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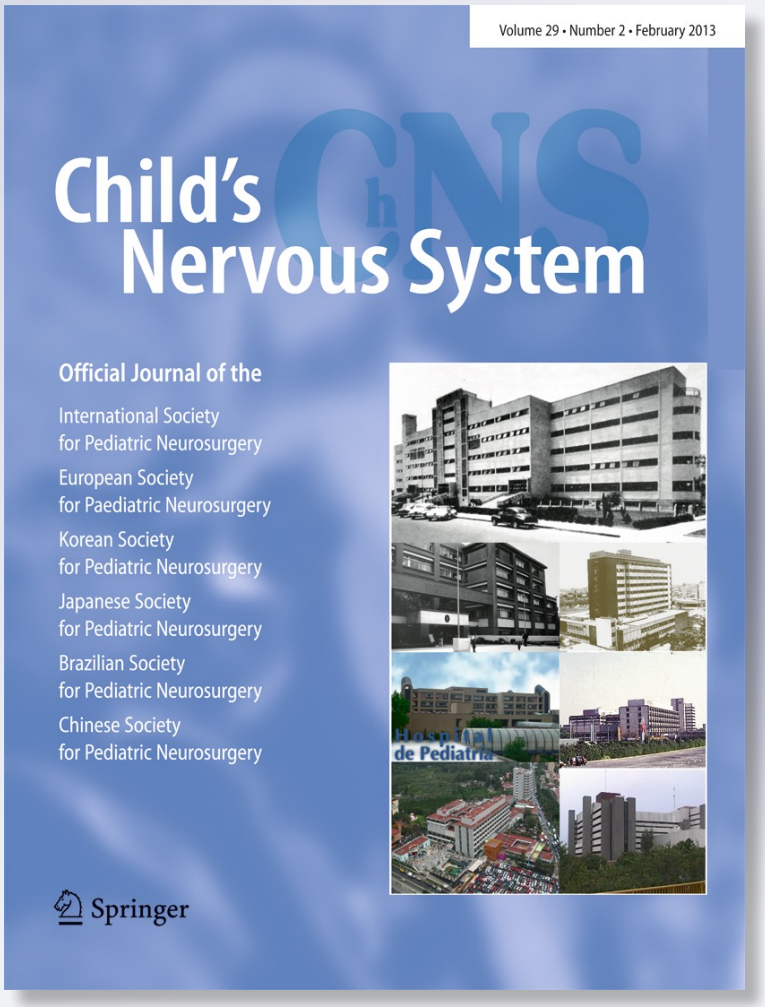

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ORIGINAL PAPER

A systematic review of the results of surgery and radiotherapy on tumor control for pediatric craniopharyngioma

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Abstract
Objective Craniopharyngiomas are rare tumors with bimodal incidence in the pediatric and adult age groups. Treatment strategies range from aggressive resection to planned limited resection combined with adjuvant therapies. Currently there is no consensus for standard of care for pediatric craniopharyngioma.
Materials and methods We performed a systematic review of the published literature on pediatric craniopharyngioma. Patients were grouped based on extent of resection into gross total resection (GTR), subtotal resection (STR), and biopsy procedures. These groups were compared with respect to tumor control. Chi square was used to compare rates of recurrence. Kaplan–Meier was used to generate progression-free survival (PFS) estimates. Cox proportional hazard modeling was used to evaluate risk of progression. Each extent of resection group was also subdivided based on adjuvant therapy and compared.
Results A total of 109 studies described extent of resection resulting in a cohort of 531 patients. Recurrence data were available for 377 patients. There was no difference in 1- or 5-year PFS between the groups who underwent GTR and STR combined with radiation (XRT; log-rank; $p=0.76$; 1-year PFS 89 vs 84 %; 5-year PFS 77 vs 73 %, respectively). One-year PFS was 84 % for STR+XRT compared to 76 % for STR alone while 5-year PFS was 73 % for STR+XRT compared to 43 % for STR alone (log-rank; $p=0.003$).
Conclusion Although there are limitations of a systematic review of retrospective data, our results suggest that STR+XRT of pediatric craniopharyngioma is associated with similar rates of tumor control as GTR.

Keywords Pediatric · Craniopharyngioma · Surgery · Extent of resection · Tumor control · Radiotherapy

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Introduction

Craniopharyngiomas are rare tumors arising from Rathke's pouch, a remnant of the primitive pharynx. The incidence is bimodal with peaks occurring between 5 to 15 and 45 to 60 years. Craniopharyngiomas account for 1–3 % of all pediatric brain tumors [17]. The histopathology is typical and consists of stratified papillary epithelial tissue with either solid, cystic, or mixed components. Although classified as WHO grade I tumors, their clinical behavior is more aggressive with many patients experiencing frequent tumor recurrence and significant morbidity due to their location and/or treatment. A recent study suggests that the adamantinomatous variant which is common in children should be designated a grade II tumor due to high rates of recurrence and significant treatment-related morbidity [95].

Craniopharyngiomas typically arise in the suprasellar region but can involve the pituitary stalk, the hypothalamus, and the optic pathways. Although these tumors do not widely infiltrate the brain as do primary astrocytic tumors, they can be densely adherent to brain structures. Recurrence is influenced by extent of resection with improved disease control in patients who undergo gross total resection (GTR) [100, 120, 121]. Experienced surgeons have reported that

