Craniopharyngioma Clinical Status Scale: a standardized metric of preoperative function and posttreatment outcome

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Object. Controversy persists concerning the optimal treatment of craniopharyngiomas in children, and no standard outcome metric exists for comparison across treatment modalities, nor is there one that adequately reflects the multisystem dysfunction that may arise.

Methods. The authors retrospectively analyzed the records of 86 consecutive children who underwent a uniform treatment paradigm of attempted radical resection performed by a single surgeon. Excluding 3 perioperative deaths and 3 patients with inadequate follow-up, 80 children (34 girls and 46 boys; mean age 9.56 years; mean follow-up 9.6 years) composed the study group (53 primary and 27 previously treated/recurrent tumors). Building on existing classification schemes proposed by De Vile for hypothalamic dysfunction and Wen for overall functional outcome, the authors devised a more nuanced classification system (Craniopharyngioma Clinical Status Scale [CCSS]) that assesses outcome across 5 axes, including neurological examination, visual status, pituitary function, hypothalamic dysfunction, and educational/occupational status at last follow-up (there is a 4-tiered grading scale in each domain, with increasing values reflecting greater dysfunction).

Results. There was a significant increase in pituitary dysfunction following treatment—consistent with the high rates of diabetes insipidus and hypopituitarism common to the surgical management of craniopharyngiomas—and less dramatic deterioration in hypothalamic function or cognitive domains. Significant improvement in vision was also demonstrated, with no significant overall change in neurological status. Preoperative CCSS scores predicted postoperative outcome better than clinical characteristics like patient age, sex, tumor size, and the location or presence of hydrocephalus.

Conclusions. Preoperative CCSS scores predicted outcome with higher accuracy than clinical or imaging characteristics. In lieu of randomized trials, the CCSS may provide a useful outcome assessment tool for comparison across treatment paradigms and surgical approaches. Long-term follow-up is critical to the analysis of outcomes of craniopharyngioma treatment, given the often-delayed sequelae of all therapies and the high recurrence rates of these tumors. (DOI: 10.3171/2010.2.FOCUS09304)

KEY WORDS • pediatric tumor • craniopharyngioma • functional outcome • functional assessment

CRANIOPHARYNGIOMAS are the most common non-glial brain tumor of childhood—comprising 6–8% of pediatric brain tumors—but are relatively rare on a population-wide scale.^{3,5,66} They are benign neoplasms thought to arise from embryological remnants of squamous epithelium of the craniopharyngeal duct.^{49,65} They most commonly arise in the suprasellar region and

have intimate relationships with the circle of Willis, third ventricle, hypothalamus, optic pathways, and pituitary stalk. Although histologically benign, their proximity to such critical structures and their tendency to recur render them potentially dangerous. Children with these tumors are prone to significant deficits prior to or as a result of treatment.

As improvements in surgical technique, RT modalities, and supportive care have resulted in improved overall survival, attention has shifted toward analysis of the quality of survival.^{6,7,41,46,50,55,58,61} Although investigators in a handful of studies have attempted to create grading scales to assess functional outcomes and QOL in patients with craniopharyngiomas, each scale has its own limitations. Wen and colleagues⁶⁷ developed a 4-tiered outcome

Abbreviations used in this paper: ADLs = activities of daily living; BMI = body mass index; CCSS = Craniopharyngioma Clinical Status Scale; DI = diabetes insipidus; E-CCSS = educational/occupational CCSS; GTR = gross-total resection; H-CCSS = hypothalamic CCSS; N-CCSS = neurological CCSS; NYU = New York University; P-CCSS = pituitary CCSS; QOL = quality of life; RT = radiation therapy; TBI = traumatic brain injury; VA = visual acuity; V-CCSS = visual CCSS; VF = visual field.

TABLE 1: Proposed CCSS

Domain & Score	Criteria
N-CCSS	
1	no deficits or seizures
2	mild deficits (cranial nerve palsy, well-controlled seizures)
3	moderate deficits (mild hemiparesis w/ independent ambulation, moderately controlled seizures)
4	severe deficits (moderate-to-severe hemiparesis, major stroke, significant abulia, or lethargy)
V-CCSS	
1	normal VA & VFs
2	mild acuity deficits or field cut
3	unilat blindness, homonymous hemianopia, or bitemporal hemianopia
4	bilat blindness or nearly functional blindness
P-CCSS	
1	normal anterior & posterior pituitary function
2	mild anterior pituitary dysfunction (1 or 2 hormone supplements)
3	DI w/ or w/o mild anterior pituitary dysfunction (1 or 2 hormone supplements)
4	DI & panhypopituitarism
H-CCSS*	
1	normal hypothalamic function
2	postop obesity (BMI >+2 SD), lack of behavioral/psychological symptoms
3	obesity (BMI >+2 SD) w/ hyperphagia, or memory disturbance or BMI >+3 SD w/o frank hyperphagia behaviors
4	extreme obesity (BMI >+4 SD) & hyperphagia, behavioral disturbances (such as rage episodes), & disturbances of thermoregulation, sleep-wake cycles, or memory
E-CCSS	
1	excellent academic performance &/or occupational success
2	good academic performance at grade level &/or maintaining employment†
3	behind in grade academically, requires significant tutoring, or inability to maintain consistent employment‡
4	completely dependent on others for self-care (cannot perform ADLs), IQ <80, severe cognitive deficits

* Modified version of scale proposed by De Vile et al.¹²

† Meeting or exceeding developmental milestones for preschool-aged children.

‡ Not meeting age-appropriate developmental milestones for preschool-aged children.

scale that addressed overall functional outcome across domains, and De Vile et al.¹² created a grading scale focused on predicting hypothalamic dysfunction to determine the optimal extent of the intended resection. Duff et al.¹⁷ proposed a 2-tiered grading scale that dichotomized outcome into good or poor based on 8 inclusion criteria. Despite these attempts, no assessment tool currently exists that adequately addresses the myriad systems affected by craniopharyngiomas and their treatment, and none has been validated or consistently adopted by other centers.

We propose a system that assesses the following 5 axes of function in children with craniopharyngiomas, to serve as a preliminary attempt at a comprehensive evaluation of pre- and posttreatment status: vision, neurological status, pituitary function, hypothalamic function, and educational/occupational status. Given the persistent debate about the optimal treatment of craniopharyngiomas (namely, radical resection vs limited resection and RT; transcranial vs transsphenoidal approaches), we hope that such a scale could find universal appeal and allow meaningful comparisons across treatment paradigms.

