Risk factors associated with the surgical management of craniopharyngiomas in pediatric patients: analysis of 1961 patients from a national registry database

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OBJECTIVE Patient demographic characteristics, hospital volume, and admission status have been shown to impact surgical outcomes of sellar region tumors in adults; however, the data available following the resection of craniopharyngiomas in the pediatric population remain limited. The authors sought to identify potential risk factors associated with outcomes following surgical management of pediatric craniopharyngiomas.

METHODS The Nationwide Inpatient Sample database and Kids' Inpatient Database were analyzed to include admissions for pediatric patients (≤ 18 years) who underwent a transcranial or transsphenoidal craniotomy for resection of a craniopharyngioma. Patient-level factors, including age, race, comorbidities, and insurance type, as well as hospital factors were collected. Outcomes analyzed included mortality rate, endocrine and nonendocrine complications, hospital charges, and length of stay. A multivariate model controlling for variables analyzed was constructed to examine significant independent risk factors.

RESULTS Between 2000 and 2011, 1961 pediatric patients were identified who underwent a transcranial (71.2%) or a transsphenoidal (28.8%) craniotomy for resection of a craniopharyngioma. A major predilection for age was observed with the selection of a transcranial (23.4% in < 7 -year-olds, 28.1% in 7- to 12-year-olds, and 19.7% in 13- to 18-year-olds) versus transsphenoidal (2.9% in < 7 -year-olds, 7.4% in 7- to 12-year-olds, and 18.4% in 13- to 18-year-olds) approach. No significant outcomes were associated with a particular surgical approach, except that 7- to 12-year-old patients had a higher risk of nonendocrine complications (relative risk [RR] 2.42, 95% CI 1.04–5.65, $p = 0.04$) with the transsphenoidal approach when compared with 13- to 18-year-old patients. The overall inpatient mortality rate was 0.5% and the most common postoperative complication was diabetes insipidus (64.2%). There were no independent factors associated with inpatient mortality rates and no significant differences in outcomes among groups based on sex and race. The average length of stay was 11.8 days, and the mean hospital charge was \$116,522. Hospitals with medium and large bed capacity were protective against nonendocrine complications (RR 0.53, 95% CI 0.3–0.93, $p = 0.03$ [medium]; RR 0.45, 95% CI 0.25–0.8, $p < 0.01$ [large]) and total complications (RR 0.73, 95% CI 0.55–0.97, $p = 0.03$ [medium]; RR 0.68, 95% CI 0.51–0.9, $p < 0.01$ [large]) when compared with hospitals with small bed capacity (< 200 beds). Patients admitted to rural hospitals had an increased risk for nonendocrine complications (RR 2.56, 95% CI 1.11–5.9, $p = 0.03$). The presence of one or more medical comorbidities increased the risk of higher total complications (RR 1.38, 95% CI 1.14–1.68, $p < 0.01$ [1 comorbidity]; RR 2.37, 95% CI 1.98–2.84, $p < 0.01$ [≥ 2 comorbidities]) and higher total hospital charges (RR 2.9, 95% CI 1.08–7.81, $p = 0.04$ [1 comorbidity]; RR 9.1, 95% CI 3.74–22.12, $p < 0.01$ [≥ 2 comorbidities]).

CONCLUSIONS This analysis identified patient age, comorbidities, insurance type, hospital bed capacity, and rural or nonteaching hospital status as independent risk factors for postoperative complications and/or increased hospital charges in pediatric patients with craniopharyngioma. Transsphenoidal surgery in younger patients with craniopharyngioma was a risk factor for nonendocrine complications.

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KEY WORDS National (Nationwide) Inpatient Sample; Kids' Inpatient Database; craniopharyngioma; transsphenoidal; parasellar; sellar; oncology

ABBREVIATIONS DI = diabetes insipidus; HCUP = Healthcare Cost and Utilization Project; ICD-9-CM = *International Classification of Diseases, Ninth Revision; Clinical Modification*; KID = Kids' Inpatient Database; LOS = length of stay; NIS = Nationwide Inpatient Sample; RR = relative risk.

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CRANIOPHARYNGIOMAS are benign intracranial tumors derived from residual cell rests of embryonal tissue, and they have an incidence of 0.5–2.0 cases per million people.^{3,11} It is estimated that 30%–50% of craniopharyngiomas arise in pediatric patients, and although these tumors are considered benign, they can adversely impact a child's physical and psychosocial functioning.^{16,16,17} Surgical intervention is frequently the first step in management for tissue diagnosis and tumor debulking.¹¹ However, given their proximity to critical structures of the brain such as the hypothalamus, complete resection is often difficult and postoperative complications include new neurological deficits, endocrine dysfunction, and visual deterioration.^{11,21,23,28,30} Additionally, increased morbidity rates associated with surgical treatment may have long-standing physical and social effects on patients, and can contribute to increased total cost of health care.^{14,25,26,29} Therefore, it is important to identify preoperative risk factors associated with poor surgical outcomes in pediatric patients with craniopharyngiomas.

Previous national database registry studies investigating the resection of sellar region tumors have shown that patient demographic characteristics, hospital volume, or hospital admission subtypes are associated with postoperative endocrine and nonendocrine complications, mortality rates, or hospital charges.^{2,26,29} Recently, the Nationwide Inpatient Sample (NIS) was analyzed for adult patients undergoing surgery for craniopharyngiomas.²⁹ The authors reported that hospitals with a low procedural volume had greater postoperative complications and inpatient charges. The analysis was limited to the adult population, and factors associated with surgical outcomes in pediatric patients remain unclear. Therefore, we sought to investigate the impact of demographic characteristics, hospital type, and route of admission on postoperative complications and hospital charges in children undergoing surgical treatment for craniopharyngiomas.