GTR can be achieved in 50–79 % of patients with craniopharyngiomas [32, 48, 84]. The factors that prevent GTR are hypothalamic involvement, significant calcification, and involvement of critical vessels [32]. Perioperative mortality is low, ranging from 0 to 3 % even in the setting of planned aggressive resection [31, 84]. Perioperative morbidity, however, ranges from 8 to 14 %, including CSF leaks, infections, and visual worsening [31, 48]. In a large series of adult and pediatric craniopharyngioma patients treated with the initial goal of GTR [32], when GTR was achieved, the 5-year progression (PFS)/recurrence-free survival was 87 % as compared to 49 % in the subtotal resection (STR) group. Elliott et al. in a large series of exclusively pediatric patients also noted significantly longer progression/recurrence free survival in GTR patients [31]. They also noted worse outcomes in patients being treated for a recurrent tumor, which led them to propose that aggressive resection at initial presentation is most important. In contrast, Mechant et al. reported similar rates of tumor control in patients undergoing planned attempted GTR and planned STR followed by radiotherapy (XRT) [84]. They noted decreased IQ and quality of life metrics in the aggressive surgical group. They also reported a 73 % rate of diabetes insipidus in the aggressive surgical group compared to 33 % in the conservative surgical group. Diabetes insipidus can have long-term negative effects on children and has been suggested to be a predictor of poor response to adjuvant XRT [85]. These data suggest that the treatment for craniopharyngioma should be planned STR followed by XRT. Still others recommend biopsy followed by intracystic chemotherapy for certain craniopharyngiomas [20].

The current literature that is focused on pediatric craniopharyngioma consists mainly of single institution or single surgeon case series. Due to the rarity of this tumor, some series combine adult and pediatric age groups [32, 95]. Currently, there is no consensus regarding standard treatment of craniopharyngioma in pediatric patients and it is unlikely that prospective randomized trials will be performed to definitively address this issue. In order to place the reported experience with craniopharyngioma into context, we reviewed the published literature on to in order to determine if tumor control was dependent on degree of resection [1–8, 10–16, 18, 19, 21–30, 33–47, 49–62, 64–83, 86–99, 101–119, 122].

Materials and methods

Article selection

In order to determine overall recurrence rates and progression-free survival after treatment of craniopharyngioma, data from the existing English language literature were systematically reviewed. Articles were identified using a PubMed search combining the key word "craniopharyngioma" with "pediatric." After reviewing these articles, all referenced sources were compiled and analyzed, yielding a total of 1,451 publications. All references that contained disaggregated data specifically describing patients who had undergone surgery (biopsy or resection) of histologically confirmed craniopharyngioma were included in our analysis. Disaggregated data are defined as individual patient information presented in a manner that allowed assignment of pre- and postoperative factors and outcomes to the individual patient described in the report. Any paper which did not provide follow-up data on these patients with follow-up imaging was excluded, as these would not facilitate Kaplan–Meier analysis.

Data extraction

Median largest dimension and median tumor volume were not reportable or analyzable in our analysis, as the identified studies did not consistently report either value. The data were stratified into three groups based on extent of resection data presented in each reference: biopsy, subtotal resection, and gross total resection. The data were then further stratified based on subtotal resection with or without radiotherapy, or biopsy followed by intracystic chemotherapy. Tumor control data were included if adequate radiographic follow-up data were presented and stated in the study, demonstrating evidence of recurrence or continued tumor control. Time to progression was defined as time from diagnosis to radiographic evidence of progression. PFS was calculated at the 1- and 5-year time points.

Statistical analysis

Pearson's χ^2 test was used to analyze for differences in preoperative categorical factors, including gender and preoperative endocrine and visual deficits. Fisher's exact test was used if there were less than five values per cell. Analysis of variance was used to evaluate for statistical differences in preoperative continuous factors, including age. Chi-square test was used to evaluate differences in postoperative outcomes between the different treatment groups. Cox proportional hazard modeling was used to determine hazard ratios associated with each outcome measure. Kaplan–Meier estimates were used to generate progression curves. Differences in progression-free survival were analyzed by the log-rank test. Analyses were carried out using SPSS version 16.0 (SPSS, Inc.).

Results

Clinical characteristics

Our search yielded a total of 109 studies that described the surgical procedures performed for craniopharygioma in 531 pediatric patients. Of these, data on recurrence were available

for 377 patients and were included in the analysis. Of the included studies, the median number of patients per study was 11 (range 1–29, Table 1). There was no difference in age between the cohorts analyzed (data not shown). There were significantly fewer males in the biopsy group compared to GTR and STR (29 vs 52 vs 49 %, respectively; $p=0.002$; chi-square).

Extent of resection and postoperative outcomes

To evaluate if greater extent of resection irrespective of other adjuvant treatments was associated with differences in tumor control, we separated patients into three groups based on whether they underwent biopsy, STR, or GTR, and then compared their outcomes. We specifically evaluated the rate of reported recurrence after surgical procedures (Table 2). The GTR group included patients who underwent GTR alone and those who received adjuvant XRT. Likewise, the STR group included those who received surgery alone and those who received surgery and XRT. The biopsy group was comprised of patients who underwent biopsy alone or biopsy and delivery of intracystic chemotherapy. STR was associated with a small but highly statistically significant increased rate of tumor recurrence compared to GTR ($p=0.008$; HR 1.4; 95 % CI 1.1, 1.8).

Radiotherapy after STR

Although, when taken as a whole, STR appeared to be associated with worse tumor control, we were interested in evaluating if the addition of radiotherapy could result in improvement in tumor control rates. Therefore, we next analyzed outcome differences between GTR alone and STR combined with adjunctive radiotherapy (STR+XRT). The results are described in Table 3. There was no difference in 1- or 5-year PFS between the GTR and STR+XRT groups (Fig. 1, log-rank; $p=0.76$; 1-year PFS 89 vs 84 %; 5-year PFS 77 vs 73 %, respectively).

Table 1 Clinical characteristics of the study population

Variable (no. of cases)	Value (%)
Sex (377)	
Male	171 (45)
Female	206 (55)
Age in years (374)	
Median (range)	10 (0–18)
Operation (377)	
Biopsy	91 (24)
STR	134 (36)
GTR	152 (40)
Radiation therapy (377)	
Yes	131 (35)
fXRT	95 (72)
SRS	37 (28)
No	246 (65)
Intracystic chemotherapy (377)	
Yes	22 (6)
No	355 (94)

Table 2 The association between EOR (biopsy±adjuvant therapy vs STR±XRT vs GTR±XRT) and outcomes irrespective of adjuvant therapy

Outcome	Biopsy	STR	GTR	*p*
Recurrence				
Yes (%)	31 (34)	79 (59)	55 (36)	<0.001
No (%)	60 (66)	55 (41)	97 (64)	

Addition of XRT to STR

We then compared STR alone to STR+XRT to evaluate the effect of adjunctive XRT on outcomes (Table 3). The addition of XRT was associated with a significant increase in PFS. One-year PFS was 84 % for STR+XRT compared to 76 % for STR alone ,while 5-year PFS was 73 % for STR+XRT compared to 43 % for STR alone (Fig. 2; log-rank; $p=0.003$).

Comparison of STR and biopsy procedures

Biopsy followed by intracystic chemotherapy was compared with STR+XRT (Table 3). There was no difference in PFS between the two groups (log-rank; $p=0.31$).

Discussion

There is no consensus regarding a standard treatment for craniopharyngioma in children. Aggressive resection with the goal of GTR and planned conservative resection with subsequent adjuvant radiotherapy have both been reported

Table 3 Comparison of outcomes between the different surgical and adjuvant therapy subgroups

Subgroup	Recurrence (%)	No recurrence (%)
GTR alone	51 (35)*	94 (65)
STR alone	51 (65)**	28 (35)
STR+XRT	27 (50)*, **, ***	27 (50)
Bx+chemo	9 (41)***	13 (59)

Bx+chemo biopsy followed by chemotherapy

*$p=0.06$; **$p=0.11$; ***$p=0.63$

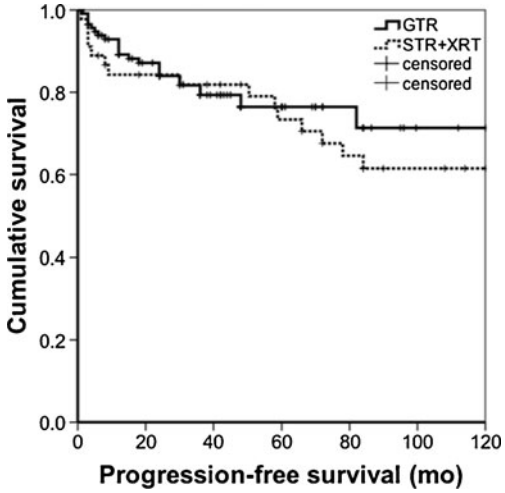

Fig. 1 Kaplan–Meier survival estimates comparing PFS between GTR and STR+XRT@@

to result in superior outcomes [32, 84]. Most reports, however, analyzed small patient cohorts undergoing heterogeneous treatments, which limits the relevance of the results. In order to exploit the advantages of a larger cohort of patients, we performed a systematic review of the literature to compare tumor control in patients treated with GTR, or STR combined with postoperative XRT.

Based on our results, GTR is not associated with significantly increased rate of tumor control or increased PFS compared to STR+XRT. It has been argued that successful GTR avoids the use of subsequent XRT its associated complications [32]. Conversely, some groups argue that aggressive resection can lead to increased postoperative neurologic and endocrine deficits [84]. We have recently reported in a systematic review of treatment-related morbidity that GTR for pediatric craniopharyngioma is associated with increased rates of anterior lobe dysfunction and new neurologic deficits (Clark et al., in press). When compared specifically to STR+XRT, GTR was associated with significantly increased rates of diabetes insipidus. Taken together, our data reported here would suggest that in the setting of increased postoperative deficits related to GTR, STR+XRT may represent the optimal treatment in this patient population yielding similar rates of tumor control.

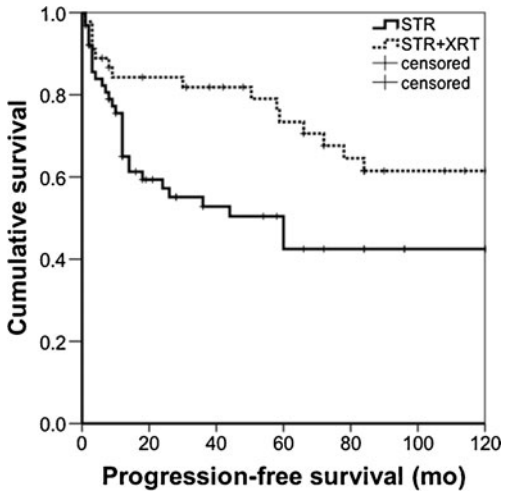

Fig. 2 Kaplan–Meier survival estimates comparing PFS between STR and STR+XRT

In this study, the addition of XRT to STR was associated with significant increases in PFS. STR is targeted at improving neurologic symptoms including vision by tumor debulking, restoring more normal CSF flow, and decreasing the tumor volume that will be targeted by XRT. However, radiotherapy in close proximity to the optic nerves carries the risk of visual deterioration as well as the risk of new or worsening of endocrinopathies and worse cognitive outcomes [63]. Tumor control benefits of XRT must be weighed against these risks. It is possible that future techniques for improved targeting of XRT will lead to decreased morbidity with preserved tumor control [85].

As a secondary comparison, we evaluated the difference between STR+XRT and biopsy followed by intracystic chemotherapy. A recent systematic review has described the current literature on intracystic chemotherapy [9]. Catheters are placed into the cyst either under direct visualization through an open craniotomy, stereotactically through a burr hole, or endoscopically. The catheter is then connected to a subcutaneous reservoir which is used to receive the agent. The goal of the agent is to destroy the secretory capacity of the epithelial cells lining the cyst to cause cyst shrinkage. The agents which have been used are radioisotopes, bleomycin, and interferon. We found similar effects on tumor control between STR+XRT and intracystic chemotherapy. Unfortunately, tumor size was not consistently reported in a disaggregated fashion and could not be included. This may partially explain the lack of difference in recurrence noted between biopsy procedures followed by intracystic chemotherapy and other more aggressive resections. We can assume that patients treated with intracystic chemotherapy likely harbored smaller monocystic tumors compared to patients who underwent open resection.

