



Original Article

Is Postoperative Radiotherapy Needed in the Management of Adult Craniopharyngiomas?

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ABSTRACT: Background: The optimal treatment of adult craniopharyngioma (CP) remains controversial. Although benign, these tumors tend to recur locally. The choice between gross total resection (GTR) versus subtotal resection (STR) with adjuvant or delayed radiotherapy (RT) is debated. The objective of this study is to review our experience with adult CPs over a 20-year period and identify an optimal management strategy. **Methods:** From 1999 to 2020, we reviewed all patients diagnosed with CP at our institution. We collected data regarding tumor characteristics, treatments, and toxicity. Disease progression was defined as growth on imaging. Descriptive statistics were used to assess patient characteristics. The Kaplan Meier method was used to assess progression-free survival (PFS) and corresponding 95% confidence intervals (CI) from the time since treatment initiation. **Results:** Twenty-four patients with a median age of 50 were included in this study. The median follow-up was 85 months. Seven patients had initial GTR, 10 STR, and 7 STR + RT. The overall 5-year PFS was 56% (95% CI: 38–83%): 100% in the STR + RT group, 69% in the GTR group, and 18% in the STR group ($p = 0.01$). Of the 17 patients initially treated with surgery alone, 3 with GTR and 6 with STR required salvage RT at a median of 46 months, with no further progression after salvage RT. **Conclusions:** Our study underscores the importance of RT for local control and suggests that STR + RT should be considered a viable option in the management of these tumors as it may be associated with improved PFS compared to surgery alone.

RÉSUMÉ : La radiothérapie postopératoire : nécessaire dans la prise en charge des craniopharyngiomes chez l'adulte? Contexte : Le traitement optimal des craniopharyngiomes (CP) chez l'adulte suscite la controverse. Bien que ces tumeurs soient bénignes, elles comportent des risques de récurrence locale. Il sera donc question du choix entre l'exérèse totale brute (ETB) et la résection partielle (RP) suivie de radiothérapie (RT) d'appoint ou de radiothérapie différée. Pour ce faire, l'étude visait à passer en revue l'expérience du traitement des CP chez des adultes, sur une période de plus de 20 ans, et à dégager la meilleure stratégie de prise en charge qui soit. **Méthode :** Ont été examinés les dossiers de tous les patients chez qui avait été posé un diagnostic de CP, de 1999 à 2020, dans l'établissement des auteurs. Il y a eu collecte de données sur les caractéristiques des tumeurs, les traitements et leur toxicité. L'évolution de la maladie était définie par le développement d'une masse à l'imagerie. L'évaluation des caractéristiques des patients repose sur des statistiques descriptives. La méthode d'estimation de Kaplan-Meier a servi à l'évaluation de la survie sans évolution (SSE) et des intervalles de confiance (IC) à 95 % correspondants, établis depuis le début du traitement. **Résultats :** L'étude comptait 24 dossiers de patients d'un âge médian de 50 ans, et la durée médiane du suivi était de 85 mois. Au départ, 7 patients ont subi une ETB; 10, une RP; et 7, une RP+RT. La SSE générale au bout de 5 ans était de 56 % (IC à 95 % : 38–83 %) et elle se répartissait ainsi : 100 % dans le groupe de RP + RT; 69 % dans le groupe d'ETB et 18 % dans le groupe de RP ($p = 0,01$). Sur les 17 patients traités initialement par la chirurgie seule, 9 d'entre eux, soit 3 par l'ETB et 6 par la RP, ont dû subir une RT de rattrapage au bout d'une période médiane de 46 mois, sans évolution ultérieure de la tumeur. **Conclusion :** Les résultats de l'étude font ressortir l'importance de la RT dans la lutte contre la réapparition locale du CP, et donnent à penser que la RP + RT devrait être considérée comme une intervention offrant une perspective favorable dans la prise en charge de ce type de tumeurs, le traitement pouvant être associé à une amélioration de la SSE, comparativement à la chirurgie seule.

