National UK Guidelines for the Investigation, Treatment & Long-Term Follow-Up of Paediatric Craniopharyngioma

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BACKGROUND

- Craniopharyngiomas are rare benign central nervous system tumours arising from embryological remnants of Rathke's pouch, but account for 80% of all suprasellar lesions in children and young people (CYP).
- 30-year overall survival rates are high (up to 80%[1]) but patients often suffer multiple relapses requiring repeated interventions and long-term neuroendocrine, cognitive and visual tumour- and treatment-related morbidity.
- Treatment is usually by a combination of neurosurgery and/ or radiotherapy but the rarity of these tumours and the lack of randomised-controlled trials means that there are large variations in management between centres with no previous evidence-based national or international guidelines.

AIM

- To provide, for the first time, an evidence- and consensus-based standard for best practice for the diagnosis, assessment, management and follow-up of craniopharyngiomas in CYP aged <19 years under the auspices of the Royal College of Paediatrics & Child Health (RCPCH), Children's Cancer & Leukaemia Group (CCLG) and the British Society for Paediatric Endocrinology & Diabetes (BSPED).

METHODS

Clinical questions formulated in PICO (**P**opulation, **I**ntervention, **C**omparison, **O**utcome) format and approved by stakeholders → 44 clinical (PICO) questions

Systematic searches of the English literature conducted using Ovid MEDLINE (1946-April 2019), CENTRAL (2016, Issue 12), DARE (2015, Issue 1) → 2023 primary research articles identified

3-tier exclusion filter:
Tier 1: Excluded based on title
Tier 2: Excluded based on abstract
Tier 3: Excluded based on detailed reading of full paper → 300 primary research articles included

GRADE assessment[2] of quality of evidence → 32 statements of recommendation

Consensus recommendations made based on Guideline Development Group expert opinion for statements where no/ insufficient published evidence was obtained → 33 consensus recommendations

2 rounds of DELPHI consensus (>70% agreement included)[3] → 28 consensus recommendations included (total 60 recommendations made)

KEY RECOMMENDATIONS

Recommendation	Strength	GRADE
All CYP with a suspected or confirmed craniopharyngioma should be managed in a specialist paediatric endocrine centre by an age-appropriate endocrinologist with experience in pituitary tumours, in liaison with the designated multidisciplinary neuro-oncology team.	Strong	Delphi consensus
Age-appropriate MDT support (neurosurgery, radiation oncology, endocrinology, neuroradiology, neuropathology) should be offered and include adult pituitary specialists where appropriate.	Strong	Low, GDG Consensus
The pre-operative MRI report should include grading of the extent of hypothalamic involvement according to the 'Paris' system[4].	Strong	High
Visual acuity, visual fields and fundoscopy should be formally assessed before treatment in all cooperative CYP. Pattern VEPs may be substituted in infants/ disabled children but should not be used for long-term surveillance.	Strong	Low, GDG consensus
Baseline endocrine biochemistry should be performed in all CYP at presentation and include an urgent AFP, β-hCG and PRL before any definitive surgery, as well as IGF-1, TSH, fT_4, LH, FSH, testosterone/ oestradiol, morning cortisol, ACTH and paired early morning plasma/ urine osmolalities.	Strong	Delphi consensus
Combined dynamic pituitary function tests of GH and cortisol reserve +/- gonadotrophin secretion should be performed at presentation, before any steroid therapy, when possible.	Strong	Delphi consensus
Clinicians should offer access to a surgeon with specific experience in paediatric craniopharyngioma surgery as evidence suggests that this may improve overall outcomes.	Strong	Low, GDG Consensus
Surgical procedures (complete/ subtotal resection or cyst aspiration) should be considered in all CYP given the better overall and progression-free survival compared with conservative (watch and wait) management alone.	Strong	Moderate
Complete resection should not be attempted where there is clear evidence of hypothalamic involvement on 'Paris' grading.	Strong	Moderate
Where tumour resection is incomplete, upfront external beam radiotherapy can be offered.	Weak	Low
Clinicians should be aware of the availability of proton beam therapy as a radiation treatment modality for CYP with craniopharyngiomas.	Weak	Low
All patients should undergo repeat formal visual acuity +/- visual field assessment within 3 months of definitive treatment.	Strong	Delphi consensus
A basal & combined dynamic anterior pituitary function test should be undertaken off replacement therapy within 6 weeks of initial tumour treatment (if not performed at diagnosis) to assess the GH/ ACTH/ TSH +/- LH/FSH axes.	Strong	Delphi consensus
Endocrinology follow-up for evolving hypopituitarism should be lifelong, with the frequency determined on an individual basis.	Strong	Delphi consensus
Recombinant hGH replacement therapy is safe, does not increase tumour progression and should be considered in confirmed GH deficiency to re-establish normal linear growth.	Strong	Moderate
CYP with identified neuropsychological and neurological deficits and those who have undergone cranial radiotherapy require ongoing neuropsychological follow-up until adulthood.	Strong	Delphi consensus

CONCLUSION

These UK RCPCH/ CCLG/ BSPED-endorsed guidelines provide the first evidence-based recommendations for the management of paediatric craniopharyngiomas, by which better consistency in the quality of care of such patients may be achieved with the aim of improving long-term quality of survival.

References
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