Methods

Patient Population

Between 1986 and 2008, a total of 86 consecutive children younger than 21 years of age underwent 104 operations for excision of craniopharyngiomas by the senior author (J.H.W.) at NYU's Langone Medical Center. Following approval by the NYU Institutional Review Board, data were retrospectively collected by reviewing clinic/office and inpatient records, pre- and postoperative and last follow-up CT and/or MR imaging studies, and operative and pathology reports. Patient characteristics, prior treatments, imaging features, extent of resection, recurrence rate, time to progression, and other oncological treatments were recorded. Long-term follow-up information was obtained between 2006 and 2009 by contacting patients, families, and referring physicians, and from records of the last follow-up office visit. Current follow-up data were not available in 3 patients, and their follow-up duration was censored at the time of last visit (6, 131, and

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180 months). Three patients died perioperatively, and in 3 no follow-up data were available. These latter 6 patients were excluded from the study. Primary tumors were those treated at NYU at the time of initial presentation; recurrent tumors were those referred to NYU for surgery after failure of prior treatment at other hospitals. It should be noted that some patients in this series were included in other reports on various aspects of the management of craniopharyngiomas in children.^{20–23,58,66,70,71}

A GTR was the primary aim of treatment in all children and was defined as the lack of residual tumor on visual inspection intraoperatively and no residual soft-tissue mass or enhancement suspected to be tumor on postoperative imaging, as determined by an independent neuroradiologist. The outcome variables measured included BMI (weight [in kilograms]/height² [in square meters]) with Z scores (SDs),⁵⁶ endocrine replacement regimen, VA and VF testing performed pre- and postoperatively by pediatric ophthalmologists, neurological examination pre- and postoperatively, subsequent seizures requiring medications, and highest level of education attained and need for educational assistance.

Children were scored using a 4-tiered grading scale across 5 domains prior to surgery at NYU and at last follow-up (Table 1). The scoring of deficits and function is as follows: 1, normal/excellent function; 2, mild deficit/good function; 3, moderate deficit/fair function; and 4, severe deficit/poor function.

Neurological status was assessed by the neurooncologist, pediatric or adult neurologist, or, less commonly, the senior author. To minimize bias, all possible attempts were made to limit the extent of involvement by the treating neurosurgeon in the neurological evaluation of the patients. Patients with an N-CCSS score of 1 had normal results on neurological examination and were without seizures. Patients receiving an N-CCSS score of 2 had mild deficits like cranial nerve palsy and/or seizures that were well controlled with medications. Patients with an N-CCSS score of 3 had moderate deficits, which included hemiparesis with independent ambulation, or epilepsy. Patients with an N-CCSS score of 4 had significant hemiparesis that prevented ambulation, hemispheric stroke, significant abulia, or abnormal level of consciousness.

All ophthalmological examinations were performed by a pediatric ophthalmologist or neuroophthalmologist, and were composed of detailed VA and VF examinations. Patients with a V-CCSS score of 1 had normal VA and VF function. Patients with a V-CCSS score of 2 had mild deficits in VA (< 20/100) and VF (quadrantanopia or unilateral nasal or temporal field deficit). Patients with a V-CCSS score of 3 had unilateral blindness, bitemporal hemianopia, or homonymous hemianopia. Patients with a V-CCSS score of 4 had bilateral blindness or enough visual compromise in both eyes to be considered functionally blind.

Pituitary function and supplementation needs were assessed by a pediatric endocrinologist. The presence of DI and anterior pituitary deficits were recorded. Patients with a P-CCSS score of 1 had normal anterior and posterior pituitary function and required no supplementation. Patients with a P-CCSS score of 2 had mild anterior pituitary dysfunction requiring supplementation of 1 or 2

TABLE 2: Functional classification scale*

Class	Criteria
I	grossly normal & independent mild hormonal disturbances seizures well controlled w/ medication
II	independent panhypopituitarism mild-to-moderate visual compromise cranial nerve deficits mild psychological dysfunction
III	partially dependent serious visual compromise serious neurological deficits (hemiparesis, refractory seizures) learning disabilities or poorly controlled psychological disorders
IV	entirely dependent on others for self-care

* Based on data in the article by Wen et al.

hormones. Patients with a P-CCSS score of 3 had DI with or without mild anterior pituitary dysfunction. Patients with a P-CCSS score of 4 had DI and panhypopituitarism (requiring ≥ 3 supplemental hormones).

Hypothalamic dysfunction scoring is primarily based on the assessment scale created by De Vile et al.,¹² with only slight modifications for more objective reporting of “obesity” by using BMI with Z scores. In addition to BMI analysis, hypothalamic dysfunction was assessed by parental, family, or primary physician reporting of behavioral disturbances. Patients with an H-CCSS score of 1 exhibited no signs of obesity or behavioral disturbances indicative of hypothalamic injury. Patients with an H-CCSS score of 2 had evidence of postoperative obesity (BMI > +2 SD), but lacked behavioral or psychological symptoms. Patients with an H-CCSS score of 3 exhibited obesity (BMI > +2 SD) with food-seeking behaviors, severe obesity (BMI > +3 SD) without overt hyperphagia, memory disturbance, and no evidence of psychosocial dysfunction. Patients with an H-CCSS score of 4 had one or more of the following signs: extreme obesity (BMI > +4 SD), behavioral disturbances such as rage episodes, severe social isolation, and disturbances of thermoregulation, sleep-wake cycles, or severe memory deficits.

Educational (for school-aged children) and developmental (for preschool-aged children) outcomes were based on neuropsychological testing when available, and on evaluations by pediatric neurologists or primary pediatricians specifically documenting developmental or educational status. Assessments of occupational functioning were obtained from patients, their family members, or their primary medical doctors. Outcomes (E-CCSS) were classified as excellent (E-CCSS score of 1) in children who achieved good or excellent grades at the appropriate level, entered and/or graduated from college, or in adults excelling in their chosen vocation. Good outcomes (E-CCSS score of 2) applied to children who were achieving passing grades at the appropriate level with or without tutoring, in young children meeting or exceeding age-ap-

TABLE 3: Comparison of baseline demographic characteristics of patients with primary and recurrent craniopharyngiomas*

Variable	Primary Group	Recurrent Group	p Value
age (yrs)	8.26 ± 4.5	12.1 ± 4.7	0.001
sex distribution (% M)	58.9	50.0	0.48
tumor size (cm)	4.1 ± 1.5	4.0 ± 1.7	0.91
retrochiasmatic location	43.6%	57.7%	0.34
hydrocephalus present	29.1%	53.8%	0.048
ventriculoperitoneal shunt	14.5%	46.2%	0.005
follow-up (yrs)	11.4 ± 6.5	6.1 ± 5.5	<0.0001

* Values for age, tumor size, and follow-up are given as the mean ± SD.

propriate developmental milestones, and in adults maintaining steady employment. Fair outcomes (E-CCSS score of 3) were cases in which children were behind in school, required special education/tutoring, were not meeting age-appropriate developmental milestones, and in which adults were unable to maintain steady employment. Poor outcomes (E-CCSS score of 4) were those in which patients had severe cognitive deficits, IQ < 80, or required significant assistance with ADLs. For preschool-aged children, those meeting or exceeding their age-appropriate developmental milestones were given an E-CCSS score of 2, and those not meeting milestones were given a score of 3.