Keywords: Craniopharyngioma; Radiotherapy; Surgery; Adult; Toxicity

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Table 1: Patient characteristics overall and stratified by treatment

Characteristic	Overall (n = 24)	GTR (n = 7)	STR (n = 10)	STR + RT (n = 7)
Female, n (%)	13 (54.2)	5 (71.4)	4 (40.0)	4 (57.1)
Male, n (%)	11 (45.8)	2 (28.6)	6 (60.0)	3 (42.9)
Age (median, IQR)	49.5 (27.0-63.5)	29.0 (20.0-41.0)	61.5 (49.0-69.0)	50.0 (48.0-56.0)
Adamantinomatous histology, n (%)	22 (91.7)	7 (100)	9 (90.0)	6 (85.7)
Papillary histology, n (%)	2 (8.3)	0 (0)	1 (10.0)	1(14.3)
Maximal diameter at time of treatment, mean (SD)	3.1 (1.4)	2.6 (1.0)	3.4 (1.6)	3.0 (1.5)
Maximal diameter at time of treatment, median (IQR)	2.9 (2.3-3.5)	3.0 (1.6-3.4)	3.0 (2.4-4.5)	2.7 (1.6-3.5)

n: number; IQR: interquartile range; SD: standard deviation; GTR: gross total resection; STR: subtotal resection; RT: radiotherapy.

Introduction

The optimal management of adult craniopharyngioma (CP) remains controversial. These rare intracranial tumors arise from remnants of Rathke's pouch in the sellar and parasellar areas.¹ Although benign, CP can cause significant morbidity and mortality¹ through compression of important adjacent structures such as the hypothalamic–pituitary axis, optic apparatus, and third ventricle. CP has a bimodal distribution with peak incidence at ages 5–14 and 50–74.² Data regarding the management and outcomes of adult CP is limited.³ Initial treatment options for CP include gross total resection (GTR) or subtotal resection (STR) with or without adjuvant or delayed radiotherapy (RT). Additional treatments with intracavitary radioisotope brachytherapy or chemotherapy, stereotactic radiosurgery (SRS),^{4,5} and systemic therapy have also been investigated.^{6,7} With this multitude of options, the optimal upfront management strategy remains debatable.^{1,7–9}

Treatment of CP is challenging, particularly due to its high recurrence rate and morbidity associated with a total resection and with disease recurrence.^{7,8,10,11} In most series, recurrences are seen, on average, in 20% of patients undergoing GTR and 60% of patients undergoing STR.^{7,8,12} While resection helps alleviate some of the compressive symptoms caused by CP, it can also cause iatrogenic complications. GTR can result in significant morbidity, particularly pan-hypopituitarism, diabetes insipidus, hypothalamic obesity, and visual impairment.^{8,13,14} Although these issues may be present prior to surgery, they may worsen in 40–100% of patients undergoing resection.^{8,9,15} To avoid extensive sequelae from GTR, one may opt for STR followed by observation. However, this treatment strategy would carry a high risk of recurrence and need for salvage treatment. The role of RT thus far has been to decrease the risk of recurrence, particularly after incomplete resection.^{1,8,11,13,16–18} However, the optimal timing of RT has yet to be established, as it may be used immediately after STR or as salvage with or without preceding debulking.¹

The purpose of this study is to present our institution's experience with the treatment of adult CP and compare disease control outcomes based on the initial treatment strategy.

Methods

After obtaining institutional review board approval, data were collected retrospectively through chart review. All patients diagnosed with adult CP at our institution from 1999 to 2020 were identified through a pathology database search. Data collected included age at diagnosis, gender, tumor location, histologic subtype, size prior

to treatment and after initial surgery, initial treatment modality and dates, RT gross tumor volume (GTV), RT dose, relapse dates and salvage treatments, last follow-up dates and imaging, secondary neoplasms, and, when available, long-term visual, endocrine, and cerebrovascular outcomes.

Twelve patients had an initial craniotomy, and the others had a transsphenoidal resection of their CP. The extent of resection was determined intraoperatively and on postoperative imaging studies. Seven patients received adjuvant RT and another nine received salvage RT. The median delivered RT dose was 54 Gy (range: 46.8–54) in 1.8–2 Gy per fraction. All patients received linear accelerator-based stereotactic intensity-modulated RT (IMRT) with 6 MV photons. The earliest RT treatment in this cohort was in 2008. Patients were simulated supine with a thermoplastic mask for immobilization. Thin-cut contrast-enhanced computed tomography (CT) and, when available, magnetic resonance imaging (MRI) simulation scans with 1–3 mm slices were done. Image registration and fusion were done with diagnostic contrast-enhanced preoperative and postoperative CT and MRI. Treatment volumes included a GTV, defined as the tumor seen on simulation scans, and a planning target volume (PTV). A 2–15 mm margin was used for PTV expansion, with 88% (14/16) ranging between 2 and 5 mm. Image-guidance RT was done using the ExacTrac system or weekly cone-beam CT. Images were monitored closely for potential tumor changes requiring cyst drainage or re-planning.

Local control was evaluated on follow-up contrast-enhanced CT and/or MRI every 6–12 months. Disease progression was defined as growth on imaging requiring further intervention. Physician follow-up included evaluations by ophthalmology, endocrinology, neurosurgery, and radiation oncology, if treated with RT. Follow-up time was measured from initial treatment to last imaging, physician or laboratory follow-up documentation, or death, whichever occurred last.

Data were collected with Microsoft Excel 2021. Statistical analyses were performed using SAS version 9.0 (SAS Institute, Cary, NC) and R (R foundation for statistical computing, Vienna, Austria). Descriptive statistics were used to assess patient characteristics. The Kaplan Meier curve was used to assess progression-free survival (PFS) and corresponding 95% confidence intervals (CI) from time since treatment initiation in the overall study population and by treatment group. Log-rank test was used to compare PFS between treatment arms up to 10 years.

Results

We identified 24 patients with adult CP (Table 1). Upon archived chart review, one patient was found to have had a GTR for a CP at

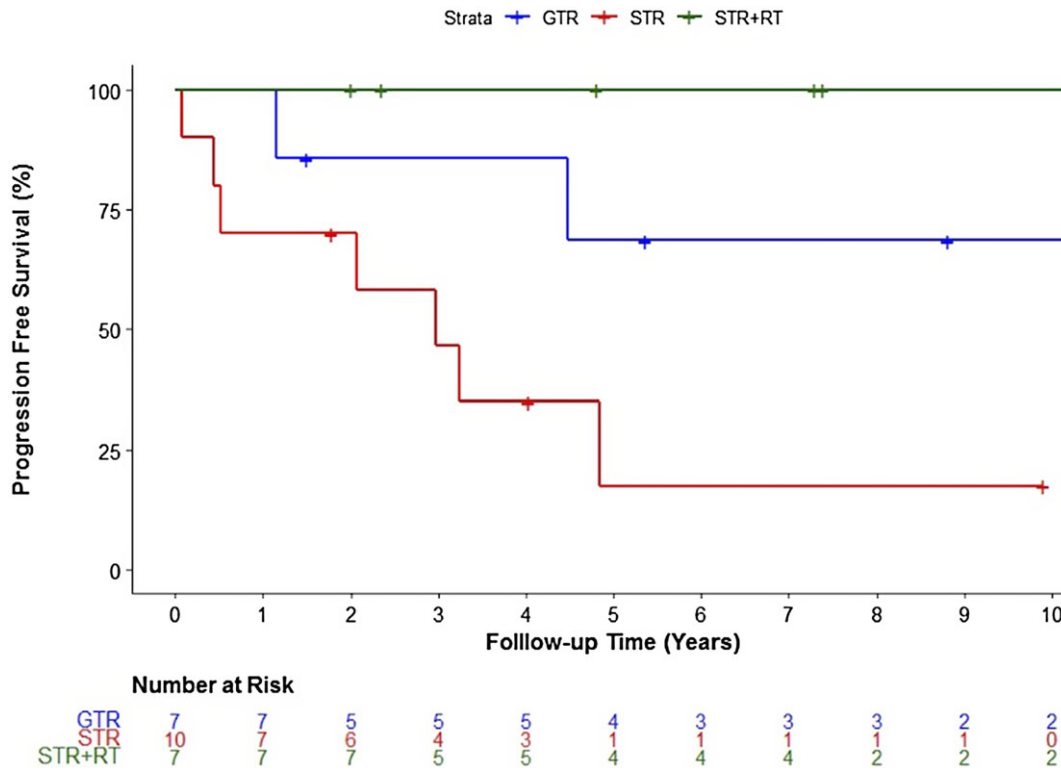


Figure 1: Kaplan Meier for progression-free survival stratified by treatment group with the start of follow-up corresponding to treatment initiation. GTR: gross total resection; STR: subtotal resection; RT: radiotherapy. Log rank p-value = 0.01

an outside institution at the age of 13. All other patients were 18 years of age or older. Presenting signs and symptoms included visual deficits, behavioral or cognitive changes, headaches, and endocrine disturbances in 16, 9, 8, and 6 patients, respectively. Six tumors were abutting the optic chiasm, and nine were extending to the third ventricle.

Initial Treatment

Seven patients had an initial GTR, 10 had an initial STR alone, and 7 had an initial STR followed by adjuvant RT. Of the GTR patients, four had a transsphenoidal surgery (TSS) while three had craniotomies. Of the STR alone patients, six had a TSS, and four had a craniotomy. Of the STR and adjuvant RT patients, two had a TSS, and five had craniotomies. Patients undergoing GTR did not receive adjuvant RT. The median residual disease volume for patients who had initial STR alone was 3.2 cm³. Patients in the STR plus adjuvant RT group-initiated RT shortly after STR (mean: 2.9 months, standard deviation: 2.5 months). The median GTV volume for patients who received RT at our institution was 6.4 cm². Two patients did not have complete information regarding their RT treatment as they were treated at another institution. RT dose and duration were, however, available for all patients. Patients managed with initial surgery alone required a median of two surgeries for the management of their CP (range: 1–5). Patients who received adjuvant RT required no more than one surgery, meaning the only surgery required for the management of their CP was the initial resection.

Follow-up

The median follow-up was 85 months (range: 19–258). Follow-up imaging was available for all patients included in the study, with

the latest imaging being at a median of 77 months after initial treatment (range: 14–255). Median follow-up since adjuvant RT was 71 months (range 15–148) and 37 months for salvage RT (range 3–111).

Outcomes

A total of 4 out of 7 patients (57%) with initial GTR and 7 out of 10 patients (70%) with initial STR had a relapse. None of the patients treated with STR followed by adjuvant RT developed disease progression or relapse. Of the 17 patients initially treated with surgery alone, 9 (53%, 3 GTR and 6 STR) underwent salvage RT due to disease progression at a median time of 46 months. There was no disease progression after salvage RT. Of the 10 patients treated with STR alone initially, 5 underwent a median of 2 additional surgeries (range: 1–3), whereas patients having undergone STR with adjuvant RT required no additional surgeries. Four patients treated with initial GTR required a median of one additional surgery (range: 1–2). None of the patients having undergone STR with immediate adjuvant RT required further resection.

The 3-year overall PFS was 73% (95% CI: 57–94%). The 3-year PFS was 100% in the STR plus RT group, 86% (95% CI: 63–100%) in the GTR group, and 47% (95% CI: 23–94%) in the STR alone group. The 5-year overall PFS was 56% (95% CI: 38–83%). The 5-year PFS was 100% in the STR plus RT group, 69% (95% CI: 40–100%) in the GTR group, and 18% (95% CI: 3–91%) in the STR alone group (Figure 1).

Toxicity

RT was well-tolerated with only mild acute toxicity such as headaches in nine patients, fatigue in nine patients, nausea and vomiting in two patients, and ocular dryness in two patients. One patient could not complete RT due to shunt dysfunction requiring repair

and stopped RT at 46.8 Gy. Endocrine disturbances were seen in 13 patients after surgery and 3 patients after RT. Four patients had no endocrine changes after treatment. Seven patients had no visual changes after treatment, five had improved vision after surgery, and two after RT. Six patients had worsening of their vision after surgery. Two patients were reported to have a cerebrovascular event (ischemic stroke) at the age of 70. One 2 years after adjuvant RT, and the other 4 years after salvage RT. The first patient had undergone multiple shunt repairs after salvage RT, while the second had a poor baseline performance status prior to treatment and had preexisting cardiac comorbidities and major cognitive disorder. No secondary neoplasm or malignant transformation was noted. There were no treatment-related deaths. Further detailed toxicity outcomes are reported in Table 2.

Discussion

As CP patients typically live a near-normal lifespan,¹⁹ disease control after initial treatment and the use of salvage interventions need to be balanced with iatrogenic treatment toxicity. Recurrences are seen in up to 62% of patients having undergone GTR⁷ and up to 75% with STR^{7,18} at 10-year follow-up. In our cohort, we observed comparable recurrence rates after surgery with 57% seen after GTR alone and 70% after STR alone. The extent of surgery has not been shown to impact on survival,^{19,20} and conflicting data exist regarding the morbidity associated with GTR versus STR. While some reports suggest no difference in long-term visual, endocrine, and hypothalamic outcomes in adults treated with STR compared to GTR,^{18,21} others show increased postoperative and long-term morbidity²² with GTR, particularly regarding endocrine dysfunction.^{13,23} However, with the high recurrence rates seen with STR alone, adjuvant RT has been used and shown to compensate for a more limited surgical approach by decreasing recurrence rates to that of a GTR.^{1,11,13,18}

Our results suggest that RT is effective and may even offer a potential benefit over surgery alone in the management of adult CP. STR followed by adjuvant RT as a definitive management, compared to resection alone, seems to result in superior PFS and obviate the need for subsequent surgical interventions. In addition, in our experience, salvage RT resulted in no disease progression upon a median follow-up of 37 months postRT. Interestingly, adjuvant RT is underutilized in adults compared to the pediatric population. Lehigh et al. reported significantly higher rates of adjuvant RT in the pediatric population (34.3% compared to 22.3% in adults), as well as a better overall survival (OS) and a lower 90-day mortality.²⁰ In our cohort, the median age of patients having undergone an initial GTR was lower than those having undergone STR (27 versus 62 and 50). However, no correlation was found between age and disease progression, and none has been reported in the literature.²⁰

Morbidity from CP, regardless of treatment, remains high.^{1,22} In our study, all patients having received either adjuvant or salvage RT remained with their disease controlled. Toxicity profiles also did not appear to differ significantly compared to surgical management alone. In fact, endocrine dysfunction seems to be more frequently seen in GTR patients.^{13,23} In our cohort, development or worsening of endocrine function was observed in 4/7 (57%) patients having had an initial GTR. In general, endocrine function deficits were seen more commonly in patients postresection with 13 patients (54%) developing deficits postsurgery and 3 (19%) postRT (Table 2). Schoenfeld et al. also reported similar outcomes with panhypopituitarism seen in 56% of GTR patients and 13% of

STR + RT patients.²⁴ Visual outcomes were improved in five patients postsurgery and two patients postRT. Due to risks associated with attempting GTR, some centers favor opting for a STR followed by observation. The main drawbacks of undergoing STR without immediate adjuvant RT are higher recurrence rates and need for additional surgical interventions. In our cohort, out of the 10 patients treated with STR alone, 6 recurred and all but one required a median of two additional surgeries prior to salvage RT. The risk of disease-progression-related and surgical morbidity is thus increased. After repeat resections and before salvage RT, two patients had worse visual defects, three had worse endocrine deficits, and one developed seizures. Four patients treated initially with GTR alone required additional surgery, with two of them developing worsened visual outcomes after re-resection. As in our study, disease control after adjuvant versus salvage RT remains similar.^{25,26} Where adjuvant RT may be better than salvage is in regards to morbidity. As seen in our cohort, patients recurring after STR often undergo additional surgeries and may develop worsening symptoms after relapse. Although disease control appears to be similar with adjuvant versus salvage RT, additional surgeries prior to RT may result in worse progression-free survival.²⁷ Literature regarding the quality of life and toxicity from adjuvant versus salvage RT is limited. Moon et al.²⁵ looked specifically at this issue and found that visual field and acuity were better with adjuvant RT, as well as improvement of diabetes insipidus. Interestingly, this is similar to our findings with increased visual morbidity after relapse. Pemberton et al.,²⁶ on the other hand, did not find any significant difference in the quality of life comparing immediate RT to salvage. Lastly, although not seen in the adult population, Regine et al.²⁸ reported worse survival outcomes in the pediatric population when RT was given upon recurrence versus upon initial treatment. The decision to favor adjuvant versus delayed RT remains to be elucidated by larger prospective studies. This being said, most patients having undergone STR alone will eventually recur, and the main benefit of adjuvant RT is to avoid worsening of morbidity from disease progression and/or re-resection. Ultimately, decision regarding adoption of one strategy versus the other remains to be made with the patient and multidisciplinary team. The main concerning long-term RT-related toxicities are cognitive deterioration, cerebrovascular events, and secondary tumors.²⁷ In our cohort, two cerebrovascular events were noted, and there were no secondary neoplasms. With increasingly precise RT allowing for smaller treatment volumes and sparing of surrounding structures, these risks are lowered.^{29,30} It is also difficult to differentiate effects of tumor growth, hormonal treatment, surgical procedures, and RT on cognitive changes,²⁴ as deterioration is often multifactorial. Direct comparison of surgery, RT, and comorbidities due to endocrinopathies in regard to the risk of cerebrovascular events is also challenging,²⁴ and no evidence exists to this date showing superiority of surgery versus RT. Disease control outcomes comparing GTR to STR with adjuvant RT are also conflicting. While some show improved control with GTR at the cost of increased toxicity,²³ others show similar or better clinical outcomes with STR and adjuvant RT.^{11,13,31–33} Furthermore, adjuvant RT has no deleterious impact on overall survival³¹ and may in fact provide a survival advantage over surgery alone.^{16,19} These findings point towards an overall superiority of STR followed by adjuvant RT for the initial management of adult CP.

In a population of patients with a long survival, minimizing the need for subsequent surgeries is important. Quality of life is significantly deterred with repeated surgery.^{3,9,14,15,34} Surgeries for recurrences also carry a higher perioperative mortality rate and lower

Table 2: Treatment toxicity outcomes

Patient	Age and gender	Initial treatment (type of surgery)	Time to disease progression (months)	Salvage RT	Follow-up (months)	Visual outcomes	Endocrine outcomes	Comments
1	41F	GTR (craniotomy)	53	Yes	175	No change	Post-op: DI and SIADH; Post-RT: PHP	Mild fatigue during RT; dry eyes postRT; PHP diagnosed 9 years postRT; RT in 2012
2	18M	STR (craniotomy)	24	Yes	189	Post-op: VF deficit	Post-op: PHP	Presented with GHD; RT in 2017
3	48F	STR + RT (TSS)	–	–	161	No change	Post-RT: central hypoT4 and GHD	Endocrine deficits developed 4 years postRT; RT in 2008
4	65F	STR (TSS)	6	Yes	121	No change	Post-op: PHP	Mild fatigue during RT; stopped RT early due to shunt repair; ischemic stroke 2 years postRT; RT in 2010
5	50M	STR + RT (craniotomy)	–	–	150	Post-op: decreased VA	Post-op: central hypoT4 and AI	Mild headache and N/V during RT; RT in 2010
6	67F	STR (TSS)	–	–	120	Post-op: VF deficit	N/A	
7	73F	STR (craniotomy)	6	No	178	No change	No change	
8	20F	GTR (craniotomy)	–	–	108	Post-op: VF improvement	Post-op: central hypoT4	
9	65F	STR + RT (craniotomy)	–	–	89	N/A	Post-op: SIADH	Mild fatigue, headaches, and N/V during RT; RT in 2012
10	33F	GTR (TSS)	149	Yes	258	N/A	Post-op: PHP	Mild fatigue and headaches during RT; ischemic stroke 5 years posttreatment; RT in 2012
11	19F	STR + RT (craniotomy)	–	–	88	No change	Post-op: PHP	Mild fatigue and headaches during RT; RT in 2014
12	58F	STR (TSS)	35	Yes	83	Post-op: VF improvement	Post-RT: central hypoT4	Mild headaches during RT; dry eyes postRT; RT in 2017
13	62F	GTR (craniotomy)	–	–	64	Post-op: decreased VA	N/A	
14	49M	STR (craniotomy)	58	Yes	64	Post-op: VA improvement	Post-op: hypogonadism	Two seizures post-op; RT in 2021
15	69M	GTR (TSS)	41	Yes	61	Post-op: VF deficit	N/A	Mild fatigue and headaches during RT; RT in 2019
16	55M	STR + RT (TSS)	–	–	63	No change	No change	Mild fatigue during RT; RT in 2017
17	25M	STR (TSS)	15	Yes	58	Post-RT: VF improvement	No change	Mild fatigue and moderate headaches during RT; RT in 2018
18	22M	STR (TSS)	–	–	52	N/A	Post-op: PHP	Post-op meningitis
19	52M	STR (TSS)	1	Yes	33	Post-RT: VA and VF improvement	Post-op: AI and central hypoT4	RT in 2020
20	56M	STR + RT (craniotomy)	–	–	29	Post-op: VF improvement	Post-op: AI and hypogonadism	Mild fatigue and headaches during RT; RT in 2019
21	13F	GTR (TSS)	218	No	247	Post-op: decreased VA	Post-op: PHP	
22	48F	STR + RT (craniotomy)	–	–	25	No change	Post-op: DI, AI and central hypoT4	Moderate headaches during RT; RT in 2019
23	69M	STR (craniotomy)	–	–	22	Post-op: VA improvement	N/A	
24	29M	GTR (TSS)	–	–	19	No change	No change	CSF leak × 2 post-op

F: female; M: male; TSS: trans-sphenoidal surgery; Post-op: postoperative; DI: diabetes insipidus; SIADH: syndrome of inappropriate antidiuretic hormone secretion; RT: radiotherapy; PHP: panhypopituitarism; VF: visual field; N/V: nausea/vomiting; GHD: growth hormone deficiency; STR + RT: subtotal resection and adjuvant radiotherapy; VA: visual acuity; hypoT4: hypothyroidism; AI: adrenal insufficiency; CSF: cerebrospinal fluid; N/A: not available.

overall survival.^{17,35} As patients in our cohort did not recur after the introduction of RT in their management, they required fewer interventions after RT. Twelve out of sixteen (75%) patients who had either adjuvant or salvage RT received 54 Gy in 1.8 Gy per fraction. Despite small numbers, there was no difference between those receiving 54 Gy versus less in terms of disease control. This raises the question of whether dose de-escalation may be done with similar results and potentially fewer toxicities. In fact, Combs et al. showed excellent 5- and 10-year PFS of 100% with a median dose of 52.2 Gy in conventional fractionation.³⁶ Definitive RT in the setting of adult CP has also been investigated.^{4,30,33,37} Zhang et al. found no difference in outcomes between definitive RT, GTR, and STR with adjuvant RT³³ in 1218 patients included in the Surveillance Epidemiology and End Results database from 2004 to 2012. Hypofractionated adjuvant RT and SRS have also shown promise with high tumor control rates, low toxicity, and shorter overall treatment time,^{4,30} and warrant further outcome and toxicity comparison with normofractionated RT. As adult CP are rare and benign tumors with heterogeneous behavior requiring a multidisciplinary approach, large randomized studies comparing surgery alone to partial surgery plus RT is nearly impossible. Lastly, the discovery of BRAF mutation in up to 95% of papillary CP has led to the use of targeted therapies in this histologic type,³⁸ which shows great promise. Although more common in the adult population, papillary CP constitutes 5–30% of adult CP.³⁹ The adamantinomatous type is more common and constitutes most of our study population (22/24). This type harbors CTNNB1 or APC mutations encoding for beta-catenin, which are being investigated for potential targeted therapy.^{40,41}

This study is limited by its relatively small number of patients and its retrospective nature with its inherent lack of standardized, centralized, and complete documentation of long-term side effects of treatment such as quality of life measures and proper cognitive assessments. Although a p-value of 0.01 is given in Figure 1, it is only assessing whether there is a statistically significant treatment difference between any of the groups without telling us which groups are statistically different. A more useful comparison would be pairwise between each of the treatment groups, but we were underpowered for that type of analysis. A major strength of the study is the long-term clinical and imaging follow-up. We also confirmed better outcomes with STR and adjuvant RT compared to GTR alone. This is an important finding that warrants further validation with larger studies.

Conclusion

Our experience in the treatment of adult CP suggests that adjuvant and salvage RT is effective in the management of these tumors, and that STR plus RT may be associated with improved PFS and less toxicity compared to GTR. Larger studies directed towards rigorous and prospectively collected outcomes are needed to corroborate these findings.

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Conflicts of Interest. None.

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