Methods

Database

This study used 2 public all-payer inpatient care datasets from the Healthcare Cost and Utilization Project (HCUP). The NIS (<https://www.hcup-us.ahrq.gov/nisoverview.jsp>) and Kids' Inpatient Database (KID) (<https://www.hcup-us.ahrq.gov/kidoverview.jsp>) have longitudinal hospital inpatient discharge data from more than 1000 hospitals. The NIS entailed 20% of all hospital discharges and the KID contained 80% of pediatric discharges. Data from the KID was available for the years 2000, 2003, 2006, and 2009. For the years that the KID did not cover, pediatric data were extracted from the 2000–2011 NIS database. The NIS also has a built-in method for obtaining national estimates of prevalence, as described by the HCUP–NIS.⁹

Criteria for Inclusion and Exclusion

The study population was limited to children (≤ 18 years) with craniopharyngiomas who underwent a transsphenoidal or transcranial craniotomy. Admission data were extracted using the *International Classification of*

Diseases, Ninth Revision; Clinical Modification (ICD-9-CM) codes.¹ The criteria for inclusion/exclusion were similar to the previous published adult report unless otherwise noted.²⁹ Patients with an ICD-9 code of 237.0 (craniopharyngioma) who underwent a transsphenoidal or transcranial procedure (07.61, 07.62, 07.64, 07.65) were included. Patients > 18 years and those with a concomitant diagnosis code of 253.8 (other disorders of the pituitary and other syndromes of diencephalohypophyseal origin, excluding a diagnosis of craniopharyngioma) were excluded from the study.

Risk Factors

Patient variables including race, payer status, sex, admission source (emergency room, another hospital, other health facility, including long-term facilities, court/law enforcement, routine), and admission type (emergency, urgent, elective, trauma center, newborn) were encoded as categorical variables in NIS. Factors that were continuous were recoded into new categorical variables, such as number of comorbidities (0, 1, or ≥ 2 comorbidities) and age (< 7 , 7–12, or 13–18 years). Hospital capacity was coded as small (< 200 beds); medium (201–400 beds); or large (> 400 beds). Other categorical hospital variables included teaching status, children's hospital type, and hospital region. Additionally, each hospital's annual transsphenoidal and transcranial procedural volume was calculated and categorized, and individual hospitals were categorized as low volume (≤ 80 th percentile for annual procedures) or high volume (> 80 th percentile for annual procedures).

Outcomes of Interest

An emphasis was placed on hospital complications that occurred during admission. We examined endocrine complications (panhypopituitarism: 253.7, diabetes insipidus [DI]: 253.50, electrolyte abnormalities: 276.00–276.52, 276.61–276.90); nonendocrine complications (CSF rhinorrhea: 349.81, postoperative neurological complications: 997.00–997.09, intracerebral hemorrhage or hematoma: 430.00–432.90, 998.11–998.13, 374.31, 378.50–378.56, cranial nerve palsy: 368.20, 374.30, cerebral arteriogram: 884.10, mechanical ventilation: 967.0–967.2, blood transfusion: 990.40, deep venous thrombosis/pulmonary embolism: 415.00, 415.11–415.19, 453.81–453.89, inferior vena cava filter installation: 387.00); or any complication (either endocrine or nonendocrine).

Statistical Analysis

Outcomes of endocrine complications, nonendocrine complications, total complications, and mortality rates were assessed for significance with socioeconomic, patient, hospital, and admission variables. Other outcomes of interest included specific endocrine complications, length of stay (LOS), and total charges. The LOS was considered increased if it was more than 7 days, and total charges were considered high if they were at or above the 90th percentile (\$217,985.08, adjusted for inflation). Patient factors included the following: race, insurance type, comorbidity, sex, and age. Hospital factors included region, teaching status, children's hospital type, bed capacity, and proce-

dures volume. Last, admission variables included admission source and admission type.

The survey weight-adjusted procedure (SAS survey-mean) was used for descriptive statistics. A multivariate Poisson regression using the Generalized Linear Mixed Model (SAS glimmix) with a log link function was used to examine the association (rate ratio) between risk factors and outcome. A 5-step approach was used as the model-building strategy (Table 1). Akaike's Information Criterion (AIC) and Bayesian Information Criterion (BIC) were used to monitor the improvement of modeling fitting after adding an additional set of covariates. Changes of beta coefficients were also monitored to inspect the impact of an existing association after adding more covariates. Given that Model 4 controlled for the most confounding variables, only the findings from this model were presented as the final result. Statistical significance was set at $p < 0.05$ for all analyses. All analyses were performed using SAS version 9.4.

Results

Patient Characteristics

Between 2000 and 2011, 1961 pediatric patients were identified who underwent a transcranial (71.2%) or transphenoidal (28.8%) craniotomy for resection of a craniopharyngioma. There was no gender predilection. Most of the patients were older (13–18 years old, 38.1%), white (43%), privately insured (60.4%), and had no comorbidity (45%) (Table 2). The majority of procedures took place in a teaching institution (94.7%), with large capacity (65.1%), and more likely to be located in the South (43.1%) (Table 3). Most of the admissions were considered elective (52%). The most common complication recorded was DI (64.2%) (Table 4) and the mortality rate was 0.5% ($n = 9$). The average LOS was 11.8 days and the mean hospital charge was \$116,522. The surgical approach in each age group is shown in Table 5.