In addition to recording neuropsychological, educational, or developmental status at last follow-up, overall functional morbidity—including visual, neurological, hypothalamic, pituitary, and psychosocial dysfunction—was assessed using the 4-tiered classification system proposed by Wen et al.⁶⁷ (criteria presented in Table 2). The Wen scores were converted into ordinal numbers for statistical analyses.

Ordinal logistic regression analysis was performed to determine the impact of age at surgery (continuous variable), sex (dichotomous variable), tumor location (dichotomous variable: retro- vs prechiasmatic), tumor size (continuous variable), presence of hydrocephalus (dichotomous variable), prior treatment (dichotomous), and baseline CCSS scoring on the ultimate CCSS outcome after treatment at NYU. Each model was tested for significance by using Cox and Snell pseudo-R² testing and model-fitting chi-square testing with p values. A p value < 0.10 on univariate testing was the cutoff for inclusion in the multivariate model.

Averages are expressed as the mean ± SD. The Student t-test was used to compare the following parametric variables: age at time of surgery, maximal tumor diameter, and follow-up duration. The CCSS scores were converted to ordinal numbers for statistical comparisons. The Fisher exact test was used to compare proportions. The Wilcoxon rank-sum test (Mann-Whitney U-test) and paired-sample Wilcoxon signed-rank test were used to compare nonparametric variables between primary and recurrent tumor groups and between pre- and postoperative outcomes, respectively, in the same patients. All statistics were calculated with SPSS software (SPSS 17.0 for Mac; SPSS, Inc.). A p value of < 0.05 on 2-tailed testing was considered statistically significant.

Results

Patients' Demographic Data

Demographic data comparing primary and recurrent tumors are summarized in Table 3. There were 46 males and 34 females in this study group, whose mean age was 9.6 ± 4.8 years at time of surgery (range 9 months–20.5 years). Twenty-seven patients (34%) had received treatment prior to referral to our center, and 53 children (66%) had primary tumors. Thirty-nine tumors (49%) were prechiasmatic, 35 were retrochiasmatic (44%), and 5 large tumors (6%) had both pre- and retrochiasmatic components. One 5-cm tumor was located entirely within the third ventricle. The mean tumor size was 4.1 ± 1.6 cm (range 1.1–8 cm). Thirty patients (37.5%) had preoperative hydrocephalus, and 20 patients (25%) either had ventriculoperitoneal shunts at presentation or required one following resection. The mean follow-up duration was 9.6 ± 6.6 years (range 6 months–23.8 years).

Children with recurrent tumors were older (p = 0.001), were more likely to have hydrocephalus (p = 0.048), were more likely to have or to need ventriculoperitoneal shunts (p = 0.005), and had shorter follow-up (p < 0.0001) compared with the primary tumor group. There was no difference in the sex distribution, distribution of tumor location, or tumor size.

Prior treatments for patients in the recurrent tumor group included one or more resections in 15 children and limited resection plus RT in 10. Two patients had aspirations, followed by Gamma Knife radiosurgery in one child and conventional RT in the other.

Neurological Status

Sixty-four children (80%) were neurologically intact at time of presentation to NYU. Of the 16 patients (20%) with deficits prior to surgery, hemiparesis was the primary deficit in 10 patients and lethargy in 3 patients. Of note, 4 patients with hemiparesis also had either unilateral third cranial nerve palsies or lethargy (2 patients each). The proportion of patients in the primary group (7 [13.2%] of 53) who had preoperative neurological deficits was less than in the recurrent group (9 [33%] of 27; p = 0.04). Preoperative N-CCSS scores are summarized in Fig. 1A. Sixty-four children (80%) had an N-CCSS score of 1; 2 children (2.5%) had a score of 2; 10 (12.5%) had a score

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Fig. 1. Histograms summarizing preoperative (A), postoperative (B), and change in (C) N-CCSS scores in children with primary and recurrent craniopharyngiomas.

of 3; and 4 (5%) had a score of 4. The mean preoperative N-CCSS score was 1.43 ± 0.90 (median 1). The children with recurrent tumors had a higher N-CCSS score prior to surgery ($p = 0.03$), indicating greater pretreatment neurological dysfunction.

Sixty patients (75%) were either improved (4 patients [5%]) or at their neurological baseline (56 [70%]) in the immediate postoperative period after the initial operation at NYU. Twenty (25%) developed new major (8 patients) and minor (12 patients) neurological deficits in the immediate postoperative period. Four patients (5%) suffered strokes, and another had a mild hemiparesis with nearly complete resolution by 6 months. Three patients had severe lethargy and abulia that either partially or completely resolved by 2 weeks postoperatively. Eleven of these new deficits were cranial nerve palsies, 9 (82%) of which completely resolved by the 6-month follow-up. Two patients

required corrective surgery for persistent strabismus. At the last follow-up, 10 patients (12.5%) had permanent postoperative neurological deficits, and 16 (20%) were taking antiepileptic drugs for postoperative seizures. No patient had epilepsy that was refractory to medications. Postoperative N-CCSS scores are summarized in Fig. 1B. Sixty-three children (78.8%) had an N-CCSS score of 1; 4 children (5%) had a score of 2; 7 (8.8%) had a score of 3; and 6 (7.5%) had a score of 4. The mean postoperative N-CCSS score was 1.45 ± 0.94 (median 1). Children with recurrent tumors continued to have higher N-CCSS scores postoperatively; however, the difference was only marginally significant at last follow-up ($p = 0.076$).

Figure 1C demonstrates the change in N-CCSS score following treatment. The mean change in the neurological score was $+0.03 \pm 0.84$ (median 0, range -3 to +3). Overall, there was no significant decline in neurological func-

TABLE 4: Comparison of CCSS scores between primary and recurrent craniopharyngiomas*

Domain	Primary Group	Recurrent Group	p Value
preop score			
N-CCSS	1.26 ± 0.71	1.74 ± 1.13	0.03
V-CCSS	1.79 ± 0.93	2.67 ± 0.78	<0.001
P-CCSS	1.51 ± 0.72	2.78 ± 0.85	<0.001
H-CCSS	1.17 ± 0.64	1.96 ± 1.06	<0.001
E-CCSS	1.55 ± 0.67	1.81 ± 0.79	0.13
postop score			
N-CCSS	1.34 ± 0.85	1.67 ± 1.07	0.076
V-CCSS	1.62 ± 0.81	2.48 ± 0.80	<0.001
P-CCSS	3.23 ± 0.89	3.15 ± 0.72	0.42
H-CCSS	1.55 ± 0.93	2.19 ± 1.00	0.003
E-CCSS	1.79 ± 0.88	2.37 ± 1.12	0.02
change in score			
N-CCSS	0.08 ± 0.70	-0.07 ± 1.07	0.60
V-CCSS	-0.17 ± 0.83	-0.19 ± 0.68	0.82
P-CCSS	1.72 ± 1.04	0.37 ± 0.56	<0.001
H-CCSS	0.38 ± 0.74	0.22 ± 0.58	0.32
E-CCSS	0.25 ± 0.73	0.56 ± 0.70	0.03

* Values are given as the mean $\pm$ SD.

