

Craniopharyngiomas: Analysis of 68 Surgical Cases

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ABSTRACT

Objective: Although craniopharyngiomas are benign pathologies, they have surgical challenges due to their locations, infiltrations, and potential for neuroendocrine problems. We evaluated the surgical outcomes, complications, the neuroendocrine problems in patients who underwent total or subtotal resection, and to reveal the ideal treatment regimen. **Materials and Methods:** We retrospectively reviewed 68 patients who received pathologic results of craniopharyngioma between 1999 and 2019 in our neurosurgery clinic. The demographic characteristics, hormone levels, resection ratio (total/subtotal), residue and recurrence rate, and the complications after surgery were used in the analysis. **Results:** Twenty-six (38.2%) patients underwent total tumor removal, and 42 (61.8%) had subtotal removal. Fifteen (22%) patients had recurrence. Of the total tumor removal group, only one patient was determined as having recurrence. We detected hypothalamic–pituitary system deficiency in 15 patients with total removal and nine patients with subtotal removal. Of the 37 patients who had lesions smaller than 4 cm, only one died and 30 were in good health after surgery. Of the 31 patients who had lesions larger than 4 cm, five died and 15 were in poor or moderate health. **Conclusion:** Tumor size is one of the most important factors affecting surgical results. Subtotal tumor removal is associated with tumor recurrence and total removal with serious hypothalamic deficiency symptoms.

KEYWORDS: Craniopharyngioma, hypothalamic–pituitary system, partial resection, total resection

Submitted: 29-Apr-2020

Revised: 12-Jul-2020

Accepted: 03-Aug-2020

Published: ***

INTRODUCTION

Craniopharyngiomas are benign, epithelial neoplasms that are thought to arise from residual embryologic squamous epithelium of the craniopharyngeal canal. Craniopharyngiomas are classified as Grade I by the World Health Organization. Although they are benign tumors, total surgical removal is difficult due to infiltration to the surrounding tissues such as optic nerves, chiasm, the carotid and middle cerebral arteries, hypothalamus, and pituitary gland and the potential to create neuroendocrine problems.^[1,2] Although the tumors were thought to be cured completely after the total removal of craniopharyngiomas, it could cause serious morbidity correspondingly to the injury to hypothalamic–pituitary system. Therefore, it is still hotly debated as to whether total or subtotal resection is useful or detrimental.^[3,4]

Our aim in this study was to determine the long-term clinical course and pathologic changes in patients who

underwent surgical resection and accordingly to reveal the requirement of the ideal radical therapy.

MATERIALS AND METHODS

We retrospectively reviewed 68 patients who underwent surgery for sellar-suprasellar masses and had a pathologic result of craniopharyngioma between 1999 and 2019. The median follow-up period was 36 (range, 7–120) months. We performed cranial magnetic resonance imaging (MRI), pituitary MRI, and cranial computed tomography (CT) on all patients before the surgery. Tumor location, tumor calcification, optic nerve and chiasm compression, stalk compression,

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How to cite this article: Akçay E, Yılmaz H, Benek HB, Tabanlı A, Yurt A. Craniopharyngiomas: Analysis of 68 surgical cases. *Neurol Sci Neurophysiol* 2020;XX:XX-XX.

Access this article online

Quick Response Code:



Website: www.nsnjournal.org

DOI: 10.4103/NSN.NSN_56_20

and expansion to the third ventricle, lateral ventricle and interpeduncular cistern, and hydrocephalus were evaluated. The mass dimensions were measured, and it was confirmed whether the mass was cystic or solid. All the patients were examined for the visual field by an experienced ophthalmologist. Blood hormone levels were measured, and all patients were consulted by the endocrinology department for treatment regulation.

Electrolyte levels 24 h after surgery were monitored routinely. The tumor resection ration and potential intracranial complications were evaluated using cranial CT 24 h after the procedure. The hormone levels were checked in the 1st week, and the recommendations of the endocrinologist were performed. One to 3 months after the operation, visual acuity and visual field were examined. A gadolinium-enhanced cranial MRI was performed for residue or relapse 1–3 months postoperatively. Patients with no residue were followed up every 12 months.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as mean $\pm$ standard deviation in all tables. The paired-samples *t*-test and independent-samples *t*-test were run to determine if there were differences within-subjects and between-subjects. $P = 0.05$ was used to determine significance.

All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

RESULTS

Thirty-nine (57.3%) of the 68 patients were male and 29 (42.7%) were female. The mean age of the patients was 31.7 (range, 16–78) years [Table 1]. Regarding the presentation symptoms of the patients, 22 (32.3%) had headache, 21 (30.8%) had a vision defect, 16 (23.5%) had diabetes insipidus, five (7.3%) had anterior pituitary deficiency symptoms, and four patients (5.8%) had worsened consciousness and general condition.

During neurologic examinations, we detected visual field defects in 36 (52.9%) patients, papilledema in 22 (32.3%), and optic atrophy in 23 (33.8%) patients. There were endocrine disorders in 55 (80.8%) patients. Twenty-two (32.3%) patients had hypothyroidism, 17 (25%) were hypoadrenal, and clinical diabetes insipidus was apparent in 16 (23.5%) patients.

Table 1: The demographic data and distribution of patients according to the Glasgow Outcome Scale results at discharge

	<i>n</i> (%)
Sex	
Male	39 (57.3)
Female	29 (42.7)
GOS	
1	6 (8.8)
2	1 (1.5)
3	4 (5.9)
4	16 (23.5)
5	41 (60.3)

GOS: Glasgow Outcome Scale

Craniopharyngioma was localized retrochiasmatic in 32 (47%) cases, infra- and suprasellar in 19 (27.9%), prechiasmatic in 10 (14.7%), intraventricular in five (7.3%), and intrasellar in two (3%) patients. We detected calcification in forty cases in CT examinations. There was a cystic component in 38 cases, solid cystic component in 27 cases, and parenchymatous component in three cases. Twenty-eight patients had moderate-to-severe hydrocephalus.

Regarding admission Glasgow Coma Scores (GCSs), 64 (94.1%) patients had scores ranging between 14 and 15, two (2.9%) patients scored 9–13, and two (2.9%) patients scored 3–8 [Table 1].

The pterional approach was the most used surgical procedure (60 cases) [Figure 1]. Combined transcortical-pterional ($n = 3$) and transcallosal-pterional approaches ($n = 2$) were used for tumors involving the third ventricle, the transsphenoidal approaches ($n = 2$) were used for intrasellar tumors [Figure 2], and the suboccipital transmeatal approach was used for one case.

We achieved total removal in 26 patients (38.2%) and subtotal removal in 42 patients (61.8%). Total removal was performed in seven of 10 cases with tumor dimensions <2 cm, in 13 of 27 cases with tumor dimensions 2 cm–4 cm, in three of 20 cases with tumor dimensions 4 cm–6 cm, and in three of 11 cases with tumor dimensions larger than 6 cm. Subtotal removal was performed in three of 10 cases with tumor dimensions <2 cm, in 14 of 27 cases with tumor dimensions 2 cm–4 cm, in 17 of 20 cases with tumor dimensions 4 cm–6 cm, and in eight of 11 cases with tumor dimensions larger than 6 cm. Fifteen (22%) patients had recurrence. There was only one case of recurrence in the total removal group [Figure 3]. The recurrence rate was significantly higher in the subtotal tumor removal group ($t = 3.21$, $P < 0.05$) and who had no postoperative radiation ($t = 2.31$, $P < 0.050$). We

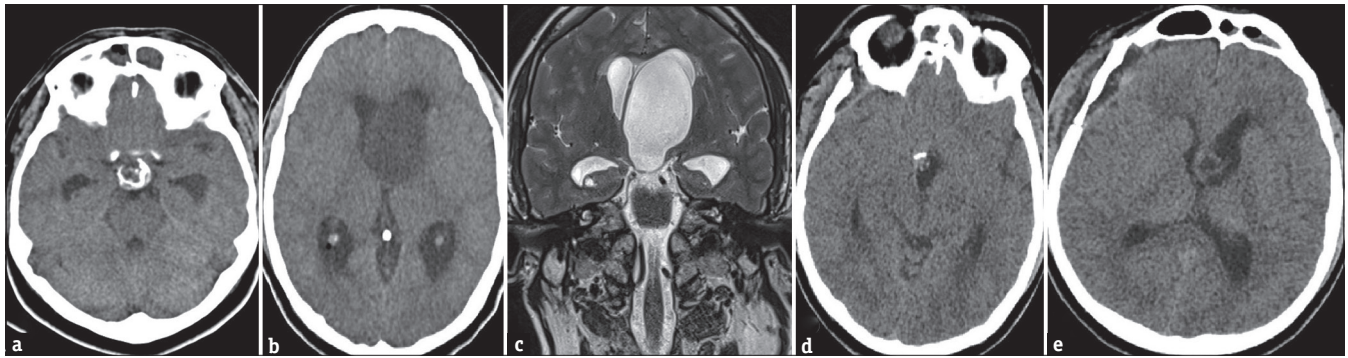


Figure 1: Preoperative axial computed tomography (a and b), coronal T2-weighted magnetic resonance imaging images (c), and postoperative axial computed tomography images (d and e) of a patient with total removal of a large craniopharyngioma protruding into the third and lateral ventricles

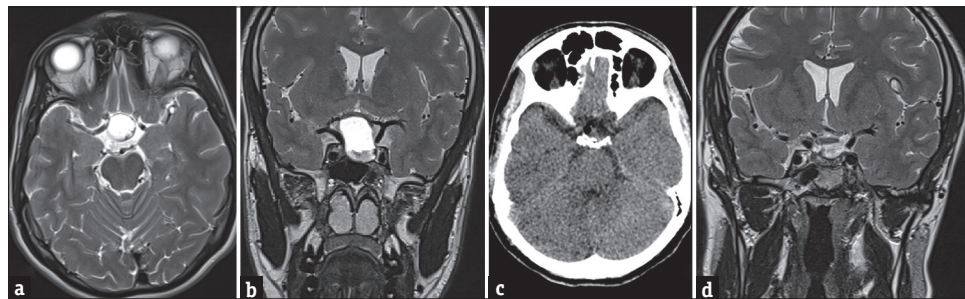


Figure 2: Preoperative axial and coronal T2-weighted magnetic resonance imaging images (a and b), postoperative axial computed tomography (c), and coronal T2-weighted magnetic resonance imaging images (d) of a patient operated through the transsphenoidal approach

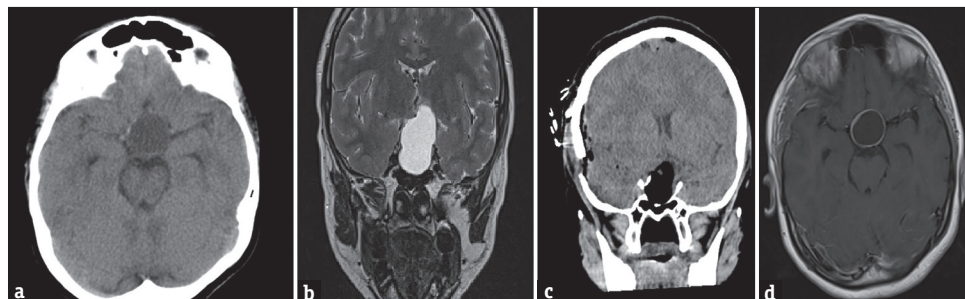


Figure 3: Preoperative axial computed tomography (a), coronal T2-weighted magnetic resonance imaging images (b), and postoperative axial computed tomography images (c) of a patient with total removal of a suprasellar craniopharyngioma. Postoperative axial T1-weighted magnetic resonance imaging (d) in 3 months showed recurrence

detected hypothalamic–pituitary system deficiency in 15 patients with total tumor removal and nine patients with subtotal resection. Hypothalamic–pituitary system deficiency was found to be significantly higher in the total tumor removal group ($t = 3.32$, $P < 0.05$) [Table 2].

Postoperative morbidity and mortality was appendant to the volume of the tumor and also its relationship to vital structures [Table 3]. In patients with vision field defects preoperatively (36 cases 52%: 15 cases in the total removal group and 21 cases in the subtotal removal group), vision improved in 11 patients (30%) (seven in the total removal group and four in the subtotal removal group) and vision partially improved in 14 patients (36%) (seven in the total removal group and seven in the subtotal removal group). Vision remained

Table 2: Relationship of surgical procedure and recurrence with early hypothalamic-pituitary failure

Surgical procedure	Cases	Recurrence, n (%)	Postoperative hypothalamic-pituitary failure, n (%)
Total resection	26	1 (3.8)	15 (57)
Subtotal resection			
Radiotherapy+	24	5 (21)	9 (21)
Radiotherapy–	18	9 (50)	
Total	68	15 (22)	24 (35.2)

the same in seven (20.5%) patients and vision worsened in four (13%) patients postoperatively. Postoperative vision improvement was seen in 25 of 36 cases, mostly in the total removal group. Postoperative endocrine instability occurred in 24 patients.

Extrahypothalamo-pituitary deficits developed predominantly in patients with total excision. Additional hormone therapy achieved normal hormone levels in these patients. Twenty-four patients required hormone replacement. Radiation therapy (RT) was administered in 24 patients. The median interval between the day of surgery and the first dose of RT was 50 (range, 30–130) days. Fifty-four Gy radiation was administered over thirty fractions for conformal radiation treatment. Five patients became disabled due to vision defects and neurologic deficits. As a postoperative complication, there was a patient with cerebellar infarction following total mass excision [Figure 4]. The histopathologic results of our surgical specimens were compatible with craniopharyngioma [Figure 5].

Six patients died in the intensive care follow-up period postoperatively (mortality rate: 8.8%). Two of these patients had a low preoperative GCS (between 3 and 5). Two patients died of panhypopituitarism postoperatively, one patient died of intracerebral hematoma postoperatively, and one patient died of pulmonary embolism.

When we evaluated the Glasgow outcome scales (GOS), 41 patients had low disability (GOS 5), 16 patients had moderate disability (GOS 4), four patients had severe disability (GOS 3), and one patient had persistent vegetative state (GOS 2) (morbidity rate = 30.8%).

DISCUSSION

Craniopharyngiomas are benign and rare tumors that develop from the squamous epithelium found in the Rathke bladder residues and settle in the sellar/suprasellar region. Total removal of craniopharyngiomas is difficult and the recurrence rate is high because they have a high degree of invasion into the surrounding neural and vascular structures such as the hypothalamus, pituitary gland, optic pathways, and the Willis polygon.^[4-6]

Treatments of craniopharyngiomas are always discussed, and there are different ideas about the most appropriate surgery. The main principles for craniopharyngioma surgery are arachnoid dissection for neurovascular protection, progressive tumor extraction, microsurgical extracapsular dissection, and protection of neurovascular structures. In the previous series, the recurrence rate was significantly higher in patients who underwent subtotal mass excision compared with those who underwent total excision.^[6-8] For this reason, although total excision is the main target in the publications, it is stated that additional RT with subtotal or partial excision is an alternative goal when total excision cannot be achieved due to a close relation with the hypothalamus, pituitary, and optical paths.^[9,10] In our study, recurrence was observed in 15 of 68 cases. Only one patient with recurrence had undergone total excision and 14 underwent subtotal excision.

Craniopharyngiomas cause endocrine and visual symptoms due to their close relationship with hypothalamic, pituitary, and visual pathways.^[11-13] Craniopharyngiomas may cause serious hypothalamic deficiency symptoms after total removal because of their infiltrative nature.^[14-16] In our study, hypothalamohypophyseal insufficiency was significantly higher in patients who underwent total mass excision compared with subtotal excision. A total of 24 patients had postoperative hypothalamic–pituitary insufficiency, 15 of whom

Table 3: Tumor size correlated with operative results

Size of tumor (cm)	Number of cases	Operative results			
		Good	Moderate	Poor	Death
<2	10	8	2	-	-
2-4	27	22	4	-	1
4-6	20	8	7	3	2
>6	11	3	3	2	3
Total	68	41	16	5	6