Patient Demographic Variables

There were no significant differences among sex and race for all measured outcomes. There were no significant factors associated with the surgical approach (transcranial vs transphenoidal; $p > 0.05$), except that 7- to 12-year-old patients had a higher risk of nonendocrine complications

TABLE 2. Cohort demographic variables—patient factors in 1961 patients with craniopharyngioma

Variable & Category	Percentage
Sex	
Male	50.3
Female	47.2
Missing	2.5
Age	
<7 yrs old	26.3
7–12 yrs old	35.6
13–18 yrs old	38.1
Race	
White	43.0
Black	8.7
Hispanic	18.8
Asian/Pacific	2.1
Native American	1.2
Other	5.8
Missing	20.4
Payer status	
Medicare	NA
Medicaid	33.0
Private/HMO	60.4
Self-pay	2.6
No charge	NA
Other	3.5
Missing	NA
Comorbidity	
No comorbidity	45.0
1 comorbidity	28.1
≥2 comorbidities	26.9

HMO = health maintenance organization; NA = not available.

The risk of individual identification of persons is increased when the number of observations in any given cell is ≤ 10 .

(relative risk [RR] 2.42, 95% CI 1.04–5.65, $p = 0.04$) with the transphenoidal approach when compared with 13- to 18-year-old patients. Compared with patients 13–18 years old, 7- to 12-year-olds were more likely to have higher total hospital charges (RR 3.44, 95% CI 1.55–7.64, $p < 0.01$), and patients < 7 years old were more likely to have a longer hospital stay (RR 1.5, 95% CI 1.11–2.02, $p < 0.01$).

The presence of one or more comorbidities (Table 6) increased the risk of endocrine-related complications (RR 1.38, 95% CI 1.1–1.72, $p < 0.01$ [1 comorbidity]; RR 2.18, 95% CI 1.77–2.69, $p < 0.01$ [≥ 2 comorbidities]); electrolyte abnormality (RR 2.15, 95% CI 1.12–4.1, $p = 0.02$ [1 comorbidity]; RR 9.2, 95% CI 5.29–15.99, $p < 0.01$ [≥ 2 comorbidities]); higher total complications (RR 1.38, 95% CI 1.14–1.68, $p < 0.01$ [1 comorbidity]; RR 2.37, 95% CI 1.98–2.84, $p < 0.01$ [≥ 2 comorbidities]); and accrued higher hospital charges (RR 2.95, 95% CI 1.08–7.81, $p = 0.04$ [1 comorbidity]; RR 9.16, 95% CI 3.74–22.12, $p < 0.01$ [≥ 2 comorbidities]) compared with patients with no comorbidities (Tables 7 and 8). Two or more comorbidities

TABLE 1. The 5-step model used to perform statistical analysis

Step	Description
1	A univariate model was created to validate variables for multivariable regressions analysis
2	Model 1 was created to adjust for patient-level factors (race, insurance status, age category, no. of comorbid conditions, & sex)
3	Model 2 added hospital variables (bed size, region, teaching status, location, children's specialty status, procedure vol) to Model 1
4	Model 3 added the variable admission type to Model 2
5	Model 4 added the variable admission type & source to Model 2

TABLE 3. Patient demographic variables—hospital factors in 1961 patients with craniopharyngioma

Variable & Category	Percentage
Hospital region	
Northeast	18.2
Midwest	15.8
South	43.1
West	22.9
Teaching status	
Nonteaching	3.3
Teaching	94.7
Missing	2.0
Hospital capacity	
Small	10.9
Medium	22.1
Large	65.1
Missing	2.0
Hospital location	
Rural	2.3
Urban	95.7
Missing	2.0
Hospital type	
Not children's	6.8
Children's general	12.8
Children's unit	16.0
Missing	64.4
Hospital vol	
<2 ops annually	50.0
≥2 ops annually	50.0
Admission type	
Emergency	19.4
Urgent	13.1
Elective	52.0
Newborn	NA
Trauma center	NA
Missing	15.4
Admission source	
ER	10.1
Another hospital	2.4
Other facility	1.2
Routine	58.5
Missing	27.5

ER = emergency room.

placed the patients at higher risk for DI (RR 1.54, 95% CI 1.2–1.97, $p < 0.01$) and nonendocrine complications (RR 3.11, 95% CI 2.15–4.49, $p < 0.01$). Medicaid patients were more likely to have postoperative panhypopituitarism than patients with private insurance (RR 2.28, 95% CI 1.14–4.56, $p = 0.02$).

Hospital Factors and Admission Status

Hospitals with medium (201–400) and large (> 400)

TABLE 4. Outcomes in 1961 patients with craniopharyngioma

Event	Percentage	95% CI
DI	64.2	59.1–69.2
Electrolyte abnormality	19.7	15.7–23.8
RBC transfusion	8.1	5.2–11
Neurological complications	7.3	4.8–9.7
Panhypopit	6.8	4.6–8.9
Cranial nerve palsy	6.3	3.5–9.2
Mechanical ventilation	5.9	3.6–8.3
Any ICH	2.7	1.3–4.1
CSF rhinorrhea	0.9	0.2–1.7
Cerebral arteriogram	0.6	0–1.3
IVC filter	0.5	0–1.2
Pneumonia	0.4	0–0.9
DVT/PE	0.3	0–0.7

DVT/PE = deep venous thrombosis/pulmonary embolism; ICH = intracerebral hemorrhage or hematoma; IVC = inferior vena cava; panhypopit = panhypopituitarism; RBC = red blood cell.

bed capacity were protective against nonendocrine complications (RR 0.53, 95% CI 0.3–0.93, $p = 0.03$ [medium]; RR 0.45, 95% CI 0.25–0.8, $p < 0.01$ [large]) and total complications (RR 0.73, 95% CI 0.55–0.97, $p = 0.03$ [medium]; RR 0.68, 95% CI 0.51–0.9, $p < 0.01$ [large]) when compared with hospitals with small bed capacity (< 200 beds) (Table 9). Centers with high (≥ 2 procedures annually) and low (< 2 procedures annually) procedural volume had similar outcomes.