Fig. 2. Histograms summarizing preoperative (A), postoperative (B), and change in (C) V-CCSS scores in children with primary and recurrent craniopharyngiomas.

tion as a result of radical resection ($p = 0.42$). There was no difference in the change in N-CCSS score between primary and recurrent tumor groups following treatment ($p = 0.6$). The pre- and postoperative N-CCSS scores and changes following treatment for both primary and recurrent craniopharyngiomas are shown in Table 4.

The ordinal logistic regression model for N-CCSS was significant (pseudo- $R^2 = 0.35$; $p < 0.0005$). Predictors of higher postoperative N-CCSS scores (Table 5) included preoperative N-CCSS score ($p = 0.036$) and giant tumor size ($p = 0.03$).

Visual Status

Two children were too young for formal VA testing and were scored only on gross VF testing results. Forty-three (57.5%) of 80 children had VF deficits, and 31 (40%) of 78 children had VA deficits. Compared with those with primary tumors, a higher proportion of patients with recurrent craniopharyngiomas had VF (23 [43.4%] of 53 vs 20 [74.1%] of 27; $p = 0.01$) and VA (15 [29.4%] of 51 vs 16 [59.3%] of 27; $p = 0.015$) deficits. Two patients were blind prior to surgery at NYU (1 with a primary and 1 with recurrent tumor), 2 had unilateral blindness, and 1 patient had vision limited to the left inferior quadrant, with poor acuity. Preoperative V-CCSS scores are summarized in Fig. 2A. Thirty-two children (40%) had a V-CCSS score of 1; 11 children (13.8%) had a score of 2; 35 (43.8%) had a score of 3; and 2 (2.5%) had a score of 4. The mean preoperative V-CCSS score was 2.09 ± 0.97 (median 2). Children with recurrent tumors had significantly higher preoperative V-CCSS scores in the recurrent tumor group ($p < 0.001$).

Of the 31 patients with VA deficits, improvement occurred in 13 (42%). Deterioration in VA occurred in 12 patients overall, with only 3 patients experiencing monocular blindness. Of these, 1 patient had VA results of 20/40 in the affected eye preoperatively; 1 was too young for preoperative testing, but had decreased vision compared with the unaffected eye prior to surgery; and the final patient had vision only in the left inferior quadrant, with poor VA prior to surgery. None of the 3 patients with preoperative blindness recovered vision. One patient with 20/40 VA bilaterally prior to surgery experienced marked

deterioration in his vision postoperatively, and was using Braille for reading at last follow-up.

Of the 43 patients with VF deficits, improvement occurred in 20 (47%). Although VF deficits occurred in 15 patients, only 3 had new deficits that interfered with daily functioning. The most common new immediate postoperative VF deficit was a homonymous hemianopia contralateral to the side of approach (10 left, 1 right). This was most likely due to manipulation of the ipsilateral aspect of the optic chiasm and/or optic tract during tumor removal via the pterional approach. This deficit had resolved in 5 patients by 6 months after resection. Six patients were left with a permanent complete homonymous hemianopia or superior left quadrantanopia (3 each).

Postoperative V-CCSS scores are summarized in Fig. 2B. Thirty-one children (38.8%) had a score of 1; 28 (35%) had a score of 2; 17 (21.3%) had score of 3; and 4 (5%) had a score of 4. The mean postoperative V-CCSS score was 1.9 ± 0.90 (median 2). Children with recurrent tumors continued to have higher V-CCSS scores following surgery ($p < 0.001$).

Figure 2C demonstrates the change in V-CCSS score following treatment. The mean change in score was -0.18 ± 0.78 (median 0, range -2 to +1). There was a significant improvement in V-CCSS score following resection ($p = 0.04$). No patient had more than a 1-point increase (worsening) in V-CCSS score. There was a marginally significant trend toward a higher proportion of VF improvement in primary compared with recurrent tumors (9 [56.3%] of 16 vs 4 [27%] of 15; $p = 0.15$), but no difference in the rate of VF improvement (13 [43.5%] of 23 vs 7 [35%] of 20; $p = 0.22$). There was no difference in rate of VF (9 [17%] of 53 vs 6 [22%] of 27) or VA (7 [14%] of 51 vs 5 [18.5%] of 27) deterioration between primary and recurrent tumor groups following resection. Overall, there was no difference in the change in V-CCSS score between children with primary and recurrent craniopharyngiomas ($p = 0.82$). The pre- and postoperative V-CCSS scores and changes following treatment for both primary and recurrent craniopharyngiomas are shown in Table 4.

The ordinal logistic regression model for V-CCSS was significant (pseudo- $R^2 = 0.56$, $p < 0.0005$). Predictors of higher postoperative V-CCSS scores (Table 5) in-

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TABLE 5: Multinomial logistic regression analysis of predictors of postoperative CCSS outcomes*

Variable	p Values for Individual Functional Domains				
	N-CCSS	V-CCSS	P-CCSS	H-CCSS	E-CCSS
age at op	NS	NS	0.07	NS	NS
sex	NS	0.09	NS	NS	NS
giant tumor size	0.03	NS	NS	NS	0.10
recurrent tumor	NS	0.03	0.01	NS	0.06
hydrocephalus	NS	0.07	NS	0.05	0.005
retrochiasmatic location	NS	NS	NS	NS	0.13
preop CCSS score	0.036	<0.0005	<0.0005	<0.0005	<0.0005

* NS = not significant.

cluded preoperative V-CCSS score ($p < 0.0005$) and prior treatment ($p = 0.03$).

Pituitary Function

Twenty-five patients (31.3%) had DI prior to initial surgery at NYU, with or without hypopituitarism. Significantly more patients in the recurrent group (18 [67%] of 27) had preoperative DI compared with the primary group (7 [13%] of 53, $p < 0.001$) prior to surgery at NYU. Preoperative P-CCSS scores are summarized in Fig. 3A. Thirty-three children (41.3%) had a P-CCSS score of 1; 22 (27.5%) had a score of 2; 18 (22.5%) had a score of 3; and 7 (8.8%) had a score of 4. The mean preoperative P-CCSS score was 1.99 ± 1.0 (median 2). Patients with recurrent tumors had significantly higher P-CCSS scores than the primary group ($p < 0.001$).

