following EETS surgery.

In various studies, perioperative mortality rates ranging from 0.0% to 6.9% have been reported within the first month, attributed to reasons such as bacterial meningitis, myocardial infarction, pneumonia, and injury to intracerebral arteries (9,15,17,22). In the study herein, however, perioperative mortality was observed in one patient (3.2%) due to the development of acute pancreatitis, which is a different cause compared to other series. Additionally, in the long-term follow-ups, mortality was observed in three patients (9.7%) after the first year.

CONCLUSION

The paramount determinant of recurrence-free survival in craniopharyngiomas, evident in both the existing literature and our study, underscores the significance of gross total resection. This study went further to reveal a notable discrepancy in recurrence rates even between near-total and total resection cases. Recognizing the complexities associated with recurrent surgeries, it becomes imperative to minimize complications and maximize resection during the initial surgery, leveraging available resources judiciously.

The inherent advantages of the natural anatomical corridor and expansive field of view afforded by the EETS approach prove instrumental in reaching the third ventricle without compromising normal neural tissue. This facilitates a radical surgical resection, particularly of the optic nerves. This study

underscores that, coupled with surgical expertise, the EETS approach offers the potential to extend recurrence-free survival periods while maintaining low complication rates.

AUTHORSHIP CONTRIBUTION

Study conception and design: BE, OB, EA
Data collection: MSC, SD
Analysis and interpretation of results: BE, YK
Draft manuscript preparation: BE, OB, MSC, SD
Critical revision of the article: OT, ESH, OG
All authors (BE, OB, EA, MSC, SD, YK, OT, ESH, OG) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Akinduro OO, Izzo A, Lu VM, Ricciardi L, Trifiletti D, Peterson JL, Bernet V, Donaldson A, Eggenberger E, Olomu O, Reimer R, Wharen R, Quinones-Hinojosa A, Chaichana KL: Endocrine and visual outcomes following gross total resection and subtotal resection of adult craniopharyngioma: Systematic review and meta-analysis. World Neurosurg 127:e656-e668, 2019
2. Akutsu H: Selection of surgical approach for craniopharyngiomas: Endoscopic endonasal surgery or transcranial surgery. Jpn J Neurosurg 27:456-462, 2018
3. Almeida JP, Workewych A, Takami H, Velasquez C, Oswari S, Asha M, Bernardo A, Gentili F: Surgical anatomy applied to the resection of craniopharyngiomas: Anatomic compartments and surgical classifications. World Neurosurg 142:611-625, 2020
4. Bal E, Oge K, Berker M: Endoscopic endonasal transsphenoidal surgery, a reliable method for treating primary and recurrent/residual craniopharyngiomas: Nine years of experience. World Neurosurgery 94:375-385, 2016
5. Bosnjak R, Benedicic M, Vittori A: Early outcome in endoscopic extended endonasal approach for removal of supradiaphragmatic craniopharyngiomas: A case series and a comprehensive review. Radiol Oncol 47:266, 2013
6. Bunin GR, Surawicz TS, Witman PA, Preston-Martin S, Davis F, Bruner JM: The descriptive epidemiology of craniopharyngioma. J Neurosurgery 89:547-551, 1998
7. Campbell PG, McGettigan B, Luginbuhl A, Yadla S, Rosen M, Evans JJ: Endocrinological and ophthalmological consequences of an initial endonasal endoscopic approach for resection of craniopharyngiomas. Neurosurg Focus 28:E8, 2010
8. Cao L, Wu W, Kang J, Cai K, Li C, Liu C, Zhu H, Gen S, Zhang Y, Gui S: Feasibility of endoscopic endonasal resection of intrinsic third ventricular craniopharyngioma in adults. Neurosurg Rev 45:1-13, 2022
9. Cavallo LM, Frank G, Cappabianca P, Solari D, Mazzatenta D, Villa A, Zoli M, D'Enza AI, Esposito F, Pasquini E: The endoscopic endonasal approach for the management of craniopharyngiomas: A series of 103 patients. J Neurosurg 121:100-113, 2014
10. Cavallo LM, Solari D, Esposito F, Cappabianca P: The endoscopic endonasal approach for the management of craniopharyngiomas involving the third ventricle. Neurosurg Rev 36:27-38, 2013
11. Ceylan S, Anik I, Koc K, Cabuk B: Extended endoscopic transsphenoidal approach infrachiasmatic corridor. Neurosurg Rev 38:137-147, 2015
12. Ceylan S, Caklili M, Emengen A, Yilmaz E, Anik Y, Selek A, Cizmecioglu F, Cabuk B, Anik I: An endoscopic endonasal approach to craniopharyngioma via the infrachiasmatic corridor: A single center experience of 84 patients. Acta Neurochir 163:2253-2268, 2021
13. Chamoun R, Couldwell WT: Transcortical–transforaminal microscopic approach for purely intraventricular craniopharyngioma. Neurosurg Focus 34:1-1, 2013
14. Cossu G, Jouanneau E, Cavallo LM, Elbabaa SK, Giammattei L, Starnoni D, Barges-Coll J, Cappabianca P, Benes V, Baskaya MK, Bruneau M, Meling T, Schaller K, Chacko AG, Youssef AS, Mazzatenta D, Ammirati M, Dufour H, Laws E, Berhouma M, Daniel RT, Messerer M: Surgical management of craniopharyngiomas in adult patients: A systematic review and consensus statement on behalf of the EANS skull base section. Acta Neurochir (Wien) 162:1159-1177, 2020
15. Dho YS, Kim YH, Se YB, Han DH, Kim JH, Park CK, Wang KC, Kim DG: Endoscopic endonasal approach for craniopharyngioma: The importance of the relationship between pituitary stalk and tumor. J Neurosurg 129:611-619, 2018
16. Erkan B, Barut O, Akbas A, Akpinar E, Akdeniz YS, Tanriverdi O, Gunaldi O: Results of endoscopic surgery in patients with pituitary adenomas: Association of tumor classification grades with resection, remission, and complication rates. J Korean Neurosurg Soc 64:608-618, 2021
17. Fomichev D, Kalinin P, Kutin M, Sharipov O: Extended transsphenoidal endoscopic endonasal surgery of suprasellar craniopharyngiomas.World Neurosurgery 94:181-187, 2016
18. Gardner PA, Kassam AB, Snyderman CH, Carrau RL, Mintz AH, Grahovac S, Stefko S: Outcomes following endoscopic, expanded endonasal resection of suprasellar craniopharyngiomas: A case series. J Neurosurg 109:6-16, 2008
19. Garrè ML, Cama A: Craniopharyngioma: Modern concepts in pathogenesis and treatment. Curr Opin Pediatr 19:471-479, 2007
20. Graffeo CS, Perry A, Link MJ, Daniels DJ: Pediatric craniopharyngiomas: A primer for the skull base surgeon. J Neurol Surg B Skull Base 79:65-80, 2018
21. Guo Y, Wang Y, Ni M, Zhang Y, Zhong L: Comparative evaluation of neuroendocrine dysfunction in children with craniopharyngiomas before and after mass effects are removed. J Pediatr Endocrinol Metabol 32(2):127-133, 2019
22. Iranmehr A, Esmaeilnia M, Afshari K, Sadrehosseini SM, Tabari A, Jouibari MF, Zeinalizadeh M: Surgical outcomes of endoscopic endonasal surgery in 29 patients with craniopharyngioma. J Neurol Surg B Skull Base 82:401-409, 2020

23. Jane JA Jr, Kiehna E, Payne SC, Early SV, Laws ER Jr: Early Outcomes of endoscopic transsphenoidal surgery for adult craniopharyngiomas. Neurosurg Focus 28q:E9, 2010
24. Jane JA Jr, Laws ER: Craniopharyngioma. Pituitary 9:323-326, 2006
25. Karavitaki N: Radiotherapy of other sellar lesions. Pituitary 12:23-29, 2009
26. Karavitaki N, Cudlip S, Adams CB, Wass JA: Craniopharyngiomas. Endocrine Rev 27:371-397, 2006
27. Koutourousiou M, Gardner PA, Fernandez-Miranda JC, Tyler-Kabara EC, Wang EW, Snyderman CH: Endoscopic endonasal surgery for craniopharyngiomas: Surgical outcome in 64 patients. J Neurosurg 119:1194-1207, 2013
28. Leng LZ, Greenfield JP, Souweidane MM, Anand VK, Schwartz TH: Endoscopic, endonasal resection of craniopharyngiomas: Analysis of outcome including extent of resection, cerebrospinal fluid leak, return to preoperative productivity, and body mass index. Neurosurgery 70:110-124, 2012
29. Mou J, Wang X, Huo G, Ruan L, Jin K, Tan S, Wang F, Hua H, Yang G: Endoscopic endonasal surgery for craniopharyngiomas: A series of 60 patients. World Neurosurg 124:e424-e430, 2019
30. Moussazadeh N, Prabhu V, Bander ED, Cusic RC, Tsiouris AJ, Anand VK, Schwartz TH: Endoscopic endonasal versus open transcranial resection of craniopharyngiomas: A case-matched single-institution analysis. Neurosurg Focus 41:E7, 2016
31. Omay SB, Chen YN, Almeida JP, Ruiz-Treviño AS, Boockvar JA, Stieg PE, Greenfield JP, Souweidane MM, Kacker A, Pisapia DJ, Anand VK, Schwartz TH: Do craniopharyngioma molecular signatures correlate with clinical characteristics? J Neurosurg 128:1473-1478, 2018
32. O'steen L, Indelicato DJ: Indelicato, advances in the management of craniopharyngioma. F1000Res 7:F1000, 2018
33. Park HR, Kshettry VR, Farrell CJ, Lee JM, Kim YH, Won TB, Han DH, Do H, Nyguist G, Rosen M, Kim DG, Evans JJ, Paek SH: Clinical outcome after extended endoscopic endonasal resection of craniopharyngiomas: Two-institution experience. World Neurosurg 103:465-474, 2017
34. Qi W, Gu F, Wu C: Growth hormone replacement therapy improves hypopituitarism-associated hypoxemia in a patient after craniopharyngioma surgery: A case report. Medicine 98: e14101, 2019
35. Radovanovic I, Dehdashti AR, Turel MK, Almeida JP, Godoy BL, Doglietto F, Vescan AD, Zadeh G, Gentili F: Expanded endonasal endoscopic surgery in suprasellar craniopharyngiomas: A retrospective analysis of 43 surgeries including recurrent cases. Oper Neurosurg (Hagerstown) 17:132-142, 2019
36. Tomita T, Bowman RM: Craniopharyngiomas in children: Surgical experience at Children's Memorial Hospital. Childs Nerv Syst 21:729-746, 2005
37. Wang G, Zhang X, Feng M, Guo F: Comparing survival outcomes of gross total resection and subtotal resection with radiotherapy for craniopharyngioma: A meta-analysis. J Surg Res 226:131-139, 2018
38. Weiner HL, Wisoff JH, Rosenberg ME, Kupersmith MJ, Cohen H, Zagzag D, Shiminski-Maher T, Flamm ES, Epstein FJ, Miller DC: Craniopharyngiomas: A clinicopathological analysis of factors predictive of recurrence and functional outcome. Neurosurgery 35:1001-1010; discussion 1010-1011, 1994
39. Wu J, Wu X, Yang YQ, Ding H, Yang L, Bao YY, Zhou L, Yang CX, Hong T: Association of histological subtype with risk of recurrence in craniopharyngioma patients: A systematic review and meta-analysis. Neurosurg Rev 45:139-150, 2022
40. Yadav Y, Nishtha Y, Vijay P, Shailendra R, Yatin K: Endoscopic endonasal trans-sphenoid management of craniopharyngiomas. Asian J Neurosurg 10:10-16, 2015
41. Yang I, Sughrue ME, Rutkowski MJ, Kaur R, Ivan ME, Aranda D, Barani IJ, Parsa AT: Craniopharyngioma: A comparison of tumor control with various treatment strategies. Neurosurg Focus 28(4):E5, 2010