Compared with admissions in urban hospitals, patients admitted to rural hospitals had an increased risk for nonendocrine complications (RR 2.56, 95% CI 1.11–5.9, $p = 0.03$). Teaching hospitals were less likely to have postoperative panhypopituitarism (RR 0.27, 95% CI 0.09–0.83, $p = 0.02$), had lower daily hospital charges (RR 0.3, 95% CI 0.11–0.82, $p = 0.02$) but similar total charges when compared with nonteaching hospitals (Tables 9 and 10).

Using the Northeast region as the reference point, none of the regions of hospital location were at increased risk for postoperative complications or hospital costs. The South and Midwest had lower rates of postoperative panhypopituitarism (RR 0.33, 95% CI 0.15–0.75, $p < 0.01$; RR 0.21, 95% CI 0.06–0.77, $p = 0.02$). Admission source and type were not significant for most outcomes assessed (Tables 11 and 12), except that admission from the emergency room was associated with a longer hospital stay (RR 1.58, 95% CI 1.13–2.19, $p < 0.01$).

TABLE 5. Surgical approach in each age group in 1961 patients with craniopharyngioma

Patient Age	% Transsphenoidal	% Transcranial
<7 yrs	2.9	23.4
7–12 yrs	7.4	28.1
13–18 yrs	18.4	19.7
Total	28.8	71.2

Discussion

The surgical management of craniopharyngiomas is complex and can present unique challenges in the pediatric population.^{5,11,21,28,30} By analyzing the NIS and KID national databases, we identified the clinical outcomes and key risk factors for complications in children undergoing surgical management of craniopharyngiomas. The average LOS (11.8 days vs 7.6 days), postoperative DI (64.2% vs 48%), and hospital charge (\$116,522 vs \$92,300) were greater in children compared with adults.²⁹ According to our analysis, the mortality rate was still low (0.5%). We identified age, comorbidities, insurance type, hospital bed capacity, and rural or nonteaching hospital status as independent risk factors associated with postoperative complications and/or increased hospital charges.

Patient Demographic Variables

Outcomes between the transphenoidal and transcranial

approach were similar, except that younger patients were found to have a higher risk of nonendocrine complications with the transphenoidal approach. These complications included any postoperative neurological complications (17.5%), cranial nerve palsy (4.6%), mechanical ventilation (3.0%), need for postoperative cerebral arteriogram (1.1%), intracerebral hemorrhage or hematoma (0.9%), and blood transfusion (0.9%). The transphenoidal approach was more commonly used in children > 12 years old. Transphenoidal pituitary surgery is generally associated with a shorter LOS, lower cost, and lower complication rates than transcranial surgery.²⁴ The risk for neurological complications from the endonasal approach could be due to age-related anatomical differences found at the skull base. A quantitative radio-anatomical cross-sectional study of pediatric patients found that the maximum sellar floor thickness decreased with age in pediatric patients.²² The varied sellar floor thickness, with a more limited surgical corridor in younger children, may place the 7- to 12-year-olds at great-

TABLE 6. Frequency and percentage of comorbidity in patient cohort in 1961 patients with craniopharyngioma

Comorbidity	Surgical Patients				Nonsurgical Patients				All Patients Freq
	KID		NIS		KID		NIS		
	Freq	%	Freq	%	Freq	%	Freq	%	
Other neurological disorders	143	8.4	313	18.3	255	7.8	550	16.7	1260
Hypothyroidism	118	6.9	364	21.3	192	5.9	375	11.4	1050
Fluid & electrolyte disorders	98	5.8	246	14.4	196	6.0	368	11.2	907
Obesity	41	2.4	76	4.5	83	2.5	191	5.8	391
Paralysis	16	0.9	60	3.5	53	1.6	157	4.8	286
Chronic pulmonary disease	39	2.3	73	4.3	67	2.1	94	2.9	274
Anemia (deficiency)	32	1.9	NA	NA	37	1.1	63	1.9	131
Depression	NA	NA	NA	NA	26	0.8	57	1.7	83
DM (uncomplicated)	NA	NA	NA	NA	25	0.8	52	1.6	77
Hypertension	21	1.2	NA	NA	26	0.8	NA	NA	46
Coagulopathy	NA	NA	NA	NA	25	0.8	NA	NA	25
AIDS	NA	NA	NA	NA	NA	NA	NA	NA	NA
Alcohol abuse	NA	NA	NA	NA	NA	NA	NA	NA	NA
RA/collagen vascular disease	NA	NA	NA	NA	NA	NA	NA	NA	NA
Anemia (chronic blood loss)	NA	NA	NA	NA	NA	NA	NA	NA	NA
Congestive heart failure	NA	NA	NA	NA	NA	NA	NA	NA	NA
DM w/ chronic complication	NA	NA	NA	NA	NA	NA	NA	NA	NA
Drug abuse	NA	NA	NA	NA	NA	NA	NA	NA	NA
Liver disease	NA	NA	NA	NA	NA	NA	NA	NA	NA
Lymphoma	NA	NA	NA	NA	NA	NA	NA	NA	NA
Metastatic cancer	NA	NA	NA	NA	NA	NA	NA	NA	NA
Peripheral vascular disease	NA	NA	NA	NA	NA	NA	NA	NA	NA
Psychosis	NA	NA	NA	NA	NA	NA	NA	NA	NA
Pulmonary circulation disorder	NA	NA	NA	NA	NA	NA	NA	NA	NA
Renal failure	NA	NA	NA	NA	NA	NA	NA	NA	NA
Solid tumor w/o metastasis	NA	NA	NA	NA	NA	NA	NA	NA	NA
Peptic ulcer disease w/o bleeding	NA	NA	NA	NA	NA	NA	NA	NA	NA
Valvular disease	NA	NA	NA	NA	NA	NA	NA	NA	NA
Weight loss	NA	NA	NA	NA	NA	NA	NA	NA	NA

DM = diabetes mellitus; Freq = frequency; RA = rheumatoid arthritis.