Postoperatively, 62 patients (77.5%) had DI, including 37 (46.3%) with new-onset DI. Overall, there was no significant difference in the rate of permanent DI between the primary (78%) and recurrent groups (89%). Postoperative P-CCSS scores are summarized in Fig. 3B. Four children (5%) had a score of 1; 9 children (11.3%) had a score of 2; 34 (42.5%) had score of 3; and 33 (41.3%) had a score of 4. The mean postoperative P-CCSS score was 3.2 ± 0.83 (median 3). There was no difference in the postoperative P-CCSS scores between the primary and recurrent tumor groups ($p = 0.42$).

Figure 3C demonstrates the change in P-CCSS score

following treatment. The mean change in score was $+1.21 \pm 1.1$ (median 1, range 0 to +3), indicating significant worsening of pituitary function following resection ($p < 0.001$). No patient experienced improvement in pituitary function following treatment. Patients with primary tumors had a greater increase in P-CCSS scores following treatment, indicating a significantly greater decline in pituitary function following resection compared with the recurrent tumor group ($p < 0.001$). The pre- and postoperative P-CCSS scores and changes following treatment for both primary and recurrent craniopharyngiomas are shown in Table 4.

The ordinal logistic regression model for P-CCSS was significant (pseudo- $R^2 = 0.28$; $p = 0.002$). Predictors of higher postoperative P-CCSS scores (Table 5) included preoperative P-CCSS score ($p < 0.0005$) and prior treatment ($p = 0.01$). Of note, no predictors of P-CCSS outcomes were identified when subgroup analysis of children with primary tumors was performed. This was due to the nearly universal endocrinopathy that occurred subsequent to treatment—yielding poor correlations between pre- and postoperative status.

Hypothalamic Function

Hypothalamic disturbance was present in 17 children (21%; 4 primary and 13 recurrent) preoperatively (De Vile classifications: mild in 4, moderate in 9, and severe in 4) and was more prevalent in children in the recurrent

FIG. 3. Histograms summarizing preoperative (A), postoperative (B), and change in (C) P-CCSS scores in children with primary and recurrent craniopharyngiomas.

Fig. 4. Histograms summarizing preoperative (A), postoperative (B), and change in (C) H-CCSS scores in children with primary and recurrent craniopharyngiomas.

group ($p < 0.001$). Eight patients had mild (5 patients) or moderate (3 patients) dysfunction in short-term memory prior to surgery at NYU. Preoperative H-CCSS scores are summarized in Fig. 4A. Sixty-three children (78.8%) had an H-CCSS score of 1; 4 children (5%) had a score of 2; 9 (11.3%) had a score of 3; and 4 (5%) had a score of 4. The mean preoperative H-CCSS score was 1.42 ± 0.88 (median 1). Patients with recurrent tumors had significantly higher H-CCSS scores than the primary group ($p < 0.001$), indicative of greater pretreatment dysfunction.

Eighteen children (22.5%) developed new or worsened hypothalamic dysfunction postoperatively (mild in 10, moderate in 7, severe in 1). Height and weight measurements were available in 62 patients at the last follow-up (85% of the primary group [45 patients], and 63% of the recurrent group [17]). The mean BMI was $+1.18$ SDs above normal for the entire cohort (median 1.23, SD 1.4). Although there was a trend toward higher BMI in the recurrent group, this difference was only marginally significant ($p = 0.058$). At last follow-up, 12 patients (19%) had obesity (BMI $> +2$ SD), 1 (1.6%) had severe obesity (BMI $> +3$ SD), and 1 had morbid obesity (BMI in this patient, $+4.11$). The only child with morbid obesity (BMI $+4.11$) had severe obesity prior to surgery. Two children experienced worsening of their premorbid short-term memory deficits, and another child's deficits improved following resection. Eleven patients experienced new mild (10 children) or moderate (1 child) short-term memory dysfunction postoperatively. Another patient with a 5-cm intraventricular tumor experienced significant lethargy and permanent bulba and cognitive deficits following transcallosal resection. Six of these patients experienced significant improvement in memory function over time. Postoperative H-CCSS scores are summarized in Fig. 4B. Forty-six children (57.5%) had a score of 1; 12 (15%) had a score of 2; 17 (21.3%) had score of 3; and 5 (6.3%) had a score of 4. The mean postoperative H-CCSS score was 1.76 ± 1.0 (median 1). Higher H-CCSS scores persisted following treatment for children with recurrent craniopharyngiomas ($p = 0.003$).

Figure 4C demonstrates the change in H-CCSS score following treatment. The mean change in score was $+0.34$

± 0.69 (median 0, range 0 to $+3$), indicating worse hypothalamic dysfunction following resection ($p < 0.001$). There was no difference in the change in H-CCSS scores following treatment between the primary and recurrent tumor groups ($p = 0.52$). There were no differences in pre- or postoperative hypothalamic dysfunction or BMI in children with pre- and retrochiasmatic tumors. The pre- and postoperative H-CCSS scores and changes following treatment for both primary and recurrent craniopharyngiomas are shown in Table 4.

The ordinal logistic regression model for H-CCSS was significant (pseudo- $R^2 = 0.58$; $p < 0.0005$). Predictors of higher postoperative H-CCSS scores (Table 5) included preoperative H-CCSS score ($p < 0.0005$) and presence of hydrocephalus ($p = 0.05$).

Educational/Occupational Status

Preoperative E-CCSS scores are summarized in Fig. 5A. Thirty-nine children (48.8%) had an E-CCSS score of 1; 32 (40%) had a score of 2; 7 (8.8%) had a score of 3; and 2 (2.5%) had a score of 4. The mean preoperative E-CCSS score was 1.65 ± 0.75 (median 2). There was no significant difference between children with recurrent tumors and the primary group in terms of their E-CCSS scores ($p = 0.136$).

Postoperative E-CCSS scores are summarized in Fig. 5B. Thirty-two children (40%) had a score of 1; 25 (31.3%) had a score of 2; 15 (18.8%) had score of 3; and 8 (10%) had a score of 4. The mean postoperative E-CCSS score was 1.99 ± 1.0 (median 2). Of the poor-outcome group (E-CCSS score of 4), 4 children had significant deficits on formal IQ testing (IQ < 80), and 4 were disabled enough to require significant assistance with ADLs. Seven of the 8 children in this group had preoperative cognitive deficits (mild in 3, moderate in 2, severe in 2). The final patient in this group experienced a midbrain stroke that left him physically dependent but cognitively normal. Among the 15 children who experienced a fair outcome (E-CCSS score of 3), 8 had preoperative cognitive deficits. One child in the fair-outcome group made significant gains in cognition following resection, but social isolation remained prominent. Three children who experienced good

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Fig. 5. Histograms summarizing preoperative (A), postoperative (B), and change in (C) E-CCSS scores in children with primary and recurrent craniopharyngiomas.

outcomes (E-CCSS score of 2) had mild preoperative deficits that improved postoperatively. No children with excellent outcomes (E-CCSS score of 1) had documented preoperative cognitive deficits, and 3 experienced gains in IQ scores of > 10 points. Thirty-five (73%) of 48 patients 18 years of age or older at the time of last follow-up were either currently attending, had matriculated into, or had graduated from college. Three patients experienced improvement in their social interactive skills, and 1 child worsened in that domain following surgery. Higher E-CCSS scores persisted following treatment for children with recurrent craniopharyngiomas ($p = 0.02$).

Figure 5C demonstrates the change in E-CCSS score following treatment. The mean change in score was $+0.34 \pm 0.73$ (median 0, range -1 to +3), indicating significant worsening of educational/occupational function following resection ($p < 0.001$). Children with recurrent craniopharyngiomas tended to have a greater increase in E-CCSS score at the last follow-up compared with primarily treated patients ($p = 0.017$), indicating a greater decline in overall performance following treatment. The pre- and postoperative E-CCSS scores and changes following treatment for both primary and recurrent craniopharyngiomas are shown in Table 4.

The ordinal logistic regression model for E-CCSS was significant (pseudo- $R^2 = 0.62$; $p < 0.0005$). Predictors of higher postoperative E-CCSS scores (Table 5) included preoperative E-CCSS score ($p < 0.0005$) and presence of hydrocephalus ($p = 0.005$).

Wen Functional Outcome

Preoperatively, patients in the recurrent tumor group had significantly worse functional status compared with the primary group ($p = 0.001$). These differences were mostly attributable to panhypopituitarism and, less so, to visual deficits following initial treatment.

Postoperatively, there was no significant difference in Wen class between the primary and recurrent groups. Following treatment, there was a significant increase in Wen class for children in the primary group, mostly attributable to hypopituitarism and/or DI following surgery ($p < 0.001$). No significant change in Wen class occurred in the recurrent group following surgery, consistent with

the fact that many were already Class II due to hypopituitarism, DI, or visual deficits following the original treatment.

Excluding 1 patient who lacked detailed imaging data, subgroup analysis was performed to determine the effects of tumor location and size on functional status before and after surgery. There was no significant difference in good pre- and postoperative functional status between patients with pre- and retrochiasmatic tumors ($p = 0.45$ and $p = 0.85$, respectively). In children with giant tumors, there was a marginally significant trend toward worse functional status before surgery and significantly worse functional outcomes following resection ($p = 0.051$ and $p = 0.03$, respectively).

Discussion

Debate persists regarding the optimal treatment of craniopharyngiomas in children,^{4,12,14,20,41,52,54,73} and currently no consistent metric of functional outcome exists to allow meaningful comparisons across treatment paradigms or surgical approaches. We have created a simple grading scale that addresses the clinical status of patients with craniopharyngiomas across the 5 major axes of morbidity, both at presentation and following treatment. We have attempted to overcome the limitations of subjectivity of assessment and excess binning of functional domains to provide a useful metric for intermodality comparison—the CCSS. The criteria for each of the first 4 grades (neurological examination, vision, pituitary function, and hypothalamic function) are objective in nature. Potential for subjectivity exists for our assessment protocol of educational and occupational performance.

In our model, we used a 4-tiered scale to rate educational/occupational success that was based on actual achievement and not formal neuropsychological testing. Starting early on in our series, we advocated for neuropsychological testing in all patients before and after surgery. However, due to financial considerations, poor overall preoperative functional status, need for emergency surgery for high intracranial pressure or vision compromise, poor compliance with follow-up appointments, or logistical reasons, fewer than half of the patients underwent any testing, and only 19% completed both pre- and postoperative testing.

Although neuropsychological testing comprehensively assesses cognitive, attentional, memory, and task-specific performance skills, in our series it did not often predict or correlate with the patient's current level of academic or vocational success and achievement. Defined as performing well at grade level but scoring below the 50th percentile in multiple domains of testing, we noted discrepancies in more than one-third of children tested. Similar findings addressing such "ecological validity" of neuropsychological testing have been noted in patients following TBI—that is, a significant disparity between the deficits noted on formal testing and the patient's performance in school or at work.^{39,59,62} In a study of patients with TBI, Sbordone⁵⁹ noted that neuropsychological tests "were never designed to predict how these patients were likely to function in real-world settings, live independently, return to work, or maintain competitive employment."

Such discrepancies are probably due to the high sensitivity of formal testing in detecting such specific and task-oriented deficits. We continue to believe that neuropsychological testing is a crucial part of the initial assessment and postoperative follow-up for children with craniopharyngiomas to maximize their educational and vocational potential; however, we believe strongly that their current level of success and achievement should be the ultimate measure of good functional outcomes. Fischer and colleagues²⁷ shared this belief, and noted that performance after high school is a critically important indicator of overall function.

Compared with preoperative baseline status, we noted a significant increase in pituitary dysfunction following treatment—consistent with the high rates of DI and hypopituitarism common to the surgical management of these tumors—and less dramatic deterioration in hypothalamic function or cognitive domains. Significant improvement in vision was also demonstrated, with no significant overall change in neurological status. Although increasing tumor size, prior treatment, and the presence of hydrocephalus were associated with postoperative deterioration in multiple domains in children with craniopharyngiomas, the preoperative CCSS scores correlated most highly with ultimate outcomes in all domains of function. We believe these results demonstrate the utility of this standardized outcome assessment tool, and can be used to predict morbidity and to offer better counsel to patients, their families, and their primary physicians.

Functional Outcome in Reported Surgical Series

Currently, no Class I or II evidence exists demonstrating the optimal treatment of primary and recurrent craniopharyngiomas in children. Most would agree that complete resection for these benign but tenacious lesions is ideal, but the cost of attempted GTR in all cases has been questioned.^{12,29,47,57,63} The 2 major treatment paradigms—complete resection aiming for surgical cure and limited resection followed by RT—offer similar rates of disease control and long-term survival.^{4,15,20,29,31,41,44,52,64,73} Given the improved rates of survival with treatment advances over the past few decades, the focus has turned toward functional outcome and QOL metrics.^{6,7,41,46,48,50,55,58,61}

Neuropsychological testing of small series of pa-

tients has revealed cognitive and intellectual sequelae in as many as 60% of children treated for craniopharyngioma.^{6,7,10} Merchant et al.⁴² reported increased neurological deficits, increased DI, and statistically insignificant trends toward greater IQ decline and worse QOL in 15 patients in whom attempts at complete resection were made (GTR was successful in 8 of 15), compared with 15 children who underwent limited resection as intended, followed by RT. These differences were small, as were the numbers of children in each group. Prior work by our group demonstrated overall QOL and neuropsychological outcomes following radical resection to be within the normal range seen in children with other chronic diseases. Specific to craniopharyngiomas, however, some children experienced deficits in social function and emotional reactivity. These disturbances were more common in children with retrochiasmatic or recurrent tumors.⁵⁸

