ANNEX A.

Summary of the literature review of 21st century series.

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Author	N Study design	Mean/Median FU (yr)	Study goal	Treatment recommendations	Outcome parameters	Disease control	Complications or Sequelae
Saint Rose. 2005 [1]	66. Retrospective Aim of GTR in 100% at first surgery (33 STR) FSRT 18.18%	7 years (mean)	To classify PCPG at presentation to allow rationalization of multimodal therapy to decrease morbidity.	Treatment strategy may be adapted according to the **degree of preoperative hypothalamic involvement** in order to minimize morbidity.	BMI, HUI index related to hypothalamic types and surgeon experience.	36% recurrence GTR 54% recurrence STR	90% hormonal therapy. Visual function was improved in 68% but worse in 21%. A degree of hyperphagia 70% of the cases (18% severe leading to morbid obesity) 15% of the children had an impaired neuropsychological evaluation post-operatively.
Thompson. 2005 [2]	75 historical/ 48 current 25/48 GTR 23/48 STR 6 STR (<5y) 17 STR+FSRT	5.58 years (mean in current series)	To compare current conservative approach (STR + FSRT) with previous policy (GTR)	**Avoidance of radical surgery as a primary curative treatment option** is associated with a reduction in post-operative morbidity without subsequent fall in rates of cure.	Degree of hydrocephalus Size of tumor Age less than 5y Signs of hypothalamic disturbance Intra-operative complication Removal of tumor observed to be adherent to hypothalamus	Current series: 48% recurrence GTR 100% recurrence STR alone 17.64% recurrence STR+FSRT	Historical series vs current series: Mortality rates 12% vs 4% Neurological sequelae 67% vs 20% Hormonal impairment 99% vs 92% DI 80% vs 73%

Pierre-Kahn. 2005 [3]	14 Prospective GTR		Incidence of hypothalamic syndrome after GTR of PCPG	**CPG with preop hypothalamic involvement** (abnormal BMI, behavioral disturbances, and/or intraventricular extension) are **not amenable to "total" resection.**	A large defect at the level of the III V floor on post-surgical MRI is a factor of bad prognosis.		At 2-year follow-up, only two children (14.3%) were symptom-free, considered as intellectually normal, and at tending normal schooling. The 12 others presented with at least two of the six symptoms constituting the hypothalamic syndrome
Zuccaro. 2005 [6]	153 Retrospective	A follow up of 1 to 16 years	Results of a radical surgery perspective.	**The treatment of choice in CPG in childhood is total resection** in order to avoid radiation therapy and recurrence.	Surgeon experience	0% recurrence GTR 51% recurrence STR+RTEF	85% supplemental hormonal therapy. Visual status improved markedly after surgery. Surgical complications: Subdural hematoma (12%) Seizures (9%) Vascular (6%), Neurological (4%) Infection (4%) Transplanted craniopharyngioma (1%). Shunt malfunction (68%). Until December 1994, the overall mortality was 12.5%; 7% (2005). 3.2% perioperative deaths.
Puget. 2007 [5]	66 Retrospective cohort (GTR) 22	Retrospective: 7 years (median) Prospective: 13.8 months (mean)	A retrospective analysis to identify pre-operative prognostic factors that would allow stratification of patients, that was applied prospectively to	**Multimodal treatment** for PCPG.	Surgeon experience Hydrocephalus Pre- and post-operative classification of hypothalamic involvement.	53% recurrence (retrospective series) Recurrence rate 36% after GTR and 54% after STR, (intergroup	

	Prospective cohort (treatment stratified according to risk factors)		another cohort of patients.		Hyperphagia Neuropsychological dysfunction.	difference was not significant)	
Elliott. 2010 [23]	86 Retrospective	9 years (mean)	Overall and progression-free survivals and outcomes in a large series of children who underwent GTR of primary and recurrent CPG performed by a single surgeon.	**The treatment of choice in CP in childhood is total resection.**	Surgeon experience Risk factors for STR: prior RT, size of the tumor. Risk factors affecting OS and PFS after radical resection of CP were hydrocephalus, VP shunt and size > or equal to 5 cm.	20% recurrence GTR. There was no difference in the rate of recurrence between the primary and the recurrent tumors.	15% died during the study period. Overall operative mortality rate of 3%. Neurological morbidity (53%) Non neurological complications (8%) 78% had DI. 24.6% post-operative hypothalamic dysfunction.
Cavalheiro. 2010 [16]	60 Prospective and multicenter > 60% of the tumor volume was cystic	44 months (mean)	To demonstrate that the use of ICC with INFα is a simple method, with a very low cost, that allows the control of cystic CPG	The **use of INFα for the treatment of cystic forms of CPG** is efficacious, easy to handle, and available at a low cost; it is also associated with a low morbidity rate.		Disease control was achieved in 78.3% of the patients (they considered disease to be controlled when a tumor decreased more than 50%)	30% of the patients had some kind of side effect due to INFα2A therapy (headache, palpebral edema, fever, chronic fatigue syndrome and arthritis) Only 13% of patients developed a worsening of endocrine function, no patient developed severe hypothalamic disturbances or

							became obese and the mortality rate was 0%.
Mallucci. 2012 [7]	20 Prospective Endoscopic drainage of tumor cyst + risk grade and surgical strategy. Definitive surgery was performed in 4–6 weeks' time.	3 years (median)	To review their management of patients with CPG using a risk stratification system that combines the CCLG guidelines and the Paris staging system.	**Re-stratification before and after endoscopic decompression** of the cystic component and hydrocephalus.	Hypothalamic syndrome at presentation, hydrocephalus, tumor size and the radiological three-point Paris grading, were combined to produce four subgroups: very high, high, medium and low risk.	GTR (30%), NTR (25%) or STR (45%)	No complications associated with the neuroendoscopic procedures. No surgical-related mortality. Two new visual field defects. No hypothalamic complications. Post-operative complications: one extradural hematoma, seizure and a cerebrospinal fluid fistula. 47 % patients were deficient in all anterior pituitary hormones and 16 patients had DI.
Cohen. 2013 [17]	33 (2001-2011) 43 (1990-2001) 50 (1975-1989) Retrospective	4 years (mean)	They aim to compare long-term outcomes of pediatric CP treated over the last decade vs historical series.	Treatment approach to CP has shifted from a goal of "curative" tumor resection to use of **minimalistic surgery plus adjuvant treatment to reduce tumor symptoms**.	Younger age at diagnosis and degree of hypothalamic involvement.	Recurrence rates were not significantly different among the 3 time periods, shifting from 34% and 30% in the past to 52% in the last decade.	Prevalence of pituitary hormone deficiency has decreased significantly compared with the last decade, including both anterior panhypopituitarism and DI. The prevalence of obesity decreased by 10% and that of severe obesity by 36% (not significant.) Survival rate in this series was 97%.

Hoffman. 2014 [15]	120 KPHG2000. 106 KPHG 2007. Prospective and multicenter	6.78 years (mean) KPHG2000 2.22 years (mean) KPHG2007	To analyzed childhood CPG patients of the studies KPHG 2000/2007.	A trend towards **more hypothalamus-sparing surgical strategies** in childhood CPG. **FSRT is recommended for treatment and/or prevention of progression after STR**	Surgical expertise.	Comparing KPHG 2000 vs 2007, 3-year event free survival rates were higher in patients after GTR (89% vs 77%) when compared to patients after STR (33% vs 32%)	The 3-year overall survival rate in KPHG 2000 was 0.97 ± 0.015. In KPHG 2007, no lethal event was encountered up to now (September 2013)
Amayiri. 2017 [8]	24 Retrospective	4.5 years (median)	To review the experience in the management of pediatric CPG in a LMIC, with emphasis on the QoL.	It is important, to have a **locally feasible plan** to care of children with CPG. It may be practical **to accept less than a GTR to avoid further hypothalamic injury and morbidities**. Multidisciplinary teams and second opinions, from experts.		54% needed multiple surgical resections, with a median of two interventions (range 2–4)	Post-operative complications were mainly related to electrolyte imbalance. Four patients had significant post-operative hypothalamic symptoms. 17% died and 13% were lost to follow-up. One immediate postoperative mortality was due to major cerebral infarction following STR. At last follow-up, VA stabilized in 33 (69%). Almost all patients were on multiple hormonal supplements. All GTR were overweight or obese. Hyperlipidemia (41%), and liver with fatty changes (67%). 11/17

						patients (65%) were attending school. 53% low self-esteem and difficulties to engage with peers. Two patients had significant behavioral difficulties and attention seeking behaviors.
Fouda. 2020 [18]	45 old era/90 new era Retrospective	10 years (median)	To demonstrate the paradigm shift in management strategies.	Aggressive resection-related **morbidities are balanced** by the avoidance of radiation-induced morbidities and the contrary.	29% recurrence (new era) 31% recurrence (old era) STR/cyst drainage + FSRT has similar rate of recurrence in comparison with GTR. STR without adjuvant FSRT was associated with a 71% risk of recurrence.	4% patients died. Visual function improved in 13% patients while it deteriorated in 18% Panhypopituitarism was evident in 75%. New-onset DI in 61% patients. Radiation induced moyamoya was 11%. Intracranial aneurysm was evident in 5%. Psychological impairment was documented in 22% and learning disabilities in 28%. New-onset hypothalamic obesity in 34% patients.

							Radiation-induced secondary malignancies were seen 4% patients. Seizures were evident in 15 patients (three had seizures preoperatively). Motor dysfunction was evident in seven patients.
Al Shail. 2020 [25]	35. Retrospective.	156.9 months (median)	To investigate factors related to recurrence of CPG.	Twenty-four patients (70.6%) had GTR. There were 12/35 patients who received radiotherapy.	VP shunt presence at presentation.	Rate of disease recurrence was 42.9% (15 patients)	Probability of 10-year overall survival was observed at 0.889 ± 0.105. Postsurgical panhypopituitarism was observed in nine (25.7%) patients. VP shunt was inserted in 12 (34.3%) patients
Liu. 2020 [24]	28 Retrospective	6.1 years (median)	To review the experience of managing CP over the past 20 years. To investigate patient survival, predictors of outcome, and long-term morbidities.	The treatment approaches were heterogeneous. GTR/NTR in 39% STR 50% and Biopsy+IFN 11% patients. Adjuvant RT 32%	Patients treated in a high-volume center had significantly better outcomes.	43% patients experienced disease progression (median time to progression = 1.4 years)	Among the survivors (n = 25), 60% had chronic visual impairments. Endocrinopathies were present in 92% patients. 64% patients were overweight or obese at their last evaluation, with one patient requiring bariatric surgery.

Enayet. 2021 [9]	130 Retrospective 65 Surgery “follow up group” 71 Surgery+RT “RT group” 1 Ommaya+IF	43.95 months (median)	To report their experience and management strategies for childhood CPG.	Management protocol is presented based on i**ndividualized surgical approach** (guided by preoperative imaging and intraoperative findings) **and tumor genetics** (Beta-catenin mutations)	Beta-catenin mutations more than 5% were associated with statistically trending aggressive clinical behavior.	5-year PFS was 52.3%, (34.49% for the follow-up group and 72.25% for the RT group) Median time to progression in the follow-up cohort and the radiotherapy cohort was 20.5 months and 44.3 months, respectively.	Mortality was reported in eight patients (8/137)