TABLE 7. The association of patient demographic variables with endocrine, nonendocrine, and total complications in 1961 patients with craniopharyngioma

Risk Factor & Variable	Nonendocrine	CSF Rhinorrhea	Endocrine	Electrolyte Abnormalities	DI	Panhypopit	Total Comp
Insurance							
Medicaid	0.96 (0.68–1.35)	0.16 (0.01–2.18)	0.99 (0.81–1.2)	0.76 (0.5–1.16)	0.98 (0.77–1.24)	2.28 (1.14–4.56)	0.98 (0.83–1.16)
Missing	NA	NA	0.77 (0.11–5.62)	NA	0.82 (0.11–6.05)	NA	0.67 (0.09–4.83)
Other	0.8 (0.32–1.99)	NA	0.81 (0.48–1.34)	0.68 (0.21–2.21)	0.92 (0.52–1.62)	NA	0.81 (0.52–1.26)
Private including HMO	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Self-pay	0.83 (0.32–2.15)	NA	1.02 (0.59–1.77)	1.41 (0.47–4.18)	1.02 (0.54–1.96)	NA	0.96 (0.6–1.55)
Race							
Asian/Pacific	0.76 (0.29–1.99)	NA	0.88 (0.5–1.55)	0.8 (0.23–2.75)	1.01 (0.53–1.92)	NA	0.84 (0.52–1.37)
Black	1.07 (0.57–2.01)	NA	0.94 (0.66–1.32)	1.05 (0.49–2.27)	0.91 (0.6–1.37)	0.9 (0.27–2.96)	0.97 (0.72–1.31)
Hispanic	1.35 (0.89–2.04)	4.18 (0.24–72.93)	1.03 (0.8–1.32)	1.49 (0.91–2.44)	0.95 (0.7–1.3)	0.56 (0.21–1.46)	1.11 (0.9–1.37)
Missing	1.13 (0.68–1.89)	NA	0.98 (0.75–1.28)	0.77 (0.41–1.45)	1.08 (0.79–1.47)	0.72 (0.25–2.05)	1.02 (0.8–1.29)
Native American	2.84 (0.65–12.52)	NA	0.53 (0.13–2.16)	NA	0.71 (0.17–2.92)	NA	0.89 (0.32–2.45)
Other	1.53 (0.83–2.83)	NA	0.96 (0.64–1.42)	1.06 (0.45–2.47)	0.94 (0.59–1.51)	1.01 (0.23–4.57)	1.09 (0.78–1.52)
White	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Comorbidity							
No comorbidity	Reference	Reference	Reference	Reference	Reference	Reference	Reference
1 comorbidity	1.42 (0.94–2.15)	8.99 (0.43–186.66)	1.38 (1.1–1.72)	2.15 (1.12–4.1)	1.24 (0.96–1.6)	1.97 (0.92–4.22)	1.38 (1.14–1.68)
≥2 comorbidities	3.11 (2.15–4.49)	9.83 (0.43–223.08)	2.18 (1.77–2.69)	9.2 (5.29–15.99)	1.54 (1.2–1.97)	1.05 (0.45–2.48)	2.37 (1.98–2.84)
Sex							
Female	1.15 (0.86–1.55)	3.26 (0.5–21.28)	1 (0.85–1.19)	1 (0.69–1.44)	1.04 (0.85–1.27)	0.76 (0.4–1.46)	1.04 (0.89–1.2)
Male	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Age							
13–18 yrs	Reference	Reference	Reference	Reference	Reference	Reference	Reference
7–12 yrs	1.36 (0.94–1.97)	NA	1.08 (0.87–1.33)	1.2 (0.76–1.89)	1.1 (0.86–1.41)	0.72 (0.33–1.59)	1.15 (0.95–1.37)
<7 yrs	1.22 (0.82–1.82)	NA	1.22 (0.98–1.51)	1.28, (0.79–2.07)	1.21 (0.93–1.57)	1.19 (0.54–2.61)	1.22 (1–1.47)

Total comp = total complications.

Values are expressed as RR (95% CI). Boldface type indicates statistical significance at $p < 0.05$.