In a series of 153 children reported by Zucarro⁷³ who were treated with the intent of complete removal, all children who underwent GTR (69% of the group) were in school and no more than 1 year behind in grade level, in contrast to only 62% of children who underwent subtotal resection plus RT (31% of the group). Di Rocco and colleagues¹⁵ noted improvement in mean IQ scores following radical resection in 54 children, and all but 2 of 50 surviving patients enjoy a normal social life. Riva et al.⁵⁵ reported no instances of cognitive or memory deficits in 12 children who underwent radical resection, but noted increased emotional lability and difficulty with impulse control, possibly related to the subfrontal approach or hypothalamic injury. In a series by Hoffman et al.,³² 26 of 27 children who underwent aggressive resection had IQ scores at or above average levels. Although 16 children had memory deficits, 14 of them attended regular schools. These authors contend that "memory impairment did not interfere with school progress if intelligence was adequate." A few centers have reported less favorable outcomes and lower rates of functional independence after resection of recurrent compared with primary craniopharyngiomas (58–61% vs 72–78%).^{25,72} Habrand et al.²⁹ described their 25-year experience with limited resection followed by RT, and reported panhypopituitarism in 97% and psychological disturbances and poor school performance in 29% of children. Thus, although these earlier studies are retrospective, lack control groups, and use vaguely defined outcome metrics, it is evident that both treatment paradigms can have deleterious effects on functional outcome in children with craniopharyngiomas.

Functional Outcome Scales for Children With Craniopharyngiomas

Given the limitations and subjectivity of outcome reporting in most series, a few centers have attempted to define specific outcome criteria for craniopharyngiomas. De Vile and colleagues¹² introduced a scale that is similar to ours in addressing these 5 domains of function for children with craniopharyngiomas. These investigators identified the following variables as risk factors for increased morbidity: larger lesion size, hypothalamic involvement of the tumor, clinical signs of hypothalamic dysfunction (namely obesity), and patient younger than 5 years of age.

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TABLE 6: Functional outcome grading scale*

Outcome	Criteria
good	alive at follow-up examination
	no major motor deficit related to op or tumor progression
	functional vision
	Katz Grade A (able to perform basic ADLs)
	Karnofsky Performance Scale score ≥ 80
	no more than 1 yr behind in expected school grade
	employability for adults of working age
	absence of debilitating psychological or emotional problems
poor	all patients not meeting the "good" criteria

* Based on data in the article by Duff et al.

Using these clinical and radiographic findings, they subsequently used the hypothalamic morbidity predicted by their scale to determine preoperatively the optimal surgical plan.⁶³ Specifically, they treated 23 children with larger tumors and those involving the hypothalamus with intentionally limited resection followed by RT, whereas 25 tumors were deemed completely resectable. Using this paradigm, they reported decreased hypothalamic morbidity, less cognitive decline, improved vision outcomes, and overall less severe morbidity (4 vs 20% compared with their prior series, in which GTR was attempted in all cases).

A few points should be made concerning the morbidity in their series. Using their 1996 study as the aggressive-surgery "control" group,¹² their postoperative morbidity scores are rather high. Severely compromised vision was noted in > 50% of children, 40% of children had major neurological deficits (at least mild-to-moderate motor dysfunction), and 40% had significant cognitive impairment (IQ < 80). These outcomes are worse than those in many published series, and may serve as a poor baseline for comparison as surgical experience and techniques improve over time. Furthermore, severe hypothalamic morbidity still occurred in 20% of children (down from 29% in the original study), and there was no improvement in pituitary function after using the new treatment paradigm (92% still had hypopituitarism, and DI occurred in 73%, compared with 80% in the original series). Although they concluded that their "evidence-based" treatment protocol resulted in improved outcomes, there was little improvement in hypothalamic dysfunction—the purported *raison d'être* of their new paradigm. Overall, 94% of children were "normal" academically before treatment, and only 62% maintained such normality following treatment—indicative of significant morbidity with even more conservative treatment.⁶³

Another concern regarding the De Vile outcome scale is that overall morbidity was determined as a simple sum of the morbidity profiles across each individual axis. However, the functional significance or "weight" of each 1-point score across the different domains is unlikely to be equivalent in terms of subjective morbidity in the patients. We have refrained from creating a composite total score to avoid this pitfall, and are currently attempting to

determine the impact on QOL of the individual deficits across domains.

A second major outcome measure was proposed by Wen et al.,⁶⁷ consisting of a 4-tiered classification scheme that considers morbidity across all domains (Table 2). The major benefit of this grading scale resides in its simplicity. Its major limitations are its ill-defined terms (such as "learning disabilities" and "psychological disorders") as well as its combining of the deficits in so many disparate domains into a single morbidity class. The former limitation introduces interobserver subjectivity, whereas the latter results in the loss of a more nuanced picture of the deficits in each child.

Duff and colleagues¹⁷ examined the outcomes in 121 adults and children who were treated for craniopharyngiomas, and attempted to identify patients who were "well integrated independent individuals functioning in society." They classified patient outcomes as either good or poor; patients not meeting all 8 criteria (Table 6) were considered to have had poor outcomes. Such dichotomization, however, causes a significant amount of functional data to be lost—limiting the completeness of the assessment and the conclusions that can be drawn when comparing treatment modalities.

Poretti and colleagues⁴⁸ used a variety of questionnaires to assess QOL in 25 consecutive children with craniopharyngiomas, including the Pediatric Quality of Life Inventory to address physical, emotional, social, and school functioning; the Youth Self Report scale to assess social and emotional function; the Epworth Sleepiness Scale to assess fatigue and sleepiness during daily activities; and the Child Behavioral Checklist to assess behavioral and emotional problems from the parental perspective. They reported the following as predictors of poor outcome on their QOL analyses: young age, hypothalamic involvement and/or damage, hydrocephalus, and tumor recurrence. Some authors have used the Health Utilities Index Mark 2 to assess health-related QOL.^{41,50} This index is used to classify a patient's health across 7 categories (vision, hearing, speech, mobility, emotion, cognition, self-care, pain, and fertility). Obviously, there is some overlap with the predominant deficits children suffer following craniopharyngioma treatment, but many facets of craniopharyngioma morbidity are not addressed. Other scales have been used to assess outcome after resection of brain tumors, including the Glasgow Outcome Scale,³³ the extended Glasgow Outcome Scale,³⁴ and the modified Rankin Scale.^{26,53} All are rather crude measures of outcome; the first and second are used primarily in TBI, and the third is designed to assess patients who have suffered strokes. Furthermore, they all have limitations in terms of interobserver reliability and subjectivity,^{51,68,69} and have not been reported or tested in the craniopharyngioma literature.