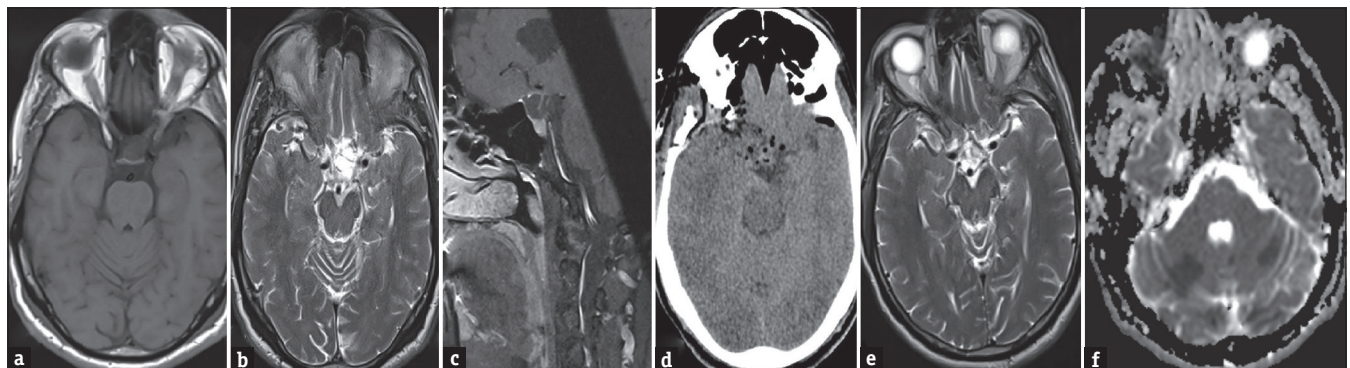


Figure 4: Preoperative axial T1-weighted, axial T2-weighted, and sagittal T1-weighted magnetic resonance imaging images (a-c), postoperative axial computed tomography (d), and axial T2-weighted magnetic resonance images (e) of a patient operated for intrasellar craniopharyngioma. Postoperative diffusion-weighted magnetic resonance imaging (f) showed cerebellar infarction

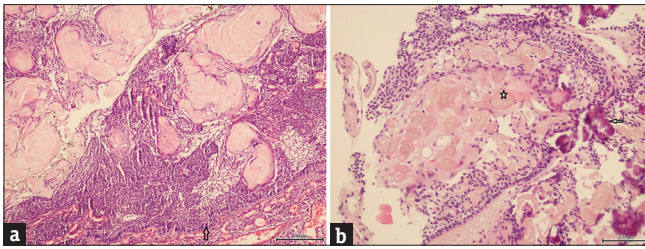


Figure 5: Pathologic images of a surgical specimen obtained from a patient with craniopharyngioma. (a) Adamantinomatous craniopharyngioma, epithelial islands (H and E, $\times 100$) containing peripheral palisading columnar cells (arrow). (b) Calcification (arrow) and “wet” keratin (star) (H and E, $\times 200$) (alone may be diagnostic)

underwent total mass excision and nine underwent subtotal excision.

Tumor size has an important effect on the postoperative general neurologic condition. As the tumor size increases, the rate of compression of the peripheral neurovascular structures, the rate of hypothalamohypophyseal insufficiency, and the rate of hydrocephalus by invasion into the ventricle significantly increase, and this negatively affects the surgical results.^[17,18] In our study, only one of 37 patients with a mass smaller than 4 cm died. Thirty patients with masses smaller than 4 cm had good postoperative status. Five of 31 patients with masses larger than 4 cm died. The postoperative status of 15 patients with masses larger than 4 cm was moderate and poor.

CONCLUSION

Tumor size affects the postoperative general neurologic condition in patients with craniopharyngiomas. Subtotal removal is correlated with recurrence and total removal is correlated with symptoms of serious hypothalamic deficiency. Total excision should be the primary aim without creating hormonal deficits and hypothalamic-stalk lesions. Our aggressive approach to totally excise craniopharyngiomas results in excellent long-term disease control with a greater risk of diabetes insipidus and panhypopituitarism.

Ethics committee approval

This is a retrospective contrastive analysis and study. This type of retrospective study did not require ethical approval. The trial is compliant with the Human Use guidelines and the Declaration of Helsinki.

Informed consent

Written informed consent was obtained from all individual participants included in the study.

Peer review

Externally peer reviewed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Mortini P, Losa M, Pozzobon G, Barzaghi R, Riva M, Acerno S, *et al.* Neurosurgical treatment of craniopharyngioma in adults and children: Early and long-term results in a large case series. *J Neurosurg* 2011;114:1350-9.
2. Cheng J, Shao Q, Pan Z, You J. Analysis and long-term follow-up of the surgical treatment of children with craniopharyngioma. *J Craniofac Surg* 2016;27:e763-66.
3. Tamasauskas A, Bunevicius A, Matukevicius A, Radziunas A, Urbonas M, Deltuva V. Extended pterional approach for initial surgical management of craniopharyngiomas: A case series. *Turk Neurosurg* 2014;24:174-83.
4. Lee EJ, Cho YH, Hong SH, Kim JH, Kim CJ. Is the complete resection of craniopharyngiomas in adults feasible considering both the oncologic and functional outcomes? *J Korean Neurosurg Soc* 2015;58:432-41.
5. Okada T, Fujitsu K, Ichikawa T, Mukaihara S, Miyahara K, Tanino S. Surgical approaches and techniques for radical resection of craniopharyngioma based on histopathological analysis of the dissection plane. *Jpn J Neurosurg* 2014;23:142-9.
6. Müller HL. Craniopharyngioma. *Handb Clin Neurol* 2014;124:235-53.
7. Komotar RJ, Roguski M, Bruce JN. Surgical management of craniopharyngiomas. *J Neurooncol* 2009;92:283-96.
8. Rock AK, Dincer A, Carr MT, Opalak CF, Workman KG, Broaddus WC. Outcomes after craniotomy for resection of craniopharyngiomas in adults: Analysis of the national surgical quality improvement program (NSQIP). *J Neurooncol* 2019;144:117-25.
9. Fahlbusch R, Hofmann BM. Surgical management of giant craniopharyngiomas. *Acta Neurochir (Wien)* 2008;150:1213-26.
10. Morisako H, Goto T, Goto H, Bohoun CA, Tamrakar S, Ohata K. Aggressive surgery based on an anatomical subclassification of craniopharyngiomas. *Neurosurg Focus* 2016;41:E10.
11. Dandurand C, Sepehry AA, Asadi Lari MH, Akagami R, Gooderham P. Adult craniopharyngioma: Case series, systematic review, and meta-analysis. *Neurosurgery* 2018;83:631-41.
12. Du C, Feng CY, Yuan XR, Liu Q, Peng ZF, Jiang XJ, *et al.* Microsurgical management of craniopharyngiomas via a unilateral subfrontal approach: A retrospective study of 177 continuous cases. *World Neurosurg* 2016;90:454-68.
13. Erfurth EM, Holmer H, Fjalldal SB. Mortality and morbidity in adult craniopharyngioma. *Pituitary* 2013;16:46-55.
14. 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* 2018;226:131-9.
15. Rao YJ, Hassanzadeh C, Fischer-Valuck B, Chicoine MR,

- Kim AH, Perkins SM, *et al.* Patterns of care and treatment outcomes of patients with craniopharyngioma in the national cancer database. *J Neurooncol* 2017;132:109-17.
16. Lee MH, Kim SH, Seoul HJ, Nam DH, Lee JI, Park K, *et al.* Impact of maximal safe resection on the clinical outcome of adults with craniopharyngiomas. *J Clin Neurosci* 2012;19:1005-8.
17. Kim YH, Kim CY, Kim JW, Kim YH, Han JH, Park CK, *et al.* Longitudinal analysis of visual outcomes after surgical treatment of adult craniopharyngiomas. *Neurosurgery* 2012;71:715-21.
18. Zhao X, Yi X, Wang H, Zhao H. An analysis of related factors of surgical results for patients with craniopharyngiomas. *Clin Neurol Neurosurg* 2012;114:149-55.