Received: 11.08.2012 / **Accepted:** 13.05.2013
DOI: 10.5137/1019-5149.JTN.6995-12.2

Extended Pterional Approach for Initial Surgical Management of Craniopharyngiomas: A Case Series

Kraniyofaringiomların Başlangıç Cerrahi Tedavisi İçin Genişletilmiş Pterional Yaklaşım: Bir Olgu Serisi

Arimantas TAMASAUSKAS[1, 2], Adomas BUNEVICIUS[1,2], Algimantas MATUKEVICIUS[1], Andrius RADZIUNAS[1,2], Mindaugas URBONAS[1], Vytenis DELTUVA[1, 2]

[1]Lithuanian University of Health Sciences, Department of Neurosurgery, Kaunas, Lithuania
[2]Lithuanian University of Health Sciences, Institute of Neurosciences, Kaunas, Lithuania

Corresponding Author: Adomas BUNEVICIUS / E-mail: a.bunevicius@yahoo.com

ABSTRACT

AIM: Treatment of craniopharyngiomas remains challenging. The aim of this study was to evaluate results of initial surgical management of craniopharyngiomas via the extended pterional approach.

MATERIAL and METHODS: Nineteen patients (10 female; median age of 23 years; ranging from 10 months to 67 years) undergone initial surgery for craniopharyngiomas through the extended pterional approach. Data were retrospectively collected by reviewing medical records, operative reports and imaging results.

RESULTS: The median size of craniopharyngiomas was 3.2 cm (range 1.3 - 4.8). Visual deterioration (n=12) and headache (n=10) were the most common symptoms on admission. After surgery, one patient died due to medical complications, 12 patients developed diabetes insipidus and eight patients developed anterior pituitary dysfunction. Median follow-up period was 9 years (range 2 – 13). Patients with progression of craniopharyngioma (n=5) when compared to patients without progression of craniopharyngioma (n=14) were significantly younger at the time of surgery, had less visual deterioration before surgery and had higher rates of not changed vision after surgery. Children had larger craniopharyngiomas when compared to adults.

CONCLUSION: Initial surgery for craniopharyngioma via the extended pterional approach is a safe and effective treatment option with low postoperative mortality, and acceptable postoperative morbidity and recurrence rate.

KEYWORDS: Craniopharyngioma, Surgery, Pterional approach, Outcome

ÖZ

AMAÇ: Kraniyofaringiomların tedavisi halen zordur. Bu çalışmanın amacı, genişletilmiş pterional yaklaşım aracılığıyla kraniyofaringiomların başlangıç cerrahi tedavi sonuçlarını değerlendirmekti.

YÖNTEM ve GEREÇLER: On dokuz hastada (10 kadın; medyan yaş 23 yıl; 10 ay - 67 yaş) genişletilmiş pterional yaklaşım yoluyla kraniyofaringiomlar için başlangıç cerrahisi yapıldı. Veriler tıbbi kayıtlar, ameliyat raporları ve görüntüleme sonuçlarının gözden geçirilmesiyle retrospektif olarak elde edildi.

BULGULAR: Kraniyofaringiomların medyan büyüklüğü 3,2 cm'di (aralık 1,3 - 4,8). Hastaneye yatma sırasında en sık görülen belirtiler görme bozukluğu (n=12) ve başağrısıydı (n=10) . Cerrahiden sonra, bir hasta tıbbi komplikasyonlar nedeniyle öldü, 12 hastada diabetes insipidus gelişti ve sekiz hastada anterior hipofiz disfonksiyonu gelişti. Medyan takip süresi 9 yıldı (aralık 2 – 13). Kraniyofaringiomun ilerlediği hastalar (n=5), kraniyofaringiomun ilerlemediği hastalarla (n=14) karşılaştırıldığında cerrahi zamanında çok daha gençti, cerrahi öncesinde daha az görme bozukluğu vardı ve cerrahiden sonra görmenin değişmeme oranı daha yüksekti. Çocuklarda kraniyofaringiomlar yetişkinlerden daha büyüktü.

SONUÇ: Genişletilmiş pterional yaklaşım yoluyla başlangıç kraniyofaringiom cerrahisi düşük postoperatif mortalite ve kabul edilebilir bir postoperatif morbidite ve rekürens oranına sahip, güvenli ve etkin bir tedavi seçeneğidir.

ANAHTAR SÖZCÜKLER: Kraniyofaringiom, Cerrahi, Pterional yaklaşım, Sonuç

INTRODUCTION

Craniopharyngiomas are rare tumors accounting for approximately 3% of all intracranial neoplasms (2,10). Craniopharyngiomas have bimodal age distribution with peak incidence rates during childhood and later in older adults (2,10). In pediatric population craniopharyngiomas account for approximately 10% of all intracranial tumors and are the most common non-glial brain tumors (10). Craniopharyngiomas most commonly develop in the sellar and suprasellar region from residual cells of Rathke's pouch; although some craniopharyngiomas may arise primarily within the third ventricle (17, 20). Craniopharyngiomas are histologically benign and do not undergo malignant transformation, but proximity to and subsequent pressure of important structures, such as optic tract, pituitary, circle of Willis, third ventricle and hypothalamus, makes them difficult to cure and be malignant in behavior (23,26).

There remains an ongoing debate regarding the optimal therapeutic approach of craniopharyngioma patients (9,12,19). Gross total resection (GTR) was the mainstream treatment approach for many decades, but fell out of favor due to technical difficulties and high rates of postoperative morbidity and mortality (11,18). Consequentially, subtotal resection (STR) combined with adjuvant radiation therapy was introduced, but yielded conflicting results with regards to local tumor control and was criticized because of significant side effects arising from radiation therapy, such as endocrine dysfunction, optic neuritis and dementia (2,5,6,22,28,32). However, due to ongoing improvements of surgical techniques, introduction of new approaches and increasing availability of neuro-navigation systems and intraoperative imaging many authors still recommend GTR as the first-line treatment option because it provides with the most favorable long-term outcomes, especially if performed by experienced neurosurgeons (5,12,28,27).

Surgical treatment with craniotomy is especially useful for craniopharyngiomas with suprasellar (SS) and parasellar extension because it allows for detailed visualization of critical anatomical structures; while endoscopic transphenoidal surgery is best suited for intrasellar tumors (12,18). The pterional approach remains the most commonly used among trans-cranial approaches. The main advantages of the pterional approach when compared to other trans-cranial approaches are versatility, short distance and most direct route to the supra-sellar region together with minimal retraction of normal brain tissue (12). The extra-ventricular tumor can be removed through three surgical windows: the optico-carotid triangle, surgical window lateral to the carotid artery and the triangle superior to carotid bifurcation. Intra-ventricular portions of craniopharyngioma can be removed through the lamina terminalis. Anterior extension of typical "keyhole" pterional craniotomy is referred to as the extended pterional approach and allows for a wider operative field that is particularly important in cases of large retro-chiasmatic craniopharyngiomas and prefixed optic chiasm (1,31). In addition, the pterional approach can be combined with other surgical approaches (33).

The aim of our study was to present the results of initial radical surgical management of craniopharyngiomas via an extended pterional approach craniotomy.

MATERIAL and METHODS

In a period from 1998 until 2010, a total of 42 patients newly diagnosed with craniopharyngiomas underwent initial surgical treatment at the Department of Neurosurgery of the Lithuanian University of Health Sciences, Kaunas, Lithuania. Thirty-three (79%) patients underwent trans-cranial surgery, 4 patients (10%) trans-sphenoidal surgery, 3 patients (7%) stereotactic aspiration and 2 (4%) patients the Torkildsen procedure (ventriculocisternostomy). In the trans-cranial surgery subgroup, 19 (58%) patients were operated through an extended pterional approach by the senior author (A.T.) and will be analyzed in the present report. The surgical approach was chosen on an individual basis, paying close attention to the size and location of the craniopharyngioma and to the patients' health status. The extended pterional approach was preferred in patients without significant medical co-morbidities and in cases of large SS extension craniopharyngiomas.

Data was retrospectively collected by reviewing inpatient medical records, outpatient medical records and reports of the surgical procedure. Preoperative, postoperative and last follow-up computed tomography (CT) scans and magnetic resonance imaging (MRI) scans were reviewed. Patients' demographic characteristics (age and gender), pre-operative and post-operative symptoms and signs, preoperative imaging features (size, location and characteristics) and histological variant of craniopharyngiomas, extent of resection, duration of surgery, and complications during perioperative period were recorded. Visual acuity (VA) and formal visual field testing were performed by a neuro-ophthalmologist before surgery and after surgery. Pituitary functions were evaluated at the time of medical assessment, and endocrine deficiencies were determined according to classic endocrine standards. In cases of pituitary dysfunction, patients received appropriate hormone replacement therapy. The size of the craniopharyngioma was recorded as the largest diameter on any plane on pre-operative imaging studies. Tumor location with respect to sella turcica and the third ventricle was classified according to the preoperative radiology report as SS, intra-sellar (IS), para-sellar (PS), retro-sellar (RS) or intra-ventricular (IV).

The primary aim of initial surgery was GTR via extended pterional approach whenever possible without damage to the hypothalamus, visual pathway and other structures. Extent of resection was based on the neurosurgeon's impression using microscopic and/or endoscopic visualization as recorded in the operative records combined with postoperative CT and/or MRI scan results. GTR was defined as no residual tumor on visual inspection after resection and no residual tumor on

postoperative imaging studies. Cases with residual tumor on visual inspection and/or with residual soft tissue mass or contrast enhancement on postoperative imaging were considered as STR. Minimal residual calcification and no evidence of soft tissue tumor mass was considered as GTR. The functional status of the patients was evaluated before surgery and at the time of discharge using the Karnofsky performance status (KPS) scale. The scores on the KPS scale range from 0 to 100 with higher scores indicating better functional status.

Surgical Protocol

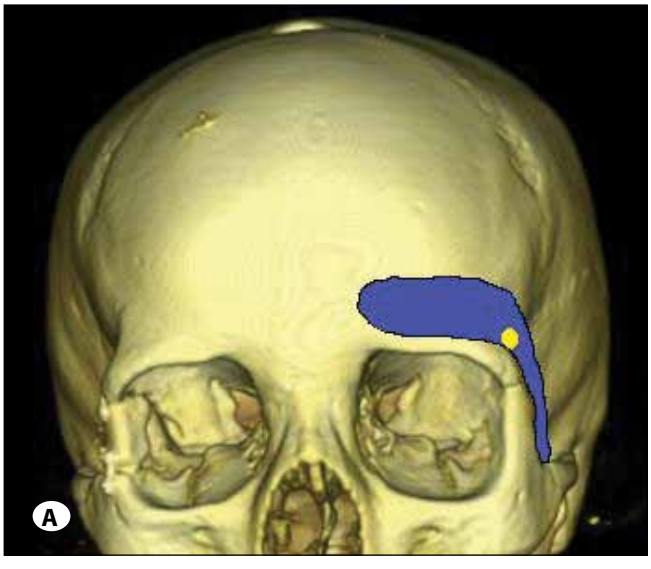
After induction of anesthesia, patients were placed in the supine position and head was fixed in a Mayfield 3-pin headholder and rotated so that the operative field was in the horizontal position. A standard curvilinear frontotemporal skin incision was performed about 1 cm in front of the tragus arch curving anteriorly from the zygomatic, staying behind the hairline and extending beyond the midline. One burr-hole was drilled at the superior-lateral aspect of the orbital rim above the intersection of the zygomatic bone and the supraorbital ridge (Figure 1A,B). Craniotomy was performed from the burr-hole extending anteriorly across the anterior margin of the superior temporal line, staying as low as possible on the orbital rim, until and about 2 cm from the sagittal sinus; then a sharp turn was made posteriorly and the opening was extended until behind the zygomatic arch and another sharp turn was made anteriorly and extended towards the burr-hole. The sphenoid wing was then removed using a rongeur. A dural flap was created over the sphenoid wing and extended frontally about 3 cm from the sagittal sinus. Cerebrospinal fluid (CSF) was gradually released through basal cisterns and the Sylvian fissure was opened to allow optimal brain relaxation. The Sylvian fissure was divided and the frontal lobe was retracted medially and upwards to allow access to the skull base structures. Anatomical structures and the pre-chiasmatic, optico-carotid, and carotid-tentorial triangles were identified (Figure 2A-C). The craniopharyngioma was then separated from the nearby structures, cysts were aspirated and the solid component was de-bulked while taking care to preserve the capsule of the craniopharyngioma that was progressively dissected from nearby structures. Attempt was always made to identify and preserve the pituitary stalk. However, when the stalk could not be separated from the tumor, it was sectioned as distally as possible to prevent undue traction of the hypothalamus. In cases of craniopharyngiomas extending into the third ventricle the tumor was removed through the lamina terminalis. After removal was completed, the entire bed was visually thoroughly inspected for residual tumor.

Statistical Analysis

Data were analyzed with SPSS 17.0 for Windows (Chicago, Illinois). Data are presented as median (range) for continuous variables and as number (percent) for categorical variables. First, we compared age, characteristic of craniopharyngiomas (size, location, quality and histological type), rates of total resection, follow-up period, functional status and symptoms of patients with tumor recurrence versus patients without tumor recurrence. Next, we compared characteristic of craniopharyngiomas (size and location), presenting symptoms, rates of total resection and recurrence, and follow-up period in adults (age ≥18 years) versus children (age <18 years). Continuous variables were compared using the Mann-Whitney U test and categorical variables were compared using the Fisher exact test. The criterion of $p \leq 0.05$ was chosen for statistical significance.

RESULTS

Age, gender, characteristics of craniopharyngiomas, extent of resection and follow-up period are presented in Table I. There were 10 female and 9 male patients. Median age at the time of surgery was 23 years (range 10 months - 67 years). Nine patients (47%) were younger than 18 years at the time of surgery. Median size of craniopharyngiomas



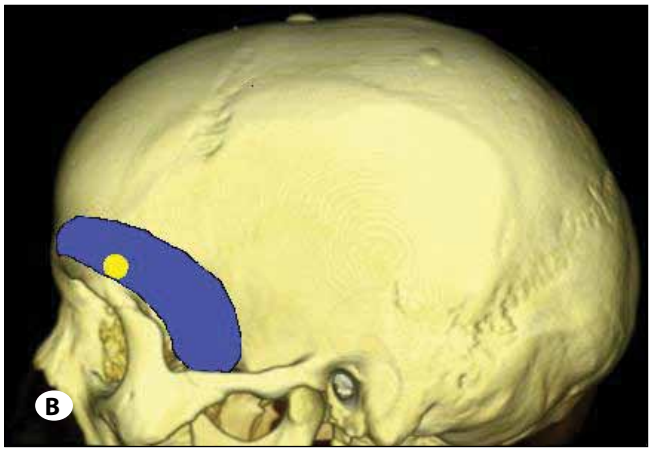


Figure 1: The site of burr hole (yellow circle) and area of craniotomy (in blue) used for extended pterional approach on **A)** anterior and **B)** lateral views.

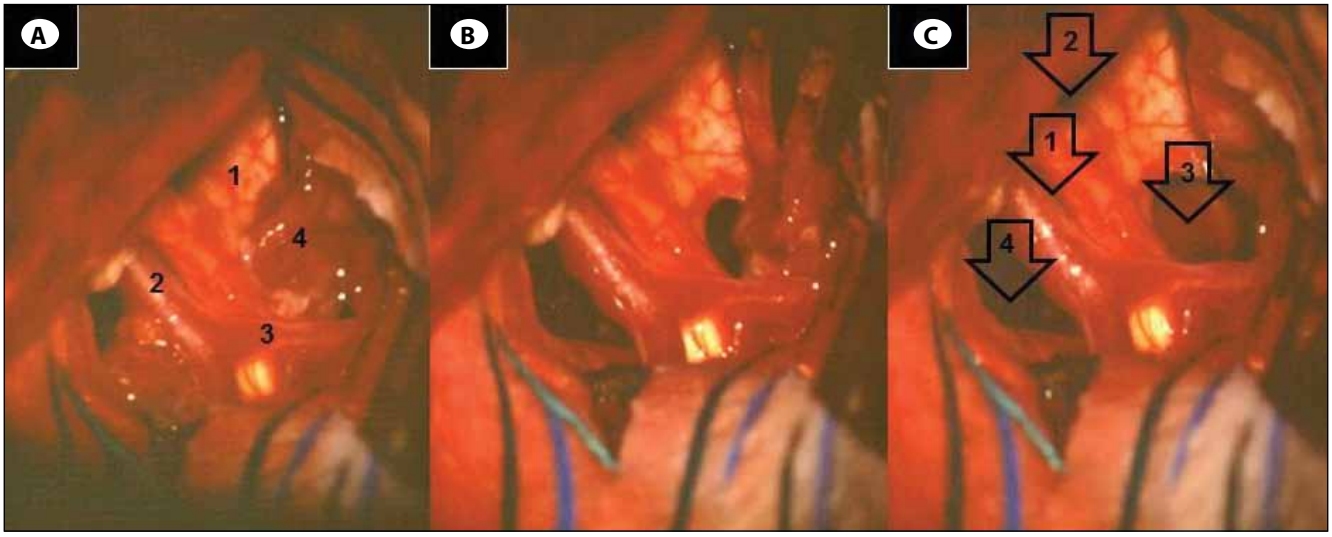
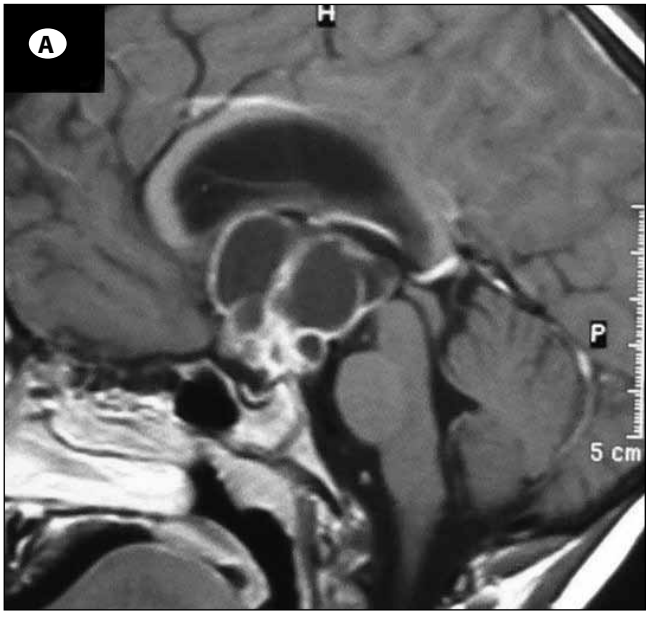


Figure 2: Intra-operative view **A)** before, **B)** during and **C)** after removal of craniopharyngioma. A: 1 – optic chiasm, 2- left carotid artery, 3 – left anterior cerebral artery A1, 4 – craniopharyngioma. C: 1 – optico-carotid triangle, 2 – pre-chiasmatic surgical corridor, 3 – lamina terminalis approach, 4 – approach lateral to carotid artery.



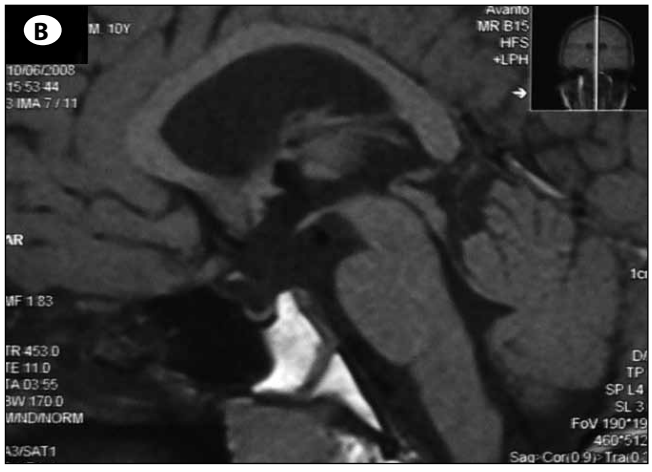


Figure 3: A) Sagittal contrast-enhanced T1-weighted MRI images demonstrate a heterogeneous tumor with solid component and cystic masses in the supra-sellar and partially intra-sellar space causing the compression of the floor of the third ventricle. **B)** No tumor recurrence is seen five years after surgery.

was 2.8 cm (range 1.3 - 4.8). Six (32%) patients had giant craniopharyngiomas, as defined by the largest diameter greater than 4 cm. The majority of craniopharyngiomas were cystic (n=18; 95%), soft (n=10; 53%) and had calcifications (n=15; 74%). All craniopharyngiomas had an SS component, seven (37%) had an IS component, four (21%) had a PS component and one (5%) had an RS component. Histological examination revealed that the majority were adamantinous craniopharyngiomas (n=16; 84%). Median follow-up period was 9 years (range 2 – 13).

Presenting symptoms, postoperative complications and follow-up results are presented in Table II. The most common symptoms at admission were visual deterioration (n=12; 63%) and headache (n=10; 53%). Four (21%) patients had anterior pituitary dysfunction before surgery. Median duration of surgery was 5 hours (range 3 – 8). Surgery was defined as total in 13 (68%) patients and as subtotal in 6 (32%) patients (Figure 3). After surgery, one patient died due to cardiopulmonary insufficiency caused by pneumonia, septicemia and pulmonary embolism (Table II; case #19). After surgery, 12 (63%) patients developed diabetes insipidus, eight (42%) patients developed new anterior pituitary dysfunction and two (11%) patients had postoperative CSF leak. After surgery, vision did not change in nine (47%) patients, worsened in five (26%) patients and improved in four (21%) patients. KPS scale

Table I: Age, Gender, Characteristics of Craniopharyngiomas, Extent of Resection and Follow-Up Duration of All Patients

No.	Age (years), sex	Tumor characteristics	Tumor location	Histology	Resection	Follow-up, years
1	17, F	2.6 cm, cystic, calcification	SS	adamantinous	Total	4
2	66, M	4.1cm, cystic	SS	adamantinous	Total	2
3	23, F	2.8 cm, cystic, calcification, soft	SS/PS	teratoid	Total	13
4	10 months, M	4.1 cm, cystic, calcification	SS/IS	adamantinous	Total	8
5	8, M	3.8 cm, cystic, calcification, soft	SS/IS/PS	adamantinous	Total	9
6	56, F	2.6 cm, cystic, calcification	SS/IS	adamantinous	Total	3
7	17, M	4.5 cm, calcification, soft	SS/PS/RS	adamantinous	Total	13
8	60, F	2.4 cm, cystic, calcification	SS/IS	adamantinous	Subtotal	8
9	28, F	1.3 cm, calcification	SS	adamantinous	Subtotal	11
10	27, F	2.5 cm, cystic, calcification	SS	adamantinous	Total	9
11	40, F	1.5 cm, cystic, calcification	SS/IS	adamantinous	Total	10
12	4, M	4.5 cm, cystic, calcification, soft	SS/PS	adamantinous	Subtotal	10
13	2, F	4.1 cm, cystic, calcification, soft	SS/IS	adamantinous	Total	7
14	10, F	3.5 cm, cystic, soft	SS/IS	adamantinous	Subtotal	9
15	7, M	4.8 cm, cystic, calcification, soft	SS	adamantinous	Total	9
16	64, M	1,8 cm ,cystic , soft	SS	papillary	Subtotal	8
17	67, M	3.7 cm, cystic, calcification	SS	adamantinous	Total	9
18	6, M	2.5 cm, cystic, soft	SS	papillary	Total	8
19	54, F	2.8 cm, cystic, soft	SS	adamantinous	Subtotal	0

***M** – male; **F** – female; **SS** – supra-sellar; **IS** - intra-sellar; **PS** – para-sellar; **IV** – intra-ventricular; **RS** - retro-sellar.*

scores before and after surgery were available in 17 patients: one patient was too young for evaluation of functional status (case #4) and another patient died soon after the surgery (case #19). Median KPS score was 80 (range 50 – 90) before surgery and 80 (range 40 - 90) after surgery. After surgery, the KPS score did not change in nine patients, decreased in four patients and increased in four patients.

Among patients who survived the initial postoperative period (n=18), progression of craniopharyngioma was documented in five (28%) patients with a median of 3 years after surgery, ranging from immediately after surgery to 8 years. In cases of craniopharyngioma progression, radiation therapy was applied only if growth of solid component of craniopharyngioma was documented (9). Accordingly, four children were referred for radiation therapy (cases # 4, 5, 12 and 13). Only one of these patients (case #5) underwent repeated surgery due to progression of craniopharyngioma nine years after initial surgery. Patients with progression of craniopharyngioma when compared to patients without progression of craniopharyngioma were significantly younger at time of surgery (p=.05), had less visual deterioration before surgery (p=.002) and had higher prevalence of unchanged vision after surgery (p=.029); see Table III.

Finally, when compared with adults, children had larger craniopharyngiomas (p=0.011) and a trend for increased prevalence of large giant craniopharyngiomas (p=.057) and soft consistency craniopharyngiomas (p=.07) (see Table IV).

DISCUSSION

The extended pterional approach was a safe and effective surgical approach for initial radical surgical management of craniopharyngiomas. The extended pterional approach was associated with low postoperative mortality, and acceptable post-operative morbidity and acceptable rate of long-term recurrence.

In adults, most fatal cases of craniopharyngioma surgery are attributed to intra-operative damage to hypothalamus or to co-existing serious medical conditions (15,30,33). With regards to the one fatal case in our series, no significant complications were documented during surgery and infectious complications (pneumonia and sepsis) were due to medical complications. Others have reported overall mortality rates ranging from 0% to 9% in patients undergoing craniopharyngioma surgery that reached 15% in aggressive resection groups (15,30,33). Variation in mortality rates across studies with a trend towards decreased mortality in the most recent surgical series can be partially attributed to ongoing improvements in medical care and microsurgical techniques. Furthermore, the experience of the neurosurgeon is of paramount importance for successful treatment of disorders with low incidence rates, such as craniopharyngiomas, and

Table II: Pre-operative and Post-operative Data of all Patients

No	Presenting symptoms	Visual disturbances		Ant. pituitary dysfunction		KPS score		Post-op complications	Progression, years after surgery, additional treatments
		Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op		
1	H/A, nanismus	No	NC	Yes	Yes	80	80	DI	NO
2	Visual deterioration, lethargy, hypopituitarism	VA lt=0, rt=6/10, BTH	NC	No	Yes	70	60	DI, transient hemiparesis of right side	NO
3	H/A, visual deterioration, lethargy/ disorientation, aphasia	VA rt=lt=8/100	W, rt HH	No	No	60	90	No	NO
4	Delayed development	N/E	NC	No	Yes	n/a	n/a	DI	YES – 7yrs, RT
5	Lethargy/ disorientation, DI	No	NC	No	Yes	90	80	DI	Yes – 4yrs, RT, RS
6	Visual deterioration	BTH, VA lt=9/100, rt=3/10	I, BTH, VA lt=9/10	No	No	70	70	No	NO
7	H/A, lethargy/ disorientation , visual deterioration, hypogonadism	BTH, VA lt=1/1000, rt=1	NC	Yes	Yes	70	80	DI- transient, hemiparesis, aphasia	NO
8	H/A, visual deterioration	BTH, VA lt=9/100, rt=9/10	I	No	No	80	90	DI	NO
9	Weight gain, amenorrhea	No	NC	Yes	No	90	90	DI	YES - immediate
10	Visual deterioration	HH lt	W, + BTH	No	No	80	80	DI	NO
11	H/A, nausea/ vomiting, gait disturbance, meningeal irritation	No	W, lt HH	No	No	70	70	No	NO
12	Lethargy/ disorientation	No	NC	No	Yes	80	80	DI	YES – 3yrs, RT
13	H/A, nausea/ vomiting	N/E	NC	No	Yes	60	60	DI	Yes – 1yr, RT
14	H/A, visual deterioration	HH lt	W, + rt HH	No	Yes	60	40	DI, CSF leak	NO
15	H/A, visual deterioration	VA rt=lt=5/10	I, VA increased	No	Yes	50	70	CSF leak	NO
16	Visual deterioration, weight gain, nanismus	VA rt=lt=1/10	W, TH, lt, VA rt=0	Yes	No	80	70	DI, pneumonia, embolization	NO
17	H/A, visual deterioration	VA rt=9/100, lt=2/10	I, VA rt=2/10, lt=6/10	No	No	90	90	No	NO
18	H/A, Nausea/vomiting, visual deterioration	BTH	NC	No	Yes	90	90	No	NO
19	Visual deterioration	BTH, VA lt=1/100, rt=1/10	N/E	No	N/E	90	n/a	Pneumonia, sepsis, death	n/a

***BTH** – bi-temporal hemianopsia; **DI** – diabetes insipidus; **H/A** – headache; HH - homonymous hemianopsia; **I** – improved; **KPS** – Karnofsky performance scale; **NC** – no change; **N/E** – not evaluated; **RT**- radiation therapy; **RS** – repeated surgery; **TH**-temporal hemianopsia; **VA** – visual acuity; **W** – worsened*

together with technological advancements contributes to improved treatment results at the same institution over time (27). Patients who underwent surgery in a period of 15 years were included in the present series; hence, a trend towards improved treatment results over time is highly expected. The incidence rate of craniopharyngiomas ranges from 0.5 to 2.0 cases per million persons per year; thus, from 2 to 7 new craniopharyngioma cases are expected each year in Lithuania (2). Our results suggest that the majority of craniopharyngioma patients underwent initial surgical treatment at our institution thus contributing to increasing experience of neurosurgeons and other members of the multi-disciplinary team.

No patients died during the follow-up period that reached 13 years after surgery, suggesting that the extended pterional approach is a safe treatment modality with respect to long-term outcomes. In a recent series of 121 patients treated for craniopharyngiomas using different modalities with a follow-up period ranging from 0.3 to 468 months, Karavitaki and colleagues (2005) reported a 5-year survival rate of 91% and 10-year survival rate of 90% (15). In the same series, the 5-year survival ranged from 30% to 93% among the operated patients. Also, postoperative mortality and morbidity rates were lower in patients undergoing first-time surgery for craniopharyngioma when compared to patients undergoing repeated surgery (15). In this context it is important to recall

Table III: Demographic and Clinical Characteristics of Patients with and without Progression of Craniopharyngioma; Median (Range); n (%).

	Progressed (n=5)	Not-progressed (n=13)	P*
Demographic characteristics			
Age, years	6 (2 - 28)	34 (6 - 67)	.051
Children	4/5 (80)	5/13 (39)	.294
Male gender	3/5 (60)	6/13 (66)	1.00
Characteristic of craniopharyngiomas			
Size, cm	4.0 (1.3 - 4.5)	2.6 (1.5 – 4.8)	.564
Size greater than 4 cm	3/5 (60)	3/10 (23)	.268
Cystic	4/5 (80)	13/13 (100)	.278
Calcifications	5/5 (100)	9/13 (64)	.234
Soft	3/5 (60)	6/13 (67)	1.00
Supra-sellar	5/5 (100)	13/13 (100)	1.00
Intra-sellar	3/5 (60)	4/13 (31)	.326
Adamantinous	5/5 (100)	10/13 (77)	.522
Total resection	3/5 (60)	10/13 (77)	.583
Follow-up, years	9.5 (7 - 11)	8.5 (2 - 13)	.584
Karnofsky performance index			
Pre-operative	85 (60 - 90)	75 (50 - 90)	.251
Post-operative	80 (60 - 90)	80 (40 - 90)	.861
Preoperative symptoms			
Headache	1/5 (20)	8/15 (57)	.303
Visual deterioration	0/5 (0)	11/13 (85)	.002
Postoperative visual symptoms			
Not-changed	5/5 (100)	4/13 (31)	.029
Improved	0/5 (0)	4/13 (31)	.278
Worsened	0/5 (0)	5/13 (39)	.249
Anterior pituitary dysfunction			
Pre-operative	1/5 (20)	3/13 (23)	1.00
Post-operative	4/5 (80)	6/13 (46)	.314

Data are presented as the number of patients with the deficiency/total number of patients with available information, with the relevant percentages in parentheses.
In bold – p <.05
** Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables.*

Table IV: Characteristics of Adult and Children Craniopharyngioma Patients; Median (Range); n (%).

	Adults	Children	P*
Characteristic of craniopharyngiomas			
Size, cm	2.6 (1.3 – 4.1)	4.1 (2.5 – 4.8)	.011
Size greater than 4 cm	5/9 (56)	1/10 (10)	.057
Cystic	9/9 (100)	9/10 (90)	1.00
Calcifications	7/10 (70)	7/9 (78)	1.00
Soft	3/10 (30)	7/9 (78)	.070
Para-sellar	1/10 (10)	3/9 (33)	.30
Presenting symptoms			
Headache	4/10 (40)	6/9 (67)	.370
Visual deterioration	8/10 (80)	4/9 (44)	.170
Anterior pituitary dysfunction	2/10 (20)	2/9 (22)	1.00
Total resection	6/10 (60)	7/9 (78)	.63
Follow-up, years	9 (2 - 13)	9 (4 – 13)	.772
Recurrence	2/9 (22)	4/9 (44)	.620

Data are presented as the number of patients with the deficiency/total number of patients with available information, and with the relevant percentages in parentheses.
In bold – p <.05
In italic – p>.05, but .1
** Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables.*

that all patients included in the present series underwent first-time surgery for craniopharyngiomas; thus, the safety and efficacy of the extended pterional approach for repeated surgery of craniopharyngiomas should be addressed.

In our series, postoperative morbidity was within an acceptable range. Specifically, among the 18 patients who survived initial postoperative period, 63% developed new DI, 42% developed new anterior pituitary dysfunction, 26% experienced worsening of visual function and 11% had postoperative CSF leak. Also, the functional status did not change in the majority of patients after surgery. However, functional status worsened after surgery in four patients and improved in four patients. DI is caused by a damage to the pituitary stalk and is a common complication after radical surgical management of craniopharyngiomas (5,33). Yasargil et al. observed permanent DI in nearly all of their craniopharyngioma patients after radical microsurgical resection (33). Another large series by Elliot et al. (2010) reported that 78% of patients had DI after surgery and 43% of patients had new onset DI following radical surgical resection of craniopharyngiomas that was performed mainly via pterional craniotomy (5). A large series of pediatric craniopharyngiomas patients from China reported postoperative DI in nearly 82% of their patients (34). Preservation of the pituitary stalk is time-consuming and challenging for neurosurgeon, because craniopharyngiomas usually originate from or are in close proximity with this structure. Nonetheless, preservation of the pituitary stalk is associated with favorable outcomes and should be attempted in all cases (14). The rate of new anterior pituitary dysfunction in our series was lower when compared to the proportion of patients (79%) who required permanent hormone substitution therapy after radical resection of craniopharyngiomas reported by Yasargil et al. (1990). Another recent series reported that hormone replacement therapy was required by 53% of craniopharyngioma patients in whom the pituitary stalk was preserved (13). The rate of postoperative worsening of visual function in our series corresponds to rates of visual deficits following surgical treatment of craniopharyngioma reported by others with average rate of 19% that reach up to 33% (5,13).

In our series, progression of craniopharyngioma was documented in five (28%) patients. Four of these patients consequentially underwent radiation therapy and one patient in the radiation therapy subgroup underwent repeated surgery nine years after the initial surgery. Craniopharyngioma recurrence was associated with younger age at the time of surgery, better preoperative visual function and higher rate of unchanged postoperative visual function. Results regarding the GTR rate correspond to results from other surgical series. For example, the GTR rate of craniopharyngiomas using the pterional approach was reported in the range of 59% to 79% of the patients in a more recent series (4,33). In three patients, resection was initially considered to be total but recurrence of craniopharyngioma was documented one year, four years and seven years after surgery. In two patients from the subtotal resection subgroup, recurrence of craniopharyngioma occurred one year and three years after surgery. These results suggest that initial impression regarding the extent of craniopharyngioma resection might be unreliable. Recurrence of craniopharyngioma usually occurs during the first year after subtotal resection. Delayed recurrence of craniopharyngioma usually occurs following what was initially thought to be

a total resection, corresponding to results from our study with the exception of one patient. Therefore, close follow-up for disease recurrence is warranted in all operated patients. However, it should be noted that the follow-up period was relatively short in our series; thus, it is expected that more patients from the current cohort will experience recurrence of craniopharyngioma in the future.

We also found that children had larger craniopharyngiomas as well as more giant and soft consistency craniopharyngiomas when compared to adults. Larger craniopharyngiomas in children partially explain why patients with documented progression of craniopharyngiomas were younger. Previous studies suggested that adults and children have different biological characteristics and different dynamics of craniopharyngiomas. For example, a previous case series from Finland reported that children presented with larger craniopharyngiomas when compared to adults (29). However, another large series by Karavitaki and colleagues did not find different radiological characteristics, including location, consistency and rates of invasion of third ventricular wall in children versus adults (15). These mixed findings suggest that more studies evaluating whether adult and children craniopharyngiomas have different biological characteristics are needed.

The most common symptoms at presentation were visual deterioration, headache and anterior pituitary dysfunction, corresponding to previous studies. Visual disturbances and headaches were reported as the most common presenting symptoms of craniopharyngioma followed by hypothalamic dysfunction, vigilance, weight gain, DI and neuropsychiatric disturbances (8,9,15,20). Therefore, one must be suspicious for supra-sellar lesions, including craniopharyngioma, in patients presenting with these symptoms.

Small sample size is a limitation of the current study. However, the major strength of this series is that all surgeries were performed in compliance with the same surgical protocol.

We agree with Powell that there is no single best surgical approach for treatment of craniopharyngiomas and advanced conservative treatment options and the full battery of skull base approaches should be available at the experienced center (24). The optimal surgical approach should be chosen on individual basis paying close attention to patients' characteristics and to craniopharyngiomas' characteristics in order to achieve the best outcomes. Various surgical approaches were employed for the treatment of craniopharyngiomas at our center, but in the present series we only presented results of the extended pterional approach as we have the most experience with this approach.

CONCLUSIONS

In conclusion, the extended pterional approach in the hands of the experienced neurosurgeon allows for radical resection of craniopharyngiomas at initial presentation in the majority of patients with low mortality and with acceptable morbidity. Further studies evaluating safety and efficacy of an extended pterional approach in patients with recurrent craniopharyngiomas are needed.

REFERENCES

1. Ammirati M, Samii M, Sephernia A: Surgery of large retrochiasmatic craniopharyngiomas in children. Childs Nerv Syst 6:13-17, 1990
2. Bunin GR, Surawicz TS, Witman PA, Preston-Martin S, Davis F, Bruner JM: The descriptive epidemiology of craniopharyngioma. J Neurosurg 89:547–551, 1998
3. De Vile CJ, Grant DB, Kendall BE, Neville BG, Stanhope R, Watkins KE, Hayward RD: Management of childhood craniopharyngioma: Can the morbidity of radical surgery be predicted? J Neurosurg 85:73–81, 1996
4. Di Rocco C, Caldarelli M, Tamburrini G, Massimi L: Surgical management of craniopharyngiomas—experience with a pediatric series. J Pediatr Endocrinol Metab 19:355–366, 2006
5. Elliott RE, Hsieh K, Hochm T, Belitskaya-Levy I, Wisoff J, Wisoff JH: Efficacy and safety of radical resection of primary and recurrent craniopharyngiomas in 86 children. J Neurosurg Pediatr 5:30-48, 2010
6. Elliott RE, Sands SA, Strom RG, Wisoff JH: Craniopharyngioma clinical status scale: A standardized metric of preoperative function and posttreatment outcome. Neurosurg Focus 28: E2, 2010
7. Fahlbusch R, Hofmann BM: Surgical management of giant craniopharyngiomas. Acta Neurochir (Wien) 150:1213-1226, 2008
8. Fahlbusch R, Honegger J, Buchfelder M: Clinical features and management of craniopharyngiomas in adults. In: Tindall GT, Cooper PR, Barrow DL (eds). The Practice of Neurosurgery. Baltimore: Williams & Wilkins, 1996:1159-1173
9. Garrè ML, Cama A: Craniopharyngioma: Modern concepts in pathogenesis and treatment. Curr Opin Pediatr 19:471-479, 2007
10. Haupt R, Magnani C, Pavanello M, Caruso S, Dama E, Garrè ML: Epidemiological aspects of craniopharyngioma. J Pediatr Endocrinol Metab 19(Suppl 1):289-293, 2006
11. Hofmann BM, Hollig A, Strauss C, Buslei R, Buchfelder M, Fahlbusch R: Results after treatment of craniopharyngiomas: Further experiences with 73 patients since 1997. J Neurosurg 116(2): 373-384, 2012
12. Honegger J, Tatagiba M: Craniopharyngioma surgery. Pituitary 11: 361-373, 2008
13. Jung TY, Jung S, Choi JE, Moon KS, Kim IY, Kang SS: Adult craniopharyngiomas: Surgical results with a special focus on endocrinological outcomes and recurrence according to pituitary stalk preservation. J Neurosurg 111:572-577, 2009
14. Jung TY, Jung S, Moon KS, Kim IY, Kang SS, Kim JH: Endocrinological outcomes of pediatric craniopharyngiomas with anatomical pituitary stalk preservation: Preliminary study. Pediatr Neurosurg 46(3): 205-212, 2010

15. Karavitaki N, Brufani C, Warner JT, Adams CB, Richards P, Ansorge O, Shine B, Turner HE, Wass JA: Craniopharyngiomas. In children and adults: Systematic analysis of 121 cases with long-term follow-up. Clinical Endocrinology 62:397-409, 2005
16. Kim SK, Wang KC, Shin SH, Choe G, Chi JG, Cho BK: Radical excision of pediatric craniopharyngioma: Recurrence pattern and prognostic factors. Childs Nerv Syst 17:531–537, 2001
17. Klein HJ, Rath SA: Removal of tumors in the III ventricle using the lamina terminalis approach. Three cases of isolated growth of craniopharyngiomas in the III ventricle. Childs Nerv Syst 5:144-147, 1989
18. Komotar RJ, Roguski M, Bruce JN: Surgical management of craniopharyngiomas. J Neurooncol 92:283-296, 2009
19. Matson DD, Crigler JF: Management of craniopharyngioma in childhood. J Neurosurg 30:377–390, 1969
20. Muller HL: Childhood craniopharyngioma. Recent advances in diagnosis, treatment and follow-up. Horm Res 69:193-202, 2008
21. Müller HL, Gebhardt U, Schröder S, Pohl F, Kortmann RD, Faldum A, Zwiener I, Warmuth-Metz M, Pietsch T, Calaminus G, Kolb R, Wiegand C, Sörensen N; Study Committee of KRANIOPHARYNGEOM 2000/2007: Analyses of treatment variables for patients with childhood craniopharyngioma--results of the multicenter prospective trial KRANIOPHARYNGEOM 2000 after three years of follow-up. Horm Res Paediatr 73:175-180, 2010
22. Ohmori K, Collins J, Fukushima T: Craniopharyngiomas in children. Pediatr Neurosurg 43:265–278, 2007
23. Pan J, Qi S, Lu Y, Fan J, Zhang X, Zhou J, Peng J: Intraventricular craniopharyngioma: Morphological analysis and outcome evaluation of 17 cases. Acta Neurochir (Wien) 153:773-784, 2011
24. Powell M: The surgery of craniopharyngiomas. Acta Neurochir (Wien)153:797-798, 2011
25. Puget S, Garnett M, Wray A, Grill J, Habrand JL, Bodaert N, Zerah M, Bezerra M, Renier D, Pierre-Kahn A, Sainte-Rose C: Pediatric craniopharyngiomas: Classification and treatment according to the degree of hypothalamic involvement. J Neurosurg 106 (1 Suppl):3–12, 2007
26. Qi S, Lu Y, Pan J, Zhang X, Long H, Fan J: Anatomic relations of the arachnoidea around the pituitary stalk: Relevance for surgical removal of craniopharyngiomas. Acta Neurochir (Wien) 153:785-796, 2011
27. Sanford RA: Craniopharyngioma: Results of survey of the American Society of Pediatric Neurosurgery. Pediatr Neurosurg 21 Suppl 1:39-43, 1994
28. Shi XE, Wu B, Fan T, Zhou ZQ, Zhang YL: Craniopharyngioma: Surgical experience of 309 cases in China. Clin Neurol Neurosurg 110:151-159, 2008
29. Sorva R, Jääskinen J, Heiskanen O: Craniopharyngioma in children and adults. Correlations between radiological and clinicalmanifestations. Acta Neurochir (Wien) 89:3-9, 1987
30. Van Effenterre R, Boch AL: Craniopharyngioma in adults and children: A study of 122 surgical cases. J Neurosurg 97:3–11, 2002
31. Wang KC, Kim SK, Choe G, Chi JG, Cho BK: Growth patterns of craniopharyngioma in children: Role of the diaphragm sellae and its surgical implication. Surg Neurol 57:25-33, 2002
32. Yang I, Sughrue ME, Rutkowski MJ, Kaur R, Ivan ME, Aranda D: Craniopharyngioma: A comparison of tumor control with various treatment strategies. Neurosurg Focus 28(4):E5, 2010
33. Yasargil MG, Curcic M, Kis M, Siegenthaler G, Teddy PJ, Roth P: Total removal of craniopharyngiomas. J Neurosurg 73:3–11, 1990
34. Zhang YQ, Ma ZY, Wu ZB, Luo SQ, Wang ZC: Radical resection of 202 pediatric craniopharyngiomas with special reference to the surgical approaches and hypothalamic protection. Pediatr Neurosurg 44:435-443, 2008