Expectations Following Treatment of Craniopharyngiomas

Based on large published series, certain generalities can be discussed concerning the expected morbidity following craniopharyngioma treatment. Neurological improvement from resolution of mass effect is common, and the rate of severe injury is low ($\leq 15\%$ in most series).

Inadvertent vascular injury appears to be a not insignificant source of acute neurological morbidity, and has been reported with intentionally complete and incomplete resections, and with transcranial and transsphenoidal approaches.^{4,11,20,37,38} This complication is probably an unpredictable event, but one that may decrease with a surgeon's experience. Reviewing the major large surgical series of pediatric craniopharyngiomas, vision improvement has been reported in > 50% of cases in the majority of studies, and visual deterioration generally occurs in < 20% of patients.^{4,17,20,25,50,57} Higher rates of visual improvement and less deterioration have been reported in many series describing tumors treated transsphenoidally.^{8,11,28} Whether this is attributable to patient selection (preponderance of intrasellar tumors) or better technique for optic apparatus decompression awaits comparisons between tumor groups of similar size and location.

As noted by Duff and colleagues,¹⁷ major endocrinopathy following radical surgery is "almost inevitable," and was not a source of significant morbidity in their series. Furthermore, a greater deterioration in pituitary dysfunction and a higher incidence of DI occurred in children with primary tumors. This is accounted for by the fact that most children with recurrent tumors already had panhypopituitarism and DI subsequent to their original (and usually conservative) treatment. Our results corroborate the findings of Duff et al.; patients, families, and primary physicians should be counseled on the very high likelihood of postoperative hypopituitarism and DI. In agreement with De Vile and colleagues,¹³ we found that DI, especially in the setting of impaired thirst (adipsia), is more persistently disabling and burdensome to patients and families compared to anterior pituitary dysfunction. With close follow-up, modern endocrinological care is very effective and successful at supplementing endocrine deficiencies, guiding catch-up growth, and nearly eliminating the risk of fatal endocrine crises. The success and safety of all paradigms of craniopharyngioma treatment, however, depend rather heavily on regular postoperative endocrinological support and the familial and societal resources to cope with these nearly universal endocrine deficiencies.⁶¹

The risk and consequences of hypothalamic dysfunction comprise the main points of contention concerning extent of resection. Hypothalamic dysfunction can manifest as a constellation of disturbances that can include obesity, hyperphagia, memory deficits, thermoregulatory abnormalities, emotionally labile behavior, and sleep-wake cycle disruption.^{12,30,43,47,50,57} Standardized assessment and reporting of hypothalamic dysfunction and "obesity" are lacking, and these conditions are poorly reported in the craniopharyngioma literature. Obesity is often undefined in many reports, but is generally < 50% in most surgical series.^{4,12,14,17,25,32,35,50,64} In a German multicenter study reported by Müller et al.,⁴⁶ in which they failed to describe their treatment protocol, severe obesity (> +3 SD BMI) occurred in 44% of 185 children with long-term "postoperative" follow-up.

As Puget and colleagues⁵⁰ noted, the risk of hypothalamic disturbance is heavily dependent on the surgeon's experience. In our series, 43 patients (81%) in the

primary group and 15 (56%) in the recurrent group had no or mild hypothalamic dysfunction following surgery, compared with 94 and 63%, respectively, before surgery. Importantly, the majority of the cases of hypothalamic morbidity in children with recurrent craniopharyngiomas occurred subsequent to treatment already received at other centers—mostly consisting of intended subtotal resection plus RT. Furthermore, obesity was rare, and significant hypothalamic disturbance was generally rare in our series, despite a significant proportion of large and retrochiasmatic tumors. We found no significant difference in pre- or postoperative hypothalamic disturbance between children with pre- and retrochiasmatic tumors. Furthermore, mild-to-moderate memory dysfunction accounted for most of the patients with moderate grades of hypothalamic dysfunction postoperatively. As noted previously, memory deficits can often be overcome as long as overall intelligence remains intact.

The aforementioned considerations are most closely associated with surgery-related morbidity, but mention should be made of the effects of RT on children. Radiation therapy has been shown to provide excellent rates of disease control and is the favored option for definitive management in many centers.^{29,41,42,52,54} Although most practitioners agree that the risk of complete resection involves the potential for higher rates of acute neurological morbidity and DI, the effects of cranial irradiation are often delayed and unpredictable in onset. More pronounced in younger children,^{41,42} side effects of RT include dysfunction of the hypothalamic-pituitary axis, vision decline, benign and malignant radiation-induced CNS tumors, cognitive dysfunction, attentional deficits, cerebrovasculopathy, and moyamoya disease.^{1,2,16,18,19,24,36,40,45,60} Prior work by our group²⁰ and others⁵⁴ has shown significantly worse surgical outcomes and survival following tumor progression after failed RT. Given the 20–30% incidence of tumor progression following RT,⁹ one must consider the potentially deleterious effects of early irradiation on the safety and efficacy of subsequent treatments.

Study Limitations

The main limitations of this study include the retrospective manner of data collection and the lack of detailed pre- and postoperative neuropsychological testing in many children. Its strengths lie in the large size of the series, lengthy follow-up, and a uniform treatment paradigm in all patients—attempted complete resection for surgical cure. However, the design of any scale involves the neglect of certain data points for the sake of grouping and meaningful comparison and analysis. We have tried to balance these opposing considerations carefully, and have created a 4-tiered classification scheme addressing the 5 major domains of morbidity in children with craniopharyngiomas. Another defect of most classification systems is the lack of direct correlation with or measurement of the effects that each type and extent of deficit may exert on a single child's everyday functioning and QOL. Ideally, we would like to determine further via interviews or questionnaires exactly what are the negative consequences of having deficits of varying degrees in the separate domains. Such a correspondence of each defi-

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cit's "weighting" to its impact on QOL would then allow further standardization of an overall morbidity profile (composite CCSS score) that would facilitate improved comparison across centers and treatment modalities. This phase of the project is currently in progress. Finally, the CCSS needs to be externally validated by comparing the results in our series with those of other large series of children with craniopharyngiomas.

Conclusions

We have created a simple grading scale that addresses the clinical status of patients with craniopharyngiomas across the 5 major axes of morbidity at presentation and following treatment. We noted a significant increase in anterior and posterior pituitary dysfunction following treatment—consistent with the high rates of DI and hypopituitarism common to the surgical management of these tumors—and less dramatic deterioration in hypothalamic function or cognitive domains. Significant improvement in vision was also demonstrated in patients with no significant overall change in neurological status. Adoption of this scale by multiple centers may allow a more standardized assessment of pre- and posttreatment functional status, and it may allow meaningful comparisons between the various treatment paradigms. Further work is needed to equate such a grading scale with the subjective quality of survival in children with craniopharyngiomas.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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