TABLE 8. The association of patient demographic variables with routine discharge, LOS, and hospital charges in 1961 patients with craniopharyngioma

Risk Factor & Variable	Routine	LOS	High Total Charge	High Daily Charge
Insurance				
Medicaid	1.01 (0.83–1.23)	1.09 (0.85–1.41)	1.57 (0.87–2.85)	0.73 (0.38–1.41)
Missing	0.94 (0.23–3.91)	0.88 (0.12–6.54)	NA	NA
Other	1.05 (0.68–1.62)	0.74 (0.37–1.46)	1.37 (0.3–6.21)	1.41 (0.41–4.85)
Private including HMO	Reference	Reference	Reference	Reference
Self-pay	1.01 (0.58–1.78)	0.98 (0.46–2.07)	2.51 (0.51–12.45)	NA
Race				
Asian/Pacific	1.04 (0.62–1.76)	1.18 (0.6–2.35)	0.89 (0.23–3.4)	0.58 (0.13–2.62)
Black	0.85 (0.6–1.19)	1.11 (0.73–1.69)	0.89 (0.23–3.34)	0.44 (0.1–1.97)
Hispanic	0.87 (0.67–1.13)	1.16 (0.84–1.61)	1.51 (0.75–3.07)	0.75 (0.35–1.58)
Missing	0.92 (0.71–1.2)	1.16 (0.82–1.66)	1.21 (0.44–3.35)	0.47 (0.15–1.48)
Native American	1.08 (0.44–2.68)	0.47 (0.06–3.46)	NA	2.19 (0.37–12.95)
Other	0.97 (0.65–1.44)	1.09 (0.67–1.78)	0.77 (0.26–2.28)	0.75 (0.22–2.61)
White	Reference	Reference	Reference	Reference
Comorbidity				
No comorbidity	Reference	Reference	Reference	Reference
1 comorbidity	0.95 (0.78–1.16)	1.24 (0.93–1.65)	2.9 (1.08–7.81)	0.92 (0.48–1.75)
≥2 comorbidities	0.83 (0.67–1.04)	1.57 (1.2–2.06)	9.1 (3.74–22.12)	0.92 (0.46–1.81)
Sex				
Female	0.99 (0.84–1.18)	1.06 (0.85–1.33)	1.49 (0.87–2.55)	0.71 (0.4–1.25)
Male	Reference	Reference	Reference	Reference
Missing	1.12 (0.58–2.18)	NA	NA	1.89 (0.39–9.16)
Age				
13–18 yrs	Reference	Reference	Reference	Reference
7–12 yrs	0.98 (0.8–1.21)	1.33 (0.99–1.77)	3.44 (1.55–7.64)	0.83 (0.43–1.58)
<7 yrs	1.03 (0.82–1.28)	1.5 (1.11–2.02)	2.36 (1–5.57)	0.89 (0.45–1.79)

Values are expressed as RR (95% CI).

Boldface type indicates statistical significance at $p < 0.05$.

er risk for postoperative complications. Seven- to 12-year-olds were 3.4 times more likely to have higher total hospital costs than 13- to 18-year-olds. This may be attributed to both the higher percentage of 7- to 12-year-old children undergoing a transcranial approach (Table 5) and greater risk for complications with the transsphenoidal approach.

Pediatric patients with preoperative comorbidities had significantly higher risks for nonendocrine and endocrine complications (including DI, electrolyte abnormalities, total complications, and higher total hospital charges). Because approximately 55% of the patients included in this study were found to have 1 or more comorbidity, their inherent risk for postoperative complications probably influenced the overall outcome in our study, and contributes to the nationwide trend in adverse clinical outcomes and increased health care costs. Whereas the management of comorbidities prior to surgical intervention is advocated to improve postoperative outcomes in patients undergoing intracranial tumor resections,^{10,27,29} surgical management of craniopharyngiomas in pediatric patients may be more complex. Unlike comorbidities in the adult population, which include cardiac, pulmonary, or renal disease, pediatric patients with craniopharyngioma generally do

not have other medical issues beyond neurological or endocrine deficiencies attributed to the tumor (Table 6). The vast majority of comorbidities found in our patient cohort were probably related to the extent of tumor invasion and complexity of the resection, thereby correlating with higher risk factors.

Disparities among patients with Medicaid continue to prevail.^{15,26} In our analysis, we found that approximately 6.8% ($n = 133$) of patients had postoperative panhypopituitarism, and that patients with Medicaid were 2.35 times more likely to have this complication than were patients with private insurance. Previous univariate analysis conducted for patients with Cushing's disease undergoing transsphenoidal craniotomy demonstrated an association between panhypopituitarism and Medicare enrollment. However, the significance was lost when controlled for admission type and source.²⁶ Given the limitation of the study design, we were unable to assess whether patients with Medicaid and at higher risk for complications were confounded by the extent of tumor involvement, resection, or other factors that could impact outcomes. Nonetheless, increased awareness of this ongoing disparity in the Medicaid population is still warranted.

TABLE 9. The association of hospital factors with endocrine, nonendocrine, and total complications in 1961 patients with craniopharyngioma

