Clinical characteristics and therapeutic outcomes after endoscopic endonasal surgery for craniopharyngioma in the elderly

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OBJECTIVE Craniopharyngiomas (CPs) in adults are rare benign epithelial tumors, and few contemporary studies have explored outcomes after surgical treatment in elderly patients, especially with regard to endoscopic endonasal surgery (EES).

METHODS A retrospective cohort study was conducted on patients aged ≥ 18 years with CP who were treated with EES from 2013 to 2022. The cohort was divided into nonelderly (18–64 years) and elderly (≥ 65 years) groups based on age. Various parameters, including patient and tumor characteristics, surgical outcomes, complications, and follow-up, were compared between the two age groups.

RESULTS A total of 193 patients met the inclusion criteria, with 161 (83.4%) patients in the nonelderly group and 32 (16.6%) patients in the elderly group. Preoperatively, older patients were more likely to have memory impairment (4.3% vs 18.8%, p = 0.010), fatigue or decreased energy (9.3% vs 34.4%, p = 0.001), hypopituitarism (68.7% vs 90.6%, p = 0.012), or hydrocephalus (18% vs 40.6%, p = 0.005), and they were more likely asymptomatic (1.2% vs 9.4%, p = 0.033) and less likely to experience headache (57.8% vs 31.3%, p = 0.006). Patients in the elderly group had a longer symptom duration (median [IQR] 5 [10] months vs 9.5 [13] months, p = 0.001) and higher comorbidity scores (p < 0.001). Postoperatively, gross-total resection was achieved in 145 (90.1%) and 28 (87.5%) patients in the nonelderly and elderly groups, respectively. Older patients were more likely to develop pneumonia (5% vs 21.9%, p = 0.004). There were no significant differences in the extent of resection (p = 0.541), pathological subtypes (88.2% vs 75.0% adamantinomatous, p = 0.089), operation time (mean ± SD 307.8 ± 68.3 minutes vs 323.5 ± 86.0 minutes, p = 0.257), estimated blood loss (median [IQR] 300 [200] ml vs 300 [238] ml, p = 0.594), length of stay (median [IQR] 15 [8] days vs 15 [22] days, p = 0.964), perioperative mortality (2.5% vs 3.1%, p > 0.99), or postoperative severe hypothalamic dysfunction (37.9% vs 50.0%, p = 0.237) between the groups. Multivariate Cox regression analysis demonstrated that tumor calcification (HR 3.406, 95% CI 1.859–27.233, p = 0.038) and preoperative hydrocephalus (HR 3.688, 95% CI 1.310–10.386, p = 0.013) were independently associated with decreased survival. The median follow-up period in the elderly group was shorter (71 months vs 44 months, p = 0.001), and no recurrence was observed (7.1% vs 0%, p = 0.132).

CONCLUSIONS This study demonstrates that EES is a viable treatment option for older CP patients. With appropriate perioperative management, EES does not significantly increase mortality and, in selected populations, is well tolerated by patients.

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KEYWORDS craniopharyngioma; elderly; endoscopic endonasal; comparative study; postsurgical outcomes; skull base

ABBREVIATIONS ASA = American Society of Anesthesiologists; CP = craniopharyngioma; DI = diabetes insipidus; EES = endoscopic endonasal surgery; EOR = extent of resection; GTR = gross-total resection; HD = hypothalamic dysfunction; HI = hypothalamic involvement; HS = hypothalamic syndrome; LOS = length of stay; PCP = papillary CP.

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Craniopharyngiomas (CPs) are rare benign epithelial tumors, but they are one of the most common destructive lesions of the hypothalamus and pituitary gland and are associated with many morbidities.[1] CP has a bimodal distribution involving children aged 5–14 years and adults aged 50–74 years, with an overall incidence of 1.34/1,000,000 each year globally.[2,3] With improvement of the healthcare system and diagnostic methods, an increasing number of CPs have been identified.

Today, the world's population of older people is growing at the fastest rate ever.[4] As of 2021, there were approximately 761 million people aged 65 years and older, and that number is projected to more than double to 1.6 billion by 2050.[4] This indicates that there will be a growing number of elderly CP patients diagnosed, and more attention should be given to this special group.

Elderly patients accounted for 14% of adult CPs in a previous study.[5] Although the incidence of CP is higher in younger patients, the aging population renders investigation of the safety of surgical interventions for CPs and other brain neoplasms increasingly crucial. Previous studies that explore outcomes after surgical treatment in this population are scarce, especially with regard to endoscopic endonasal surgery (EES).[5–7] Here, we provide the first series to systematically compare clinical characteristics, surgical outcomes, and follow-up between nonelderly adult and elderly patients. These data are likely to shed new light on this disease in the elderly and to inform future treatments.

Methods

Patient and Data Collection

This study was authorized by the Nanchang University Institutional Review Board. Informed consent was obtained from all patients. A retrospective study of patients who underwent EES for CP between 2013 and 2022 in the Department of Neurosurgery at the First Affiliated Hospital of Nanchang University was performed. The inclusion criteria were as follows: 1) patients aged 18 years and older who were histologically diagnosed with CP; 2) no previous resection or radiotherapy for the lesions; and 3) EES with complete data.

Patients were allocated to two groups according to age at diagnosis: the nonelderly group (18–64 years) and the elderly group (≥ 65 years). Demographic, radiological, clinical, surgical, and follow-up data were reviewed and compared between the two age groups. Recurrence was defined as the emergence of tumors detected on neuroimaging for patients who underwent gross-total resection (GTR) or the regrowth of a residual tumor. Meningitis was defined as positive CSF culture for a pathogen, positive CSF antigen test, organism detected in CSF microscopy, leukocyte count ≥ 50/μl, or CSF to blood glucose ratio of < 0.1 without other positive findings.[8] The American Society of Anesthesiologists (ASA) physical status classification was used to assess preoperative comorbidities.[9] The management and follow-up of elderly patients were conducted by a geriatrician (Q.F.W.).

Hypothalamic Function Evaluation

The presence of severe hypothalamic dysfunction (HD) was defined according to the diagnostic criteria for hypothalamic syndrome (HS) proposed by van Santen et al.[10] The variables in the proposed diagnostic score included eight clinical domains, namely: hyperphagia, hypophagia (diencephalic syndrome), BMI,[11] behavioral problems (obsessive compulsive symptoms, hoarding, rage), sleep disorders, temperature dysregulation, pituitary dysfunction, and radiological Müller grade. Adult diagnostic criteria were used for BMI, whereas those of other domains remained unchanged. We did not conduct a comprehensive evaluation of HD before surgery in the early part of this series. Moreover, due to the retrospective nature of the study, the evaluation could only be carried out postoperatively.

Ophthalmological and Endocrinological Evaluation

Both before and after surgery, all patients underwent a comprehensive ophthalmological and endocrinologic evaluation. Ophthalmological assessment, including visual field and visual acuity examinations in accordance with the guidelines of the German Ophthalmological Society,[12] was performed by an independent ophthalmologist (J.T.) blinded to the mode of treatment. The visual status of patients was categorized as improved, stable, or deteriorated according to preoperative and postoperative visual function changes.

The endocrinological assessment was performed by laboratory measurement.[13] Partial hypopituitarism was defined as hormone deficiencies in one or two axes, and panhypopituitarism was defined when three or more axes were deficient. Diabetes insipidus (DI) was defined as a hydroelectrolytic imbalance caused by vasopressin deficiency and consisting of hypotonic polyuria (> 300 ml/hr for 3 consecutive hours) and urine specific gravity < 1.005, in addition to at least one relative criterion: serum sodium > 145 mmol/L, serum osmolality > 300 mOsm/kg, or excessive thirst.[14] Postoperative permanent DI refers to disease with a duration greater than 6 months. The postoperative endocrine and visual outcomes were assessed on the basis of status at last follow-up.

Neuroradiological Evaluation

All patients underwent MRI and CT scans before and after surgery. Tumors were classified according to their relationship with the infundibular stalk, as proposed by Kassam et al.[15] A modified ellipsoid volume approximated tumor volume, that is, $(\pi/6) \times (A \times B \times C)$, where A, B, and C represent the dimensions of the tumor in three orthogonal planes. Hydrocephalus was documented on the basis of an Evans index ≥ 0.3 on brain imaging.[16] This refers to the ratio of the transverse diameter of the frontal horn of the lateral ventricles to the maximum inner diameter of the skull.[16] Based on the degree of hypothalamic involvement (HI) and surgical lesions, the tumors were classified into three grades: grade 0, no HI or lesion; grade 1, HI or lesions limited to the anterior hypothalamus without involving the mammillary bodies or the area beyond them; and grade 2, HI or lesions extending to both the anterior and posterior hypothalamic areas, including the mammillary bodies and the area beyond them.[17] The extent of resection

(EOR) was determined on the basis of the operative note and postoperative MRI obtained within 3 days. GTR was defined as no evidence of residual tumor; near-total resection was defined as ≥ 95% tumor removal; subtotal resection was defined as ≥ 80% removed; and partial resection was defined as < 80% removed. Follow-up MRI studies were generally performed within 3 to 6 months after surgery and then annually or every 6 months (residual tumor) thereafter. The entire radiological evaluation of all cases was carried out by an independent neuroradiologist (F.O.) and neurosurgeon (J.W.).

Statistical Analysis

All analyses were carried out using SPSS version 26.0. The Student t-test was used to analyze the continuous numerical variables following a normal distribution and describe them using mean ± SD. The Mann-Whitney U-test was used to analyze the skewed data distribution and describe it using medians (IQR). The Pearson chi-square test and Fisher's exact test were utilized to compare categorical variables. The Wilcoxon rank-sum test was applied to ordinal variables for analysis. The Cox proportional hazards model was employed for both univariate and multivariate analyses to identify factors associated with overall survival. Age groups were incorporated into the multivariate model, whereas other variables were included only if they exhibited a p value < 0.05 in the univariate analysis. A p value < 0.05 was considered significant.

Results

Patient and tumor characteristics stratified by age are tabulated in Table 1. In 10 years, 193 adult CP patients who met the inclusion criteria underwent EES. Among these patients, 32 were ≥ 65 years (median [range] age 70.8 [65–80] years), and 161 were 18–64 years (median [range] age 45 [18–64] years). Patients in the elderly group accounted for 16.6% of the cohort, with 19 males (59.4%) and 13 females (40.6%). Patients in the nonelderly group accounted for 83.4% of the cohort, with 92 male (57.1%) and 69 female (42.9%) patients. There was no significant difference in terms of sex between the groups (OR 0.912, 95% CI 0.422–1.973, p = 0.816). To characterize temporal trends, we created a year-by-year breakdown of nonelderly versus elderly patients who underwent EES for CP at our institution from 2013 to 2022 (Fig. 1). Our results showed that over the past decade, the total number of patients undergoing CP resection has steadily increased, with an increase in the number of nonelderly and elderly patients over time. Additionally, the proportion of elderly patients has been on the rise.

Regarding preoperative physical status, 90.1% of nonelderly patients were assigned an ASA class of I or II. Patients with an ASA class > II were more commonly observed in the elderly group (9.9% vs 31.3%, p < 0.001). The differences between the groups in terms of tumor classification, volume, calcification, pathology, consistency, BMI, and Müller grade before surgery were not significant (p > 0.05). Compared with younger patients, elderly patients more commonly had suprasellar tumor components, and no purely sellar tumors were observed (p = 0.142).

Table 2 summarizes the main clinical presentations. The top 5 preoperative clinical alterations were visual impairment, hypopituitarism, headache, DI, and hydrocephalus in the nonelderly group, as well as hypopituitarism, visual impairment, hydrocephalus, DI, and fatigue or decreased energy in the elderly group. Elderly patients were more likely to present with memory impairment, fatigue or decreased energy, hypopituitarism, hydrocephalus, and asymptomatic status (p < 0.05). Eight patients with preoperative hydrocephalus underwent extraventricular drainage, all of whom were nonelderly patients (27.6% vs 0%, p = 0.043). There was no significant difference in the prevalence of visual impairment, dizziness, or DI between the groups (p > 0.05). In the younger group, 57.8% of patients experienced headaches, whereas this percentage was 31.3% in older patients (p = 0.006). The nonelderly group had a shorter median symptom duration than the elderly group (5 months vs 9.5 months, p = 0.001).

Surgical outcomes are summarized in Table 3. The observed disparity in EOR between the groups did not attain statistical significance (p = 0.541). Although higher proportions of improvement were observed in the younger group for visual (76.7% vs 68.0%, OR 0.647, 95% CI 0.252–1.657, p = 0.362), endocrine (4.5% vs 0%, p = 0.583), and memory (57.1% vs 50.0%, OR 0.750, 95% CI 0.084–6.710, p > 0.99) functions, the differences in functional outcomes across all three categories did not reach significance among the two cohorts (p > 0.05). Patients in the elderly group had a higher postoperative Müller grading than patients in the nonelderly group (p = 0.007). The operation time, estimated blood loss, and length of stay (LOS) were similar between the two cohorts in our study, with no significant differences noted (p > 0.05). More variability in LOS was noted in the elderly group.

Complications and follow-up outcomes stratified by age are tabulated in Table 4. The most common complication in the younger and older age groups was hypopituitarism (82% vs 100%, OR 1.073, 95% CI 0.991–1.162, p > 0.99), followed by permanent DI (56.6% vs 73.1%, OR 2.078, 95% CI 0.822–5.253, p = 0.117). Elderly patients were more likely to develop pneumonia (5.0% vs 21.9%, OR 5.355, 95% CI 1.784–16.071, p = 0.004) after surgery. Deep vein thrombosis, postoperative hydrocephalus, seizures, and epistaxis exclusively occurred in the nonelderly group, with no significant difference observed between groups (p > 0.05). No significant differences between groups were observed in CSF leakage (8.1% vs 9.4%, OR 1.178, 95% CI 0.316–4.395, p = 0.733), meningitis (8.1% vs 6.3%, OR 0.759, 95% CI 0.163–3.539, p < 0.001), hyperphagia (20.5% vs 31.3%, OR 1.763, 95% CI 0.761–4.083, p = 0.182), or hydrocephalus (3.1% vs 0%, p = 0.593). Four younger patients (2.5%) and 1 older patient (3.1%) died perioperatively with no statistical significance (OR 1.266, 95% CI 0.137–11.715, p > 0.99).

The median (IQR) follow-up time was 71 (27) months in the nonelderly cohort and 44 (36) months in the elderly cohort (p = 0.001). Tumor recurrence occurred in only 14 patients (8.7%) in the nonelderly group, but no significant difference was observed (p = 0.132). Among the patients with recurrence, 5 underwent reoperation, 5 underwent radiotherapy, and the remaining 3 received close MRI

TABLE 1. Patient and tumor characteristics of 193 patients stratified by age group

	Total	Nonelderly	Elderly	OR (95% CI)	p Value
Age, yrs	48 (21)	44 (18)	69 (7)		**<0.001**
Sex				0.912 (0.422–1.973)	0.816
Male	111 (57.5)	92 (57.1)	19 (59.4)		
Female	82 (42.5)	69 (42.9)	13 (40.6)		
ASA class					**<0.001**
I	127 (65.8)	121 (75.2)	6 (18.8)		
II	40 (20.7)	24 (14.9)	16 (50.0)		
III	18 (9.3)	10 (6.2)	8 (25.0)		
IV	8 (4.1)	6 (3.7)	2 (6.3)		
Pathology				2.491 (0.981–6.330)	0.089
Adamantinomatous	166 (86.0)	142 (88.2)	24 (75.0)		
Papillary	27 (14.0)	19 (11.8)	8 (25.0)		
Location					0.142
Sellar	15 (7.8)	15 (9.3)	0 (0)		
Sellar-suprasellar	78 (40.4)	66 (41.0)	12 (37.5)		
Suprasellar	100 (51.8)	80 (49.7)	20 (62.5)		
Kassam classification					0.327
0*	15 (7.8)	15 (9.3)	0 (0)		
I	53 (27.5)	43 (26.7)	10 (31.3)		
II	51 (26.4)	43 (26.7)	8 (25.0)		
III	55 (28.5)	45 (28.0)	10 (31.3)		
IV	19 (9.8)	15 (9.3)	4 (12.5)		
Consistency					0.756
Cystic	58 (30.1)	48 (29.8)	10 (31.3)		
Solid	46 (23.8)	40 (24.8)	6 (18.8)		
Mixed	89 (46.1)	73 (45.3)	16 (50.0)		
Tumor vol, cm^3	6.0 (9.2)	5.9 (8.7)	6.5 (9.0)		0.413
Calcification	105 (54.4)	86 (53.4)	19 (59.4)	1.275 (0.590–2.754)	0.536
Preop Müller grade					0.303
0	25 (13.0)	24 (14.9)	1 (3.1)		
1	57 (29.5)	46 (28.6)	11 (34.4)		
2	111 (57.5)	91 (56.5)	20 (62.5)		
Preop BMI, kg/m^2	23.5 (4.0)	23.5 (4.0)	22.5 (6.0)		0.241

Values are shown as number (%) or median IQR unless indicated otherwise. Boldface type indicates statistical significance (p < 0.05).
* Type 0 refers to subdiaphragmatic craniopharyngiomas as proposed by Jamshidi et al.[32]

follow-up. The proportion of deaths during follow-up in the nonelderly group was 6.8%, whereas it was 6.3% in the elderly group (OR 0.909, 95% CI 0.192–4.312, p > 0.99). In the last follow-up, 37.9% of younger patients and 50% of older patients harbored HS, with no statistical significance (OR 1.639, 95% CI 0.765–3.515, p = 0.237) (Table 4).

Univariate and multivariate Cox regression analysis are presented in Table 5. Among variables such as sex, age, pathological type, and tumor volume, only tumor calcification (HR 3.406, 95% CI 1.859–27.233, p = 0.038) and preoperative hydrocephalus (HR 3.688, 95% CI 1.310–10.386, p = 0.013) were significantly associated with decreased overall survival.

Discussion

With extended life expectancy and widespread use of MRI, the prevalence of diagnosed CPs is predicted to increase, especially in elderly individuals.[2] Furthermore, as endoscopy is increasingly used for this lesion,[18–20] it is meaningful to explore the outcomes of EES in the elderly population. However, there are few studies on EES in elderly patients with CP. Recently, older patients were included in some reported endoscopic endonasal series, but the exact number and outcomes for this population have not been reported.[21–23] The majority of the research on the surgical treatment of CP in older patients consists of case reports.[7,24–26] It was not until 2021 that Iglesias et al. reported the first multicenter retrospective case series study

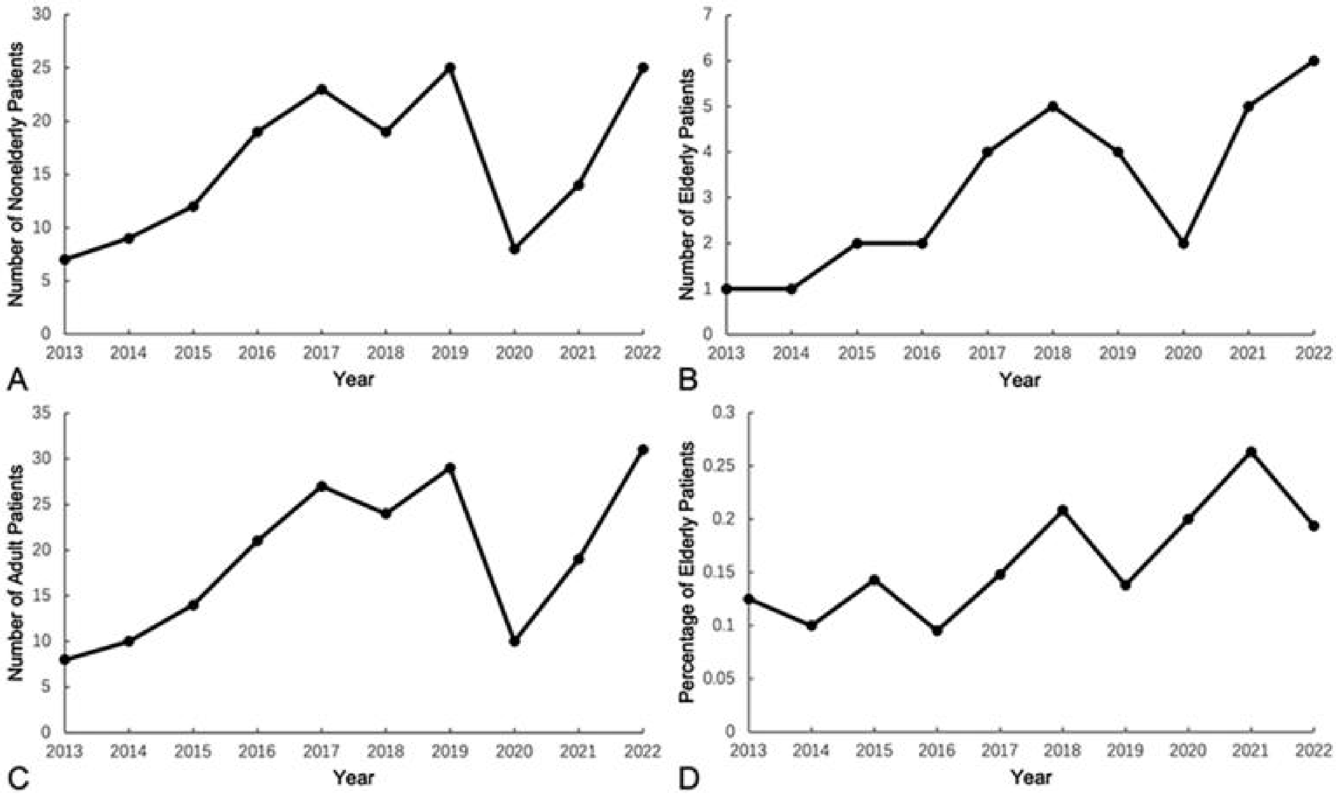

FIG. 1. Trends in nonelderly patients (**A**), elderly patients (**B**), and adult patients (**C**), as well as the proportion of elderly patients among the overall number of cases (**D**), who underwent EES for CP resection from 2013 to 2022. Data were affected by COVID-19 in 2020 and 2021.

of CP in older adults.[5] They analyzed surgically treated CP in elderly individuals, including transcranial and EES. Regrettably, the study did not make comparisons with nonelderly adults, ignoring some characteristics and outcomes of the older population.

In the present study, we aimed to investigate the EES outcomes and clinical characteristics of CP in the elderly population and to report the safety and effectiveness of this approach in select populations. To our knowledge, this is the first series to date to systematically compare the clinical characteristics, EES outcomes, and follow-up of CP in older and younger adults.

Patient Characteristics

Elderly patients accounted for 16.6% of adult CP cases, mainly among those aged 65–70 years. Symptom duration was longer in the elderly group ($p = 0.001$), which is consistent with the phenomenon observed by Hoffman et al. that the median symptom duration before CP diagnosis was positively correlated with patient age at diagnosis.[27] Compared to younger patients, elderly patients typically exhibit delayed onset of symptoms and have larger tumor volumes at diagnosis. In fact, older patients are more likely to be neglected or misdiagnosed because some symptoms and signs, such as memory deterioration, visual impairment, and hypopituitarism, may be confused with age-related diseases, leading to a delay in diagnosis.

Preoperative fatigue or decreased energy and hypopituitarism were more common in the older age group ($p < 0.05$), which were related to lower hormone levels. Moreover, memory impairment was also more common in older patients (4.3% vs 18.8%, $p = 0.010$). Normal age-related declines may contribute to hypomnesis, but the impact of the tumor is nonnegligible. Our study found that elderly patients had larger tumor volumes, a greater number of suprasellar tumor components, and higher Müller grading. These observations suggest a heightened level of tumor involvement in the mammillary body and fornix among the older population. When the mammillary body and/or fornix are damaged, memory deterioration, especially short-term memory, often results.[28,29]

Furthermore, our study revealed a higher incidence of hydrocephalus in the elderly group (18% vs 40.6%, $p = 0.005$). Notably, it was observed that elderly patients frequently exhibited an absence of symptoms related to increased intracranial pressure and did not require any preoperative interventions. This phenomenon has also been observed in other reports. In contrast, although hydrocephalus was less common in younger patients, the symptoms of increased intracranial pressure were more prominent once it occurred, and 18% of patients needed intervention prior to tumor resection. These results may be related, at least in part, to the physiological differences between younger and older patients, such as brain compliance and compensation.

Another interesting finding of our study was that older

TABLE 2. Main clinical presentations of 193 patients stratified by age group

	Total	Nonelderly	Elderly	OR (95% CI)	p Value
Visual impairment	145 (75.1)	120 (74.5)	25 (78.1)	1.220 (0.491–3.032)	0.668
Headache	104 (53.9)	93 (57.8)	10 (31.3)	0.332 (0.148–0.747)	**0.006**
Dizziness	35 (18.1)	30 (18.6)	5 (15.6)	0.809 (0.288–2.273)	0.687
Memory impairment	13 (6.7)	7 (4.3)	6 (18.8)	5.077 (1.581–16.308)	**0.010**
Fatigue/decreased energy	26 (13.5)	15 (9.3)	11 (34.4)	5.098 (2.068–12.572)	**0.001**
Preop hypopituitarism					**0.012**
Yes					
Partial hypopituitarism	85 (44.0)	68 (42.2)	17 (53.1)	1.550 (0.724–3.319)	0.257
Panhypopituitarism	55 (28.5)	43 (26.7)	12 (37.5)	1.647 (0.743–3.651)	0.217
No	53 (27.5)	50 (31.3)	3 (9.4)	4.354 (1.267–14.967)	**0.012**
DI	19 (9.8)	14 (8.7)	5 (15.6)	1.944 (0.647–5.844)	0.325
Asymptomatic	5 (2.6)	2 (1.2)	3 (9.4)	8.224 (1.316–51.394)	**0.033**
Hydrocephalus	42 (21.8)	29 (18.0)	13 (40.6)	3.114 (1.383–7.014)	**0.005**
Extraventricular drain*	8 (19.0)	8 (27.6)	0 (0)	0.618 (0.474–0.805)	**0.043**
Symptom duration, mos	6 (10)	5 (10)	9.5 (13)		**0.001**

Values are shown as number (%) or median IQR unless indicated otherwise. Boldface type indicates statistical significance (p < 0.05).
* Data were available from 42 patients.

patients had a higher rate of incidental diagnosis of CP (1.2% vs 9.4%, p = 0.033). The distinction may be attributed to the fact that elderly patients are more likely to undergo radiological examinations for various reasons, such as medical examinations, falls, or evaluations for other central nervous system disorders. In addition, we found an overall increase in the number of patients treated with EES for CP over the last decade, with a corresponding increase in the proportion of elderly patients (Fig. 1). As a result, 68.8% of elderly patients were diagnosed in the second half of the series, which directly led to a significant shortening of the median follow-up time in the elderly group (71 months vs 44 months, p = 0.001).

Tumor Characteristics

The majority of CPs have suprasellar components, both in adults and children.[5,20,30,31] Although less common, it is undeniable that purely intrasellar tumors also exist.[23,32] Interestingly, purely intrasellar tumors were not observed in the elderly population, consistent with previous reports.[5] Nonetheless, the percentages of all four resection levels were not significantly different between the two groups (p = 0.541), with similar percentages of patients achieving GTR (90.1% of nonelderly patients vs 87.5% of elderly).

In mixed-age populations, the ratio of adamantinomatous CP to papillary CP (PCP) is approximately 9:1.[33,34] Typically, CPs in pediatric populations are classified as adamantinomatous.[34] However, there is considerable variation in the histological subtype distribution among the elderly population. Iglesias et al. reported that 51% of patients had adamantinomatous CP, 45.1% had PCP, and the remainder had mixed variants.[5] In our series, PCP accounted for 11.8% of nonelderly and 25% of elderly patients. PCP is rarely found in children but is frequently found in adults, especially older individuals. This fact may further support the hypothesis that CPs arise from metaplastic squamous epithelial cells.[2] Considering the differing clinical characteristics among children, younger adults, and elderly individuals, stratified analyses by age are needed in future studies.[5,21,35]

Physical Status

Although the ASA class of the elderly group was significantly higher than that of the younger group, it would be as safe and effective for elderly patients to undergo EES for tumor removal as it would be for patients in the younger group. There were no significant differences in operation time, estimated blood loss, LOS, EOR, or the occurrence of the most common postoperative complications of EES, except for pneumonia and panhypopituitarism. These favorable results are due to our thorough preoperative preparation, which stabilized the comorbidities to the point that participants could tolerate surgery. Thus, adequate preoperative preparation time is essential for optimizing surgical outcomes in the elderly population. With early and proactive management, the long-term outcomes and prognosis of older adults with CPs are comparable to those of younger adults. Furthermore, multivariate regression analysis indicated that tumor calcification and preoperative hydrocephalus, rather than age, significantly influenced overall survival (Table 5). Given the advancement of minimally invasive surgical concepts and the development of multidisciplinary teams, perhaps the delineation of "elderly" warrants reconsideration. Overall, our experience indicates that age is not a decisive factor in deciding whether to undergo surgery.

Hypothalamic Function

The older population had higher Müller grade, which indicates more severe hypothalamic damage. Indeed, older

TABLE 3. Surgical outcomes of 193 patients stratified by age group

	Total	Nonelderly	Elderly	OR (95% CI)	p Value
Visual impairment					
Preop	145 (75.1)	120 (74.5)	25 (78.1)		
Improved	109 (75.2)	92 (76.7)	17 (68.0)	0.647 (0.252–1.657)	0.362
Stable	31 (21.4)	24 (20.0)	7 (28.0)	0.643 (0.241–1.714)	0.375
Deteriorated	5 (3.4)	4 (3.5)	1 (3.1)	1.208 (0.129–11.293)	>0.99
Endocrine impairment					
Preop	140 (72.5)	111 (68.9)	29 (90.6)		
Improved	5 (3.6)	5 (4.5)	0 (0)		0.583
Stable	26 (18.6)	22 (19.8)	4 (13.8)	0.647 (0.204–2.052)	0.457
Deteriorated	109 (77.9)	84 (75.7)	25 (86.2)	2.009 (0.642–6.288)	0.224
Memory impairment					
Preop	13 (6.7)	7 (4.3)	6 (18.8)		
Improved	7 (53.8)	4 (57.1)	3 (50.0)	0.750 (0.084–6.710)	>0.99
Stable	4 (30.8)	2 (28.6)	2 (33.3)	1.250 (0.118–13.240)	>0.99
Deteriorated	2 (15.4)	1 (14.3)	1 (16.7)	1.200 (0.059–24.472)	>0.99
Postop Müller grade					**0.007**
0	45 (23.3)	43 (26.7)	2 (6.3)		
1	101 (52.3)	83 (51.6)	18 (56.3)		
2	47 (24.4)	35 (21.7)	12 (37.5)		
EOR					0.541
GTR	173 (89.6)	145 (90.1)	28 (87.5)		
NTR	13 (6.7)	10 (6.2)	3 (9.4)		
STR	7 (3.6)	6 (3.7)	1 (3.1)		
PR	0 (0)	0 (0)	0 (0)		
Op time, mins	310.4 ± 71.5	307.8 ± 68.3	323.5 ± 86.0		0.257
Estimated blood loss, ml	300 (200)	300 (200)	300 (238)		0.594
LOS, days	15 (10)	15 (8)	15 (22)		0.964

NTR = near-total resection; PR = partial resection; STR = subtotal resection.
Values are shown as number (%), mean ± SD, or median IQR unless indicated otherwise. Boldface type indicates statistical significance ($p < 0.05$).
* New postoperative deficit in patients who did not have that particular deficit preoperatively.

patients were more likely to develop HS after surgery, although the difference was not statistically significant. In addition, 55.9% of patients with preoperative Müller grade 2 and 91.5% of patients with postoperative Müller grade 2 experienced HS. This observation suggests that, in some individuals, the hypothalamus experienced displacement rather than injury, and that radical surgical removal in such cases can be achieved without severely impairing hypothalamic function, provided that the vulnerability of this tissue is carefully taken into account. It also indicates that anatomical and functional outcomes are different aspects that should be evaluated independently. Identifying patients who will develop severe HD after aggressive resection is crucial because it may serve as an intermediate approach for determining whether to pursue radical or conservative surgical approaches.

Visual and Endocrine Function

Visual impairment is a common clinical manifestation of CP. Overall, visual improvement after EES was 70%, similar to the results in other publications.[18,33,36–38] When patients were subcategorized by age, elderly patients were more likely to have visual impairment (74.5% vs 78.1%, p = 0.668) and had a lower rate of postoperative improvement (69.6% vs 53.1%, p = 0.071). Lee and Hwang documented a duration of 5.2 ± 6.8 months in the normal visual field group and 8.9 ± 10.6 months in the abnormal visual field group.[39] According to the research by Mohd-Ilham et al., good postoperative visual acuity at 1 year was significantly correlated with duration of systemic symptoms before consultation.[40] A study by Giovinazzo et al. showed that worse long-term visual field status was associated with older age.[41] Therefore, it is unsurprising that elderly patients had worse preoperative and postoperative visual function than nonelderly patients due to their older age and generally more prolonged duration of symptoms. In other words, early diagnosis and treatment are crucial for the improvement of visual function.

The overall rates of postoperative hypopituitarism and

TABLE 4. Complications and follow-up outcomes stratified by age group

	Total	Nonelderly	Elderly	OR (95% CI)	p Value
New visual deficit*	1/48 (2.1)	1/41 (2.4)	0/7 (0)		>0.99
New hypopituitarism*	44/53 (83.0)	41/50 (82)	3/3 (100)	1.073 (0.991–1.162)	>0.99
New permanent DI†	100/169 (59.2)	81/143 (56.6)	19/26 (73.1)	2.078 (0.822–5.253)	0.117
CSF leakage	16 (8.3)	13 (8.1)	3 (9.4)	1.178 (0.316–4.395)	0.733
Meningitis	15 (7.8)	13 (8.1)	2 (6.3)	0.759 (0.163–3.539)	>0.99
Pneumonia	15 (7.8)	8 (5.0)	7 (21.9)	5.355 (1.784–16.071)	**0.004**
Hyperphagia	43 (22.3)	33 (20.5)	10 (31.3)	1.763 (0.761–4.083)	0.182
Postop hydrocephalus	5 (2.6)	5 (3.1)	0 (0)		0.593
Seizures	4 (2.1)	4 (2.5)	0 (0)		>0.99
Deep vein thrombosis	1 (0.5)	1 (0.6)	0 (0)		>0.99
Epistaxis	1 (0.5)	1 (0.6)	0 (0)		>0.99
Periop mortality	5 (2.6)	4 (2.5)	1 (3.1)	1.266 (0.137–11.715)	>0.99
Deaths during follow-up	13 (6.7)	11 (6.8)	2 (6.3)	0.909 (0.192–4.312)	>0.99
Recurrence	14 (7.3)	14 (8.7)	0 (0)		0.132
Postop BMI, kg/m^2, median (IQR)	26.1 (5.4)	26.2 (5.1)	24.7 (8.2)		0.126
HS	77 (39.9)	61 (37.9)	16 (50)	1.639 (0.765–3.515)	0.237
Follow-up, mos					**0.001**
Median (IQR)	68.5 (33)	71 (27)	44 (36)		
Mean ± SD (range)	59.5 ± 27 (3–110)	62.5 ± 26.5 (3–110)	44.8 ± 24.5 (4–99)		

Values are shown as number (%) unless indicated otherwise. Boldface type indicates statistical significance ($p < 0.05$).
* New postoperative deficit in patients who did not have that particular deficit preoperatively.
† Data were available from 169 patients. Nineteen patients had DI before surgery, and 5 patients died during the perioperative period.

permanent DI in this study were comparable to those reported by other authors.[18,20–23,35,36,38,42] It is worth noting that older patients are more likely to experience pituitary dysfunction, whether it is preoperatively or postoperatively. This finding suggests that we should enhance the management of hormone replacement therapy in older adults.

Postoperative Pneumonia

Postoperative pneumonia is one of the most common complications in older patients and an important factor of deterioration and mortality. In our series, elderly patients with CP demonstrated a higher incidence of pneumonia compared to the nonelderly counterparts (21.9% vs 5.0%, p = 0.004). The increased incidence may be attributed to poorer lung function among the elderly. Nonetheless, the impact of prolonged postoperative hospital LOS should not be disregarded. Hence, it is imperative to direct our attention toward not only the management of the primary illness in elderly individuals but also to implement effective preoperative interventions for pneumonia, including multidisciplinary consultations, meticulous postoperative nursing care, and encouragement of early ambulation. These measures are crucial to enhancing elderly patients' tolerance to surgery, leading to improved quality of life and prognosis.

Recurrence

Previous studies have found that the risk of recurrence of CP is highest during the first 3–5 years after surgery.[30,43] In our series, the overall recurrence rate was 7.3% at a median follow-up of 68.5 months. Compared with the rates reported the adult-onset CP series in the literature,[22,30,39] our lower recurrence rate was mainly attributed to the higher GTR rate. Interestingly, when we stratified by age, we found that all recurrences occurred in younger adults. A low rate of recurrence and limited sample size make it challenging to find a significant difference. Tumors appear to be more stable in the older age group. Because EOR was similar between the groups, the lower recurrence rate in older patients might be attributed to the shorter median follow-up period (71 months vs 44 months, p = 0.001). However, it is worth noting that the same phenomenon has been observed in elderly populations with other tumors such as pituitary tumors.[44,45] These phenomena imply that the growth rate of residual tumors may be influenced by patient age. There is a need for additional investigation.

Because of indolent lesions, remaining lifespan expectancy, and adverse effects, radiotherapy was not routinely recommended to older adults after surgery. Instead, they received systematic and close MRI follow-up, and radiotherapy was considered only when the tumor progressed. Nonetheless, the recurrence rate among older participants remains lower than that in younger participants. The favorable outcome strongly suggests that a strategy of delaying radiotherapy in the elderly seems to be feasible.

Limitations

The findings of this study have to be seen in light of some limitations. First, the retrospective nature of the

TABLE 5. Univariate and multivariate Cox regression model of factors associated with overall survival in patients with CP

Variable	Univariate			Multivariate		
	HR	95% CI	p Value	HR	95% CI	p Value
Sex	1.456	0.562–3.775	0.439			
Age group	1.429	0.405–5.039	0.579	0.935	0.250–3.491	0.935
Pathology	0.868	0.198–3.800	0.851			
Consistency			0.252			
Cystic						
Solid	0.180	0.022–1.449	0.107			
Mixed	0.996	0.373–2.664	0.994			
Tumor vol	1.028	1.005–1.051	**0.017**	1.016	0.990–1.042	0.232
Calcification	3.808	1.271–11.414	**0.017**	3.406	1.859–27.233	**0.038**
Preop hydrocephalus	3.848	1.436–10.313	**0.007**	3.688	1.310–10.386	**0.013**
Preop DI	2.540	0.727–8.873	0.144			
Preop BMI	1.057	0.923–1.211	0.421			
Symptom duration	1.005	0.986–1.024	0.630			
Location			0.823			
Sellar						
Sellar-suprasellar	1.514	0.190–12.082	0.695			
Suprasellar	1.146	0.142–9.239	0.898			
Preop Müller grade			0.621			
0						
1	1.350	0.257–7.105	0.723			
2	1.976	0.411–9.499	0.395			
ASA class			0.981			
I						
II	1.046	0.292–3.747	0.945			
III	1.102	0.239–5.074	0.900			
IV	1.547	0.198–12.067	0.677			
EOR			0.532			
GTR						
NTR	0.478	0.131–1.744	0.264			
STR	0.518	0.053–5.034	0.571			

Boldface type indicates statistical significance ($p < 0.05$).

analysis carries inherent limitations in our study. Second, our sample size of elderly patients was limited, making the ability to reach statistical significance between the groups less powerful. Finally, because elderly patients were mainly seen in the latter part of the decade, there was a notable disparity in the median follow-up durations between the two groups. Consequently, the follow-up time for elderly patients may have been too short to capture recurrences or additional long-term complications. It is reassuring that high consistency and completeness of results will compensate for this limitation to some extent.

Conclusions

The study results support the feasibility of using EES as a treatment approach for CP in elderly patients. With appropriate perioperative management, EES does not significantly increase mortality and, in selected populations, is well tolerated by patients. Although it is a safe procedure, elderly patients had a higher complication rate than nonelderly patients, mainly due to pneumonia. Considering that patients of various age groups exhibit distinct characteristics, a stratified analysis based on age is recommended. Given the slow growth rate of elderly CPs, radiotherapy is not routinely recommended for residual tumors unless progression occurs.

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References

1. Oskouian RJ, Samii A, Laws ERJ Jr. The craniopharyngioma. *Front Horm Res*. 2006;34:105-126.
2. Bunin GR, Surawicz TS, Witman PA, Preston-Martin S, Davis F, Bruner JM. The descriptive epidemiology of craniopharyngioma. *J Neurosurg*. 1998;89(4):547-551.
3. Nielsen EH, Feldt-Rasmussen U, Poulsgaard L, et al. Incidence of craniopharyngioma in Denmark (n = 189) and estimated world incidence of craniopharyngioma in children and adults. *J Neurooncol*. 2011;104(3):755-763.
4 United Nations Department of Economic and Social Affairs. *World Social Report 2023: Leaving No One Behind In An Ageing World*. United Nations; 2023. Accessed June 30, 2024. https://desapublications.un.org/publications/world-social-report-2023-leaving-no-one-behind-ageing-world
5. Iglesias P, Nocete I, Moure Rodríguez MD, et al. Craniopharyngioma in the elderly: a multicenter and nationwide study in Spain. *Neuroendocrinology*. 2021;111(10):925-936.
6. Kwang Sheng N, Wan Hitam WH. Acute blindness in the elderly with craniopharyngioma. *Cureus*. 2022;14(7):e26880.
7. Schroeder LE, Kritselis M, Lala N, Boxerman J, Alhusaini S. Pearls & oy-sters: Adult-onset craniopharyngioma presenting with cognitive dysfunction and obstructive hydrocephalus. *Neurology*. 2023;101(21):974-978.
8. Berkley JA, Versteeg AC, Mwangi I, Lowe BS, Newton CR. Indicators of acute bacterial meningitis in children at a rural Kenyan district hospital. *Pediatrics*. 2004;114(6):e713-e719.
9. Dripps RD. New classification of physical status. *Anesthesiology*. 1963;24:111.
10. van Santen HM, van Schaik J, van Roessel IMAA, Beckhaus J, Boekhoff S, Müller HL. Diagnostic criteria for the hypothalamic syndrome in childhood. *Eur J Endocrinol*. 2023;188(2):lvad009.
11. Goodwin S. The practical guide to the identification, evaluation and treatment of overweight and obesity in adults. *Clin Nurse Spec*. 2002;16:164.
12. Fahlbusch R, Schott W. Pterional surgery of meningiomas of the tuberculum sellae and planum sphenoidale: surgical results with special consideration of ophthalmological and endocrinological outcomes. *J Neurosurg*. 2002;96(2):235-243.
13. Mortini P, Losa M, Pozzobon G, et al. Neurosurgical treatment of craniopharyngioma in adults and children: early and long-term results in a large case series. *J Neurosurg*. 2011;114(5):1350-1359.
14. de Vries F, Lobatto DJ, Verstegen MJT, van Furth WR, Pereira AM, Biermasz NR. Postoperative diabetes insipidus: how to define and grade this complication? *Pituitary*. 2021;24(2):284-291.
15. Kassam AB, Gardner PA, Snyderman CH, Carrau RL, Mintz AH, Prevedello DM. Expanded endonasal approach, a fully endoscopic transnasal approach for the resection of midline suprasellar craniopharyngiomas: a new classification based on the infundibulum. *J Neurosurg*. 2008;108(4):715-728.
16. Evans WA. An encephalographic ratio for estimating the size of the cerebral ventricles: further experience with serial observations. *Am J Dis Child*. 1942;64(5):820-830.
17. Müller HL, Gebhardt U, Teske C, et al. Post-operative hypothalamic lesions and obesity in childhood craniopharyngioma: results of the multinational prospective trial KRANIOPHARYNGEOM 2000 after 3-year follow-up. *Eur J Endocrinol*. 2011;165(1):17-24.
18. Fan J, Liu Y, Pan J, et al. Endoscopic endonasal versus transcranial surgery for primary resection of craniopharyngiomas based on a new QST classification system: a comparative series of 315 patients. *J Neurosurg*. 2021;135(5):1298-1309.
19. Gardner PA, Prevedello DM, Kassam AB, Snyderman CH, Carrau RL, Mintz AH. The evolution of the endonasal approach for craniopharyngiomas. *J Neurosurg*. 2008;108(5):1043-1047.
20. Jeswani S, Nuño M, Wu A, et al. Comparative analysis of outcomes following craniotomy and expanded endoscopic endonasal transsphenoidal resection of craniopharyngioma and related tumors: a single-institution study. *J Neurosurg*. 2016;124(3):627-638.
21. Cavallo LM, Frank G, Cappabianca P, et al. The endoscopic endonasal approach for the management of craniopharyngiomas: a series of 103 patients. *J Neurosurg*. 2014;121(1):100-113.
22. 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*. 2013;119(5):1194-1207.
23. Solari D, d'Avella E, Agresta G, et al. Endoscopic endonasal approach for infradiaphragmatic craniopharyngiomas: a multicentric Italian study. *J Neurosurg*. 2022;138(2):522-532.
24. Lederman GS, Recht A, Loeffler JS, Dubuisson D, Kleefield J, Schnitt SJ. Craniopharyngioma in an elderly patient. *Cancer*. 1987;60(5):1077-1080.
25. Russell RW, Pennybacker JB. Craniopharyngioma in the elderly. *J Neurol Neurosurg Psychiatry*. 1961;24(1):1-13.
26. Schonder AA. Craniopharyngioma in the elderly patient: case report. *J Am Geriatr Soc*. 1975;23(12):545-547.
27. Hoffmann A, Boekhoff S, Gebhardt U, et al. History before diagnosis in childhood craniopharyngioma: associations with initial presentation and long-term prognosis. *Eur J Endocrinol*. 2015;173(6):853-862.
28. Dillingham CM, Milczarek MM, Perry JC, Vann SD. Time to put the mammillothalamic pathway into context. *Neurosci Biobehav Rev*. 2021;121:60-74.
29. Senova S, Fomenko A, Gondard E, Lozano AM. Anatomy and function of the fornix in the context of its potential as a therapeutic target. *J Neurol Neurosurg Psychiatry*. 2020;91(5):547-559.
30. Turel MK, Tsermoulas G, Gonen L, et al. Management and outcome of recurrent adult craniopharyngiomas: an analysis of 42 cases with long-term follow-up. *Neurosurg Focus*. 2016;41(6):E11.
31. Wu J, Pan C, Xie S, et al. A propensity-adjusted comparison of endoscopic endonasal surgery versus transcranial microsurgery for pediatric craniopharyngioma: a single-center study. *J Neurosurg Pediatr*. 2021;29(3):325-334.
32. Jamshidi AO, Beer-Furlan A, Prevedello DM, et al. A modern series of subdiaphragmatic craniopharyngiomas. *J Neurosurg*. 2018;131(2):526-531.
33. Nie C, Ye Y, Wu J, Zhao H, Jiang X, Wang H. Clinical outcomes of transcranial and endoscopic endonasal surgery for craniopharyngiomas: a single-institution experience. *Front Oncol*. 2022;12:755342.
34 Pekmezci M, Louie J, Gupta N, et al. Clinicopathological characteristics of adamantinomatous and papillary craniopharyngiomas: University of California, San Francisco experience 1985-2005. *Neurosurgery*. 2010;67(5):1341-1349.
35. Pang JC, Chung DD, Wang J, et al. Characteristics and outcomes in pediatric versus adult craniopharyngiomas: a systematic review and meta-analysis. *Neurosurgery*. 2023;92(6):1112-1129.
36. Komotar RJ, Starke RM, Raper DM, Anand VK, Schwartz TH. Endoscopic endonasal compared with microscopic transsphenoidal and open transcranial resection of craniopharyngiomas. *World Neurosurg*. 2012;77(2):329-341.
37. Moussazadeh N, Prabhu V, Bander ED, et al. Endoscopic endonasal versus open transcranial resection of craniopharyngiomas: a case-matched single-institution analysis. *Neurosurg Focus*. 2016;41(6):E7.
38. Wannemuehler TJ, Rubel KE, Hendricks BK, et al. Outcomes in transcranial microsurgery versus extended endoscopic endonasal approach for primary resection of adult craniopharyngiomas. *Neurosurg Focus*. 2016;41(6):E6.

39. Lee MJ, Hwang JM. Initial visual field as a predictor of recurrence and postoperative visual outcome in children with craniopharyngioma. *J Pediatr Ophthalmol Strabismus*. 2012; 49(1):38-42.
40. Mohd-Ilham IM, Ahmad-Kamal GR, Wan Hitam WH, Shatriah I. Visual presentation and factors affecting visual outcome in children with craniopharyngioma in east coast states of peninsular Malaysia: a five-year review. *Cureus*. 2019;11(4):e4407.
41. Giovinazzo S, Oliverio G, Cotta OR, et al. Persistent severe visual field impairment is associated with obesity and tumour invasiveness, but not with pituitary dysfunction, in patients with craniopharyngioma. *Endocrine*. 2023;81(1):50-53.
42. Gallotti AL, Barzaghi LR, Albano L, et al. Comparison between extended transsphenoidal and transcranial surgery for craniopharyngioma: focus on hypothalamic function and obesity. *Pituitary*. 2022;25(1):74-84.
43. Zoicas F, Schöfl C. Craniopharyngioma in adults. *Front Endocrinol (Lausanne)*. 2012;3:46.
44. Tanaka Y, Hongo K, Tada T, Sakai K, Kakizawa Y, Kobayashi S. Growth pattern and rate in residual nonfunctioning pituitary adenomas: correlations among tumor volume doubling time, patient age, and MIB-1 index. *J Neurosurg*. 2003; 98(2):359-365.
45. Shinya Y, Atkinson JLD, Erickson D, et al. Correlation of older age with better progression-free survival despite less aggressive resection in nonfunctioning pituitary adenomas. *J Neurosurg*. 2024;141(3):781-789.

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Conception and design: Bao, Zhou, Tang. Acquisition of data: Pan, Cao, Ouyang, Tan, Wang. Analysis and interpretation of data: Wu, Xie. Drafting the article: Bao, Pan. Critically revising the article: Hong, Bao, Pan. Approved the final version of the manuscript on behalf of all authors: Hong. Statistical analysis: Wu, Xie.

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