This report represents a systematic review of the published literature and therefore has inherent limitations. Currently there are no reporting standards for craniopharyngioma, so reports of extent of resection, histology, and method of radiotherapy likely vary from study to study and cannot be examined. It is entirely possible that there are features of those tumors that lend themselves to GTR are in fact important in determining overall outcome. Due to differences in reporting for each included study, potentially important variables could not be analyzed or controlled. Anatomic features that could affect extent of resection and outcomes including hypothalamic

involvement and vascular encasement were not routinely reported. Finally, all included studies were retrospective analyses and therefore are limited by potential selection biases.

Conclusions

Although subject to the limitations of a systematic review, our data support the conclusion that planned STR followed by adjuvant XRT is associated with similar rates of tumor control compared to planned GTR. Optimized multimodality treatment for craniopharygioma in the pediatric population may center around planned STR followed by adjuvant fractionated XRT.

References

1. Abe T, Ludecke DK (1999) Transnasal surgery for infradiaphragmatic craniopharyngiomas in pediatric patients. Neurosurgery 44:957–964, discussion 964–956
2. Agozzino L, Ferraraccio F, Accardo M, Esposito S, Agozzino M, Cuccurullo L (2006) Morphological and ultrastructural findings of prognostic impact in craniopharyngiomas. Ultrastruct Pathol 30:143–150
3. Al-Mefty O, Ayoubi S, Kadri PA (2007) The petrosal approach for the total removal of giant retrochiasmatic craniopharyngiomas in children. J Neurosurg 106:87–92
4. Amendola BE, Gebarski SS, Bermudez AG (1985) Analysis of treatment results in craniopharyngioma. J Clin Oncol 3:252–258
5. Amendola BE, Wolf A, Coy SR, Amendola MA (2003) Role of radiosurgery in craniopharyngiomas: a preliminary report. Med Pediatr Oncol 41:123–127
6. Ammirati M, Samii M, Sephernia A (1990) Surgery of large retrochiasmatic craniopharyngiomas in children. Childs Nerv Syst 6:13–17
7. Aquilina K, Merchant TE, Rodriguez-Galindo C, Ellison DW, Sanford RA, Boop FA (2010) Malignant transformation of irradiated craniopharyngioma in children: report of 2 cases. J Neurosurg Pediatr 5:155–161
8. Bahuleyan B, Menon G, Nair S (2009) Immediate postoperative death due to hypothalamic injury following surgery for craniopharyngioma. J Clin Neurosci 16:850–851
9. Bartels U, Laperriere N, Bouffet E, Drake J (2012) Intracystic therapies for cystic craniopharyngioma in childhood. Front Endocrinol (Lausanne) 3:39
10. Behari S, Banerji D, Mishra A, Sharma S, Chhabra DK, Jain VK (2003) Intrinsic third ventricular craniopharyngiomas: report on six cases and a review of the literature. Surg Neurol 60:245–252, discussion 252–243
11. Belen D, Er U, Yigitkanli K, Bolay H (2007) Delayed neurotoxic complication of intracavitary bleomycin therapy for craniopharyngioma in a child who had previously undergone radiosurgery. Case report. J Neurosurg 106:391–393
12. Bhagwati SN, Deopujari CE, Parulekar GD (1990) Lamina terminalis approach for retrochiasmal craniopharyngiomas. Childs Nerv Syst 6:425–429
13. Blackburn TP, Doughty D, Plowman PN (1999) Stereotactic intracavitary therapy of recurrent cystic craniopharyngioma by instillation of 90yttrium. Br J Neurosurg 13:359–365
14. Boch AL, van Effenterre R, Kujas M (1997) Craniopharyngiomas in two consanguineous siblings: case report. Neurosurgery 41:1185–1187
15. Bohn D, Davids MR, Friedman O, Halperin ML (2005) Acute and fatal hyponatraemia after resection of a craniopharyngioma: a preventable tragedy. QJM 98:691–703
16. Buhl R, Nabavi A, Fritsch M, Mehdorn HM (2001) Nasopharyngeal extension of a craniopharyngioma in a 4 year old girl. Acta Neurochir (Wien) 143:1283–1285
17. Bunin GR, Surawicz TS, Witman PA, Preston-Martin S, Davis F, Bruner JM (1998) The descriptive epidemiology of craniopharyngioma. J Neurosurg 89:547–551
18. Caceres A (2005) Intracavitary therapeutic options in the management of cystic craniopharyngioma. Childs Nerv Syst 21: 705–718
19. Cavalheiro S, Dastoli PA, Silva NS, Toledo S, Lederman H, da Silva MC (2005) Use of interferon alpha in intratumoral chemotherapy for cystic craniopharyngioma. Childs Nerv Syst 21: 719–724
20. Cavalheiro S, Di Rocco C, Valenzuela S, Dastoli PA, Tamburrini G, Massimi L, Nicacio JM, Faquini IV, Ierardi DF, Silva NS, Pettorini BL, Toledo SR (2010) Craniopharyngiomas: intratumoral chemotherapy with interferon-alpha: a multicenter preliminary study with 60 cases. Neurosurg Focus 28:E12
21. Cavallo LM, Prevedello DM, Solari D, Gardner PA, Esposito F, Snyderman CH, Carrau RL, Kassam AB, Cappabianca P (2009) Extended endoscopic endonasal transsphenoidal approach for residual or recurrent craniopharyngiomas. J Neurosurg 111: 578–589
22. Chiou SM, Lunsford LD, Niranjan A, Kondziolka D, Flickinger JC (2001) Stereotactic radiosurgery of residual or recurrent craniopharyngioma, after surgery, with or without radiation therapy. Neuro Oncol 3:159–166
23. Chung WY, Pan HC, Guo WY, Shiau CY, Wang LW, Wu HM, Lee LS (1998) Protection of visual pathway in gamma knife radiosurgery for craniopharyngiomas. Stereotact Funct Neurosurg 70(Suppl 1):139–151
24. Cinalli G, Spennato P, Cianciulli E, Fiorillo A, Di Maio S, Maggi G (2006) The role of transventricular neuroendoscopy in the management of craniopharyngiomas: three patient reports and review of the literature. J Pediatr Endocrinol Metab 19(Suppl 1):341–354
25. Clayton PE, Price DA, Shalet SM, Gattemaneni HR (1988) Craniopharyngioma recurrence and growth hormone therapy. Lancet 1:642
26. Connolly ES Jr, Winfree CJ, Carmel PW (1997) Giant posterior fossa cystic craniopharyngiomas presenting with hearing loss. Report of three cases and review of the literature. Surg Neurol 47:291–299
27. Day JD, Giannotta SL, Fukushima T (1994) Extradural temporopolar approach to lesions of the upper basilar artery and infrachiasmatic region. J Neurosurg 81:230–235
28. Economos D (1979) Systemic shunting of residual intraparenchymatous cystic craniopharyngioma. Acta Neurochir Suppl (Wien) 28:363–366
29. Eldevik OP, Blaivas M, Gabrielsen TO, Hald JK, Chandler WF (1996) Craniopharyngioma: radiologic and histologic findings and recurrence. AJNR Am J Neuroradiol 17:1427–1439
30. Elliott RE, Moshel YA, Wisoff JH (2009) Surgical treatment of ectopic recurrence of craniopharyngioma. Report of 4 cases. J Neurosurg Pediatr 4:105–112
31. Elliott RE, Hsieh K, Hochm T, Belitskaya-Levy I, Wisoff J, Wisoff JH (2010) Efficacy and safety of radical resection of primary and recurrent craniopharyngiomas in 86 children. J Neurosurg Pediatr 5:30–48

32. Fahlbusch R, Honegger J, Paulus W, Huk W, Buchfelder M (1999) Surgical treatment of craniopharyngiomas: experience with 168 patients. J Neurosurg 90:237–250
33. Feletti A, Marton E, Mazzucco GM, Fang S, Longatti P (2010) Amaurosis in infancy due to craniopharyngioma: a not-exceptional but often misdiagnosed symptom. Neurosurg Focus 28:E7
34. Filis AK, Moon K, Cohen AR (2009) Synchronous ventriculoscopic and microsurgical resection of complex craniopharyngiomas. Pediatr Neurosurg 45:434–436
35. Fraioli MF, Santoni R, Fraioli C, Contratti F (2006) "Conservative" surgical approach and early postoperative radiotherapy in a patient with a huge cystic craniopharyngioma. Childs Nerv Syst 22:151–155, discussion 158–163
36. Fraioli MF, Moschettoni L, Catena E, Fraioli C (2010) Cystic craniopharyngioma: trans-sphenoidal surgery and intra-cystic apposition of "bleomycin wax". Acta Neurochir (Wien) 152: 293–296
37. Frangou EM, Tynan JR, Robinson CA, Ogieglo LM, Vitali AM (2009) Metastatic craniopharyngioma: case report and literature review. Childs Nerv Syst 25:1143–1147
38. Frank G, Pasquini E, Doglietto F, Mazzatenta D, Sciarretta V, Farneti G, Calbucci F (2006) The endoscopic extended transsphenoidal approach for craniopharyngiomas. Neurosurgery 59: ONS75-83, discussion ONS75-83
39. Frazier JL, Chaichana K, Jallo GI, Quinones-Hinojosa A (2008) Combined endoscopic and microscopic management of pediatric pituitary region tumors through one nostril: technical note with case illustrations. Childs Nerv Syst 24:1469–1478
40. Giller CA, Berger BD, Pistenmaa DA, Sklar F, Weprin B, Shapiro K, Winick N, Mulne AF, Delp JL, Gilio JP, Gall KP, Dicke KA, Swift D, Sacco D, Harris-Henderson K, Bowers D (2005) Robotically guided radiosurgery for children. Pediatr Blood Cancer 45:304–310
41. Gleeson H, Amin R, Maghnie M (2008) 'Do no harm': management of craniopharyngioma. Eur J Endocrinol 159(Suppl 1): S95–S99
42. Golshani KJ, Lalwani K, Delashaw JB, Selden NR (2009) Modified orbitozygomatic craniotomy for craniopharyngioma resection in children. J Neurosurg Pediatr 4:345–352
43. Gurkaynak M, Ozyar E, Zorlu F, Akyol FH, Atahan IL (1994) Results of radiotherapy in craniopharyngiomas analysed by the linear quadratic model. Acta Oncol 33:941–943
44. Hader WJ, Steinbok P, Hukin J, Fryer C (2000) Intratumoral therapy with bleomycin for cystic craniopharyngiomas in children. Pediatr Neurosurg 33:211–218
45. Hamamoto Y, Niino K, Adachi M, Hosoya T (2002) MR and CT findings of craniopharyngioma during and after radiation therapy. Neuroradiology 44:118–122
46. Hamlat A, Morandi X, Riffaud L, Carsin-Nicol B, Haegelen C, Helal H, Brassier G (2008) Transtemporal-transchoroidal approach and its transamygdala extension to the posterior chiasmatic cistern and diencephalo-mesencephalic lesions. Acta Neurochir (Wien) 150:317–327, discussion 327–318
47. Hashizume C, Mori Y, Kobayashi T, Shibamoto Y, Nagai A, Hayashi N (2010) Stereotactic radiotherapy using Novalis for craniopharyngioma adjacent to optic pathways. J Neurooncol 98:239–247
48. Hofmann BM, Hollig A, Strauss C, Buslei R, Buchfelder M, Fahlbusch R (2012) Results after treatment of craniopharyngiomas: further experiences with 73 patients since 1997. J Neurosurg 116:373–384
49. Hoogenhout J, Otten BJ, Kazem I, Stoelinga GB, Walder AH (1984) Surgery and radiation therapy in the management of craniopharyngiomas. Int J Radiat Oncol Biol Phys 10: 2293–2297
50. Hukin J, Visser J, Sargent M, Goddard K, Fryer C, Steinbok P (2005) Childhood craniopharyngioma: Vancouver experience. Childs Nerv Syst 21:758–765
51. Hukin J, Steinbok P, Lafay-Cousin L, Hendson G, Strother D, Mercier C, Samson Y, Howes W, Bouffet E (2007) Intracystic bleomycin therapy for craniopharyngioma in children: the Canadian experience. Cancer 109:2124–2131
52. Im SH, Wang KC, Kim SK, Chung YN, Kim HS, Lee CH, Cho BK (2003) Transsphenoidal microsurgery for pediatric craniopharyngioma: special considerations regarding indications and method. Pediatr Neurosurg 39:97–103
53. Inoue HK, Fujimaki H, Kohga H, Ono N, Hirato M, Ohye C (1997) Basal interhemispheric supra- and/or infrachiasmal approaches via superomedial orbitotomy for hypothalamic lesions: preservation of hypothalamo-pituitary functions in combination treatment with radiosurgery. Childs Nerv Syst 13: 250–256
54. Israel ZH, Pomeranz S (1995) Intracranial craniopharyngioma seeding following radical resection. Pediatr Neurosurg 22: 210–213
55. Jackson AS, St George EJ, Hayward RJ, Plowman PN (2003) Stereotactic radiosurgery. XVII: recurrent intrasellar craniopharyngioma. Br J Neurosurg 17:138–143
56. Jakacki RI, Cohen BH, Jamison C, Mathews VP, Arenson E, Longee DC, Hilden J, Cornelius A, Needle M, Heilman D, Boaz JC, Luerssen TG (2000) Phase II evaluation of interferon-alpha-2a for progressive or recurrent craniopharyngiomas. J Neurosurg 92:255–260
57. Jang WY, Lee KS, Son BC, Jeun SS, Hong YK, Lee SW, Yang SH (2009) Repeat operations in pediatric patients with recurrent craniopharyngiomas. Pediatr Neurosurg 45:451–455
58. Jeong IH, Lee JK, Moon KS, Joo SP, Kwak HJ, Kim TS, Kim JH, Kim SH (2006) Ectopic recurrence of craniopharyngioma: a case report and review of the literature. J Neurooncol 79:191–195
59. Jooma R, Kendall BE (1982) Intracranial tumours in the first year of life. Neuroradiology 23:267–274
60. Julow J, Lanyi F, Hajda M, Simkovics M, Arany I, Toth S, Pasztor E (1985) The radiotherapy of cystic craniopharyngioma with intracystic installation of ^{90}Y silicate colloid. Acta Neurochir (Wien) 74:94–99
61. Kawahara I, Tokunaga Y, Ishizaka S, Yagi N (2009) Reversible clinical and magnetic resonance imaging of central pontine myelinolysis following surgery for craniopharyngioma: serial magnetic resonance imaging studies. Neurol Med Chir (Tokyo) 49:120–123
62. Keohane C, Hally M, Ryder DQ, Buckley TF (1994) Late recurrence of craniopharyngioma in the cerebellopontine angle in a fertile woman. J Neurol Neurosurg Psychiatry 57:873–874
63. Kiehna EN, Merchant TE (2010) Radiation therapy for pediatric craniopharyngioma. Neurosurg Focus 28:E10
64. Kim MS, Lee SI, Sim SH (1999) Brain tumors with cysts treated with Gamma Knife radiosurgery: is microsurgery indicated? Stereotact Funct Neurosurg 72(Suppl 1):38–44
65. Kim SD, Park JY, Park J, Lee JB, Kim SH, Lim DJ (2007) Radiological findings following postsurgical intratumoral bleomycin injection for cystic craniopharyngioma. Clin Neurol Neurosurg 109:236–241
66. Kitano M, Taneda M (2009) Extended transsphenoidal surgery for suprasellar craniopharyngiomas: infrachiasmatic radical resection combined with or without a suprachiasmatic translamina terminalis approach. Surg Neurol 71:290–298, discussion 298
67. Klimo P Jr, Browd SR, Pravdenkova S, Couldwell WT, Walker ML, Al-Mefty O (2009) The posterior petrosal approach: technique and applications in pediatric neurosurgery. J Neurosurg Pediatr 4:353–362

68. Kobayashi T, Tanaka T, Kida Y (1994) Stereotactic gamma radiosurgery of craniopharyngiomas. Pediatr Neurosurg 21(Suppl 1):69–74
69. Kobayashi T, Kida Y, Mori Y, Hasegawa T (2005) Long-term results of gamma knife surgery for the treatment of craniopharyngioma in 98 consecutive cases. J Neurosurg 103:482–488
70. Kodama T, Matsukado Y, Uemura S (1981) Intracapsular irradiation therapy of craniopharyngiomas with radioactive gold: indication and follow-up results. Neurol Med Chir (Tokyo) 21:49–58
71. Kramer S, Southard M, Mansfield CM (1968) Radiotherapy in the management of craniopharyngiomas: further experiences and late results. Am J Roentgenol Radium Ther Nucl Med 103:44–52
72. Kranzinger M, Jones N, Rittinger O, Pilz P, Piotrowski WP, Manzl M, Galvan G, Kogelnik HD (2001) Malignant glioma as a secondary malignant neoplasm after radiation therapy for craniopharyngioma: report of a case and review of reported cases. Onkologie 24:66–72
73. Kwon JW, Cho BK, Kim EC, Wang KC, Kim SK (2008) Herpes simplex encephalitis after craniopharyngioma surgery. J Neurosurg Pediatr 2:355–358
74. Lange M, Kirsch CM, Steude U, Oeckler R (1995) Intracavitary treatment of intrasellar cystic craniopharyngeomas with 90-Yttrium by trans-sphenoidal approach—a technical note. Acta Neurochir (Wien) 135:206–209
75. Lichter AS, Wara WM, Sheline GE, Townsend JJ, Wilson CB (1977) The treatment of craniopharyngiomas. Int J Radiat Oncol Biol Phys 2:675–683
76. Lippens RJ, Rotteveel JJ, Otten BJ, Merx H (1998) Chemotherapy with Adriamycin (doxorubicin) and CCNU (lomustine) in four children with recurrent craniopharyngioma. Eur J Paediatr Neurol 2:263–268
77. Lonjon M, Dran G, Casagrande F, Vandenbos F, Mas JC, Richelme C (2005) Prenatal diagnosis of a craniopharyngioma: a new case with radical surgery and review. Childs Nerv Syst 21:177–180
78. Maira G, Anile C, Colosimo C, Cabezas D (2000) Craniopharyngiomas of the third ventricle: trans-lamina terminalis approach. Neurosurgery 47:857–863, discussion 863–855
79. Malik JM, Cosgrove GR, VandenBerg SR (1992) Remote recurrence of craniopharyngioma in the epidural space. Case report. J Neurosurg 77:804–807
80. Mason PW, Krawiecki N, Meacham LR (2002) The use of dextroamphetamine to treat obesity and hyperphagia in children treated for craniopharyngioma. Arch Pediatr Adolesc Med 156:887–892
81. Matarazzo P, Genitori L, Lala R, Andreo M, Grossetti R, de Sanctis C (2004) Endocrine function and water metabolism in children and adolescents with surgically treated intra/parasellar tumors. J Pediatr Endocrinol Metab 17:1487–1495
82. Matthew DJ, Levin M (1986) Pulmonary thromboembolism in children. Intensive Care Med 12:404–406
83. McMurry FG, Hardy RW Jr, Dohn DF, Sadar E, Gardner WJ (1977) Long term results in the management of craniopharyngiomas. Neurosurgery 1:238–241
84. Merchant TE, Kiehna EN, Sanford RA, Mulhern RK, Thompson SJ, Wilson MW, Lustig RH, Kun LE (2002) Craniopharyngioma: the St. Jude Children's Research Hospital experience 1984–2001. Int J Radiat Oncol Biol Phys 53:533–542
85. Merchant TE, Kiehna EN, Kun LE, Mulhern RK, Li C, Xiong X, Boop FA, Sanford RA (2006) Phase II trial of conformal radiation therapy for pediatric patients with craniopharyngioma and correlation of surgical factors and radiation dosimetry with change in cognitive function. J Neurosurg 104:94–102
86. Miller ML, Kaufman BA, Lew SM (2008) Modified osteoplastic orbitozygomatic craniotomy in the pediatric population. Childs Nerv Syst 24:845–850
87. Mottolese C, Stan H, Hermier M, Berlier P, Convert J, Frappaz D, Lapras C (2001) Intracystic chemotherapy with bleomycin in the treatment of craniopharyngiomas. Childs Nerv Syst 17:724–730
88. Muller-Scholden J, Lehrnbecher T, Muller HL, Bensch J, Hengen RH, Sorensen N, Stockhausen HB (2000) Radical surgery in a neonate with craniopharyngioma. Report of a case. Pediatr Neurosurg 33:265–269
89. Nimsky C, Ganslandt O, Hofmann B, Fahlbusch R (2003) Limited benefit of intraoperative low-field magnetic resonance imaging in craniopharyngioma surgery. Neurosurgery 53:72–80, discussion 80–71
90. Niu DM, Guo WY, Pan HC, Wong TT (2002) Rapid enlargement of a residual craniopharyngioma during short-term growth hormone replacement. Childs Nerv Syst 18:164–165
91. Nomura H, Kurimoto M, Nagai S, Hayashi N, Hirashima Y, Tsukamoto E, Endo S (2002) Multiple intracranial seeding of craniopharyngioma after repeated surgery—case report. Neurol Med Chir (Tokyo) 42:268–271
92. Novegno F, Di Rocco F, Colosimo C Jr, Lauriola L, Caldarelli M (2002) Ectopic recurrences of craniopharyngioma. Childs Nerv Syst 18:468–473
93. Ohmori K, Collins J, Fukushima T (2007) Craniopharyngiomas in children. Pediatr Neurosurg 43:265–278
94. Park DH, Park JY, Kim JH, Chung YG, Lee HK, Lee KC, Suh JK (2002) Outcome of postoperative intratumoral bleomycin injection for cystic craniopharyngioma. J Korean Med Sci 17:254–259
95. Pekmezci M, Louie J, Gupta N, Bloomer MM, Tihan T (2010) Clinicopathological characteristics of adamantinomatous and papillary craniopharyngiomas: University of California, San Francisco experience 1985–2005. Neurosurgery 67:1341–1349, discussion 1349
96. Plowman PN, Wraith C, Royle N, Grossman AB (1999) Stereotactic radiosurgery. IX. Craniopharyngioma: durable complete imaging responses and indications for treatment. Br J Neurosurg 13:352–358
97. Ramnarayan R, Sreehari NR, Ninan GK, John KM (2007) Delayed postoperative extradural hematoma. Pediatr Neurosurg 43:113–114
98. Rilliet B, Vernet O, Pica A (2005) The Geneva and Lausanne (French-speaking Switzerland) experience: in favor of the trans-sphenoidal approach when feasible. Childs Nerv Syst 21: 725–728
99. Rodriguez FJ, Scheithauer BW, Tsunoda S, Kovacs K, Vidal S, Piepgras DG (2007) The spectrum of malignancy in craniopharyngioma. Am J Surg Pathol 31:1020–1028
100. Sanford RA (1994) Craniopharyngioma: results of survey of the American Society of Pediatric Neurosurgery. Pediatr Neurosurg 21(Suppl 1):39–43
101. Schmalisch K, Beschorner R, Psaras T, Honegger J (2010) Postoperative intracranial seeding of craniopharyngiomas—report of three cases and review of the literature. Acta Neurochir (Wien) 152:313–319, discussion 319
102. Sener RN, Kismali E, Akyar S, Selcuki M, Yalman O (1997) Large craniopharyngioma extending to the posterior cranial fossa. Magn Reson Imaging 15:1111–1112
103. Serowka K, Chiu Y, Gonzalez I, Gilles F, McComb G, Krieger M, Dhall G, Britt B, Ji L, Sposto R, Finlay JL (2010) Central nervous system (CNS) tumors in the first 6 months of life: the Children's Hospital Los Angeles experience, 1979–2005. Pediatr Hematol Oncol 27:90–102
104. Shinohara O, Shinagawa T, Kubota C, Oi S (1997) Spontaneous reduction of a recurrent craniopharyngioma in an 8-year-old female patient: case report. Neurosurgery 41:1188–1190
105. Shirane R, Ching-Chan S, Kusaka Y, Jokura H, Yoshimoto T (2002) Surgical outcomes in 31 patients with craniopharyngiomas

extending outside the suprasellar cistern: an evaluation of the frontobasal interhemispheric approach. J Neurosurg 96: 704–712
106. Shirane R, Hayashi T, Tominaga T (2005) Fronto-basal interhemispheric approach for craniopharyngiomas extending outside the suprasellar cistern. Childs Nerv Syst 21:669–678
107. Shuman AG, Heth JA, Marentette LJ, Blaivas M, Muraszko KM (2007) Extracranial nasopharyngeal craniopharyngioma: case report. Neurosurgery 60:E780–E781, discussion E781
108. Siomin V, Spektor S, Beni-Adani L, Constantini S (2001) Application of the orbito-cranial approach in pediatric neurosurgery. Childs Nerv Syst 17:612–617
109. Srinivasan J, Dailey AT, Berger MS (1999) The bifrontal olfactory nerve-sparing approach to lesions of the suprasellar region in children. Pediatr Neurosurg 30:245–252
110. Strenger V, Sovinz P, Lackner H, Dornbusch HJ, Lingitz H, Eder HG, Moser A, Urban C (2008) Intracerebral cavernous hemangioma after cranial irradiation in childhood. Incidence and risk factors. Strahlenther Onkol 184:276–280
111. Sutton LN, Gusnard D, Bruce DA, Fried A, Packer RJ, Zimmerman RA (1991) Fusiform dilatations of the carotid artery following radical surgery of childhood craniopharyngiomas. J Neurosurg 74:695–700
112. Taguchi Y, Tanaka K, Miyakita Y, Sekino H, Fujimoto M (2000) Recurrent craniopharyngioma with nasopharyngeal extension. Pediatr Neurosurg 32:140–144
113. Takahashi H, Yamaguchi F, Teramoto A (2005) Long-term outcome and reconsideration of intracystic chemotherapy with bleomycin for craniopharyngioma in children. Childs Nerv Syst 21:701–704
114. Thompson IL, Griffin TW, Parker RG, Blasko JC (1978) Craniopharyngioma: the role of radiation therapy. Int J Radiat Oncol Biol Phys 4:1059–1063
115. Trejos H, Caceres A, Segura JL (2005) Monstrous craniopharyngioma. Case presentations and term proposal. Childs Nerv Syst 21:1049–1053, discussion 1054–1045
116. Tsutsumi S, Yasumoto Y, Ito M (2008) Central pontine and extrapontine myelinolysis in an infant associated with the treatment of craniopharyngioma: case report. Neurol Med Chir (Tokyo) 48:351–354
117. Ulfarsson E, Lindquist C, Roberts M, Rahn T, Lindquist M, Thoren M, Lippitz B (2002) Gamma knife radiosurgery for craniopharyngiomas: long-term results in the first Swedish patients. J Neurosurg 97:613–622
118. Usanov EI, Hatomkin DM, Nikulina TA, Gorban NA (1999) Craniopharyngioma of the pineal region. Childs Nerv Syst 15:4–7
119. Vyramuthu N, Benton TF (1983) The management of craniopharyngioma. Clin Radiol 34:629–632
120. Weiner HL, Wisoff JH, Rosenberg ME, Kupersmith MJ, Cohen H, Zagzag D, Shiminski-Maher T, Flamm ES, Epstein FJ, Miller DC (1994) Craniopharyngiomas: a clinicopathological analysis of factors predictive of recurrence and functional outcome. Neurosurgery 35:1001–1010, discussion 1010–1001
121. Yasargil MG, Curcic M, Kis M, Siegenthaler G, Teddy PJ, Roth P (1990) Total removal of craniopharyngiomas. Approaches and long-term results in 144 patients. J Neurosurg 73:3–11
122. Zhou L, Luo L, Xu J, Li Q, Chen J, Jiang S, Cai B, You C (2009) Craniopharyngiomas in the posterior fossa: a rare subgroup, diagnosis, management and outcomes. J Neurol Neurosurg Psychiatry 80:1150–1154