Risk Factor & Variable	Nonendocrine	CSF Rhinorrhea	Endocrine	Electrolyte Abnormalities	DI	Panhypopit	Total Comp
Hospital capacity							
Large	0.45 (0.25–0.8)	NA	0.76 (0.55–1.06)	0.54 (0.27–1.06)	0.83 (0.56–1.25)	0.8 (0.24–2.67)	0.68 (0.51–0.9)
Medium	0.53 (0.3–0.93)	0.89 (0.01–103.81)	0.8 (0.58–1.12)	0.61 (0.3–1.26)	0.9 (0.61–1.34)	0.44 (0.12–1.62)	0.73 (0.55–0.97)
Small	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Procedure vol							
High	1.14 (0.83–1.57)	6.55 (0.55–77.66)	0.88 (0.73–1.06)	0.72 (0.48–1.08)	0.95 (0.76–1.18)	0.69 (0.35–1.4)	0.94 (0.8–1.1)
Low	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Hospital teaching status							
Teaching	1.27 (0.45–3.57)	NA	0.96 (0.59–1.53)	0.68 (0.28–1.64)	1.43 (0.72–2.85)	0.27 (0.09–0.83)	1.02 (0.66–1.56)
Nonteaching	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Hospital location							
Rural	2.56 (1.11–5.9)	NA	1.3 (0.72–2.33)	1.06 (0.23–4.79)	1.32 (0.67–2.59)	1.32 (0.15–11.52)	1.58 (0.98–2.55)
Urban	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Type of children's hospital							
Children's general or specialty	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Children's unit	1.1 (0.63–1.92)	0.28 (0–163221.08)	0.92 (0.66–1.27)	1.06 (0.53–2.12)	0.9 (0.61–1.33)	0.66 (0.21–2.1)	0.96 (0.73–1.27)
Missing	0.79 (0.51–1.23)	0.01 (0–8943.76)	1 (0.77–1.31)	1.09 (0.62–1.92)	1.03 (0.75–1.41)	0.5 (0.18–1.4)	0.95 (0.76–1.19)
Not children's hospital	1 (0.52–1.92)	NA	0.77 (0.52–1.14)	0.96 (0.42–2.17)	0.76 (0.47–1.22)	0.48 (0.12–1.98)	0.81 (0.58–1.14)
Hospital region							
Midwest	0.55 (0.29–1.03)	NA	0.91 (0.65–1.26)	1.23 (0.59–2.59)	0.98 (0.66–1.45)	0.21 (0.06–0.77)	0.81 (0.6–1.08)
Northeast	Reference	Reference	Reference	Reference	Reference	Reference	Reference
South	0.76 (0.5–1.15)	NA	0.95 (0.75–1.22)	1.11 (0.65–1.88)	1.05 (0.78–1.42)	0.33 (0.15–0.75)	0.9 (0.73–1.11)
West	0.5 (0.22–1.16)	NA	1.02 (0.69–1.51)	0.76 (0.3–1.94)	1.07 (0.67–1.71)	1.13 (0.38–3.34)	0.88 (0.62–1.25)

Values are expressed as RR (95% CI).

Boldface type indicates significance at $p < 0.05$.

TABLE 10. The association of hospital factors with routine discharge, LOS, and hospital charges in 1961 patients with craniopharyngioma

Risk Factor & Variable	Routine	LOS	High Total Charge	High Daily Charge
Hospital capacity				
Large	1.02 (0.72–1.43)	0.93 (0.58–1.47)	0.61 (0.17–2.21)	3.53 (0.7–17.75)
Medium	1.04 (0.74–1.46)	0.97 (0.62–1.52)	1.38 (0.4–4.73)	1.07 (0.21–5.51)
Small	Reference	Reference	Reference	Reference
Procedure vol				
High	0.97 (0.81–1.16)	0.95 (0.75–1.22)	0.83 (0.46–1.48)	0.96 (0.52–1.75)
Low	Reference	Reference	Reference	Reference
Hospital teaching status				
Teaching	1.08 (0.67–1.75)	1.29 (0.65–2.59)	0.37 (0.1–1.4)	0.3 (0.11–0.82)
Nonteaching	Reference	Reference	Reference	Reference
Hospital location				
Rural	0.92 (0.48–1.77)	1.39 (0.66–2.94)	1.04 (0.13–8.31)	NA
Urban	Reference	Reference	Reference	Reference
Type of children's hospital				
Children's general or specialty	Reference	Reference	Reference	Reference
Children's unit	0.96 (0.69–1.34)	1.03 (0.66–1.59)	1.96 (0.74–5.16)	0.47 (0.16–1.44)
Missing	1.01 (0.77–1.32)	1.06 (0.74–1.52)	1.04 (0.48–2.25)	0.65 (0.25–1.71)
Not children's hospital	0.9 (0.62–1.31)	1.19 (0.73–1.96)	0.65 (0.17–2.54)	0.34 (0.1–1.15)
Hospital region				
Midwest	1.26 (0.91–1.74)	0.87 (0.56–1.34)	0.38 (0.1–1.47)	1.6 (0.47–5.44)
Northeast	Reference	Reference	Reference	Reference
South	1.23 (0.95–1.6)	0.96 (0.7–1.33)	0.6 (0.28–1.26)	1.14 (0.4–3.24)
West	1.22 (0.82–1.81)	1 (0.59–1.7)	0.46 (0.13–1.63)	2.51 (0.79–8.04)

Values are expressed as RR (95% CI).

Boldface type indicates statistical significance at $p < 0.05$.

Hospital Factors

Higher hospital volume and specific surgical caseloads have previously been associated with improved health-related outcomes.^{2,6,20,29} We found no difference in complication rates and hospital charges between centers with high and low procedural volume in our patient cohort. Zaidi et al. found that patients at high-volume centers had fewer complications than patients at low-volume hospitals when assessing surgical risk factors in adult patients with craniopharyngiomas. It is possible that the finding by Zaidi et al. may have been attributed to an unmeasured confounding variable. These authors also used a dichotomized classification system, in which hospitals were classified as either low-volume (≤ 20 procedures over a 5-year period) or high-volume (> 20 procedures over a 5-year period) centers. In our analysis, the mean annual procedural volume was 1.5; therefore we dichotomized low-volume centers (those with < 2 procedures annually; ≤ 80 th percentile for annual procedures), or high-volume centers (those with ≥ 2 procedures annually; > 80 th percentile for annual procedures), which we acknowledge as a limitation of the current study. The referral pattern to high-volume hospitals can also include more complicated cases,¹⁹ thereby masking any protective effects. There could also be a threshold at which there are insufficient resources

for the volume of procedures, thereby compromising the protective impact of higher-volume centers. This is in line with the finding that hospitals with greater bed capacity were protective for total complications and nonendocrine complications when compared with hospitals with lower bed capacity (Table 8).

Differences in complication rates can also be attributed to the availability of pediatric neurosurgeons with experience in skull base surgery. Multiple studies have shown a marked difference in outcome according to the neurosurgeons' experience with craniopharyngiomas.^{13,18,21} We were unable to determine the number and level of experience of surgeons managing the patients with craniopharyngiomas. However, a small percentage of patients were treated at rural (2.3%) or nonteaching (3.3%) hospitals, which were associated with an increased risk for nonendocrine complications and panhypopituitarism, respectively. Patients treated at a children's hospital showed no difference in our analysis; however, the large number with missing data (64%) may limit the relevance of this finding. A large percentage of data were also missing for admission source (27.5%) and admission type (15.4%), which may limit interpretation of their associations. In agreement with Zaidi et al., we believe that a prospective study is needed to assess the outcomes after referring complex lesions of the sellar region to highly specialized tertiary centers.

TABLE 11. The association of admission types with endocrine, nonendocrine, and total complications in 1961 patients with craniopharyngioma

Risk Factor & Variable	Nonendocrine	CSF Rhinorrhea	Endocrine Complication	Electrolyte Abnormalities	DI	Panhypopit	Total Comp
Admission source							
Another hospital	0.76 (0.28–2.08)	NA	0.85 (0.49–1.48)	0.99 (0.3–3.27)	0.9 (0.47–1.71)	NA	0.83 (0.51–1.35)
ER	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Law/court	NA	NA	1.69 (0.39–7.35)	5.52 (0.59–51.85)	1.1 (0.14–8.48)	NA	1.57 (0.37–6.68)
Other facility	2.41 (0.85–6.81)	NA	0.91 (0.43–1.96)	0.72 (0.09–6)	1.05 (0.46–2.41)	NA	1.21 (0.66–2.22)
Routine	1.08 (0.64–1.83)	NA	0.83 (0.61–1.13)	0.99 (0.52–1.89)	0.81 (0.56–1.18)	0.82 (0.24–2.76)	0.89 (0.68–1.16)
Admission type							
Elective	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Emergency	1.14 (0.72–1.79)	2.37 (0.03–184.54)	0.96 (0.74–1.25)	0.82 (0.47–1.42)	0.99 (0.73–1.36)	1.21 (0.43–3.44)	0.99 (0.79–1.25)
Urgent	1.13 (0.71–1.82)	7 (0.09–522.56)	0.91 (0.7–1.2)	0.87 (0.48–1.56)	0.97 (0.71–1.34)	0.4 (0.12–1.41)	0.96 (0.76–1.21)

Values are expressed as RR (95% CI).

TABLE 12. The association of admission types with routine discharge, LOS, and hospital charges in 1961 patients with craniopharyngioma

Risk Factor & Variable	Routine	LOS	High Total Charge	High Daily Charge
Admission source				
Another hospital	0.89 (0.51–1.56)	1.19 (0.67–2.11)	1.49 (0.28–7.83)	NA
ER	Reference	Reference	Reference	Reference
Law/court	0.86 (0.11–6.5)	1.86 (0.24–14.59)	NA	NA
Other facility	0.76 (0.35–1.62)	1.09 (0.45–2.64)	NA	4.9 (0.43–55.79)
Routine	0.9 (0.65–1.25)	0.76 (0.52–1.11)	0.88 (0.38–2.04)	1.78 (0.49–6.39)
Admission type				
Elective	Reference	Reference	Reference	Reference
Emergency	0.98 (0.74–1.28)	1.58 (1.13–2.19)	1.09 (0.52–2.3)	0.26 (0.06–1.14)
Missing	0.91 (0.69–1.2)	1.38 (0.97–1.94)	1.45 (0.6–3.49)	0.94 (0.3–2.94)
Urgent	0.89 (0.51–1.56)	1.19 (0.67–2.11)	1.49 (0.28–7.83)	NA

Values are expressed as RR (95% CI).

Boldface type indicates statistical significance at $p < 0.05$.

Limitations and Strengths

The use of a large population-based administrative database carries many limitations. The existence of coding error has previously been shown,^{4,8} and this can have an impact on the coding of diagnoses, covariates, and complications. The database is limited to inpatient records for a single admission, and does not capture complications that occur on subsequent admissions. Therefore, we were unable to distinguish between transient and permanent DI. A large limitation of this study is that the database does not contain specific information about the tumor (size, location, invasion, and so on), which has previously been shown to have a strong impact on patient outcomes. The costs analyzed were mainly due to hospital charges, and did not include professional fees and noncovered charges.

The main strength of this study is the use of a national database to analyze a large number of patients during an 11-year period, while incorporating a multivariate model to deduce multiple confounding factors. The associations do not imply direct causes, but rather the need for prospective trials to further identify the impact of these highlighted factors. The development of national databases has made it possible to accrue enough data to investigate clinical questions that would otherwise be difficult to answer. Although these databases carry many limitations, they still provide a great deal of clinical information acquired from assessing a large pool of patients with similar conditions. We used 2 large national databases, the NIS and the KID, to evaluate risk factors associated with the surgical management of craniopharyngiomas in pediatric patients. The KID is the largest publicly available pediatric inpatient care database in the US, and it was developed through a federal, state, and industry partnership sponsored by the Agency for Healthcare Research and Quality. In future studies, other prospective databases, such as the Pfizer International Growth Database (KIGS) of patients treated with growth hormone, can be included to further investigate the impact of growth hormone treatment and the presence of obesity in patients undergoing surgery for craniopharyngioma.⁷

Conclusions

This analysis identified age, comorbidities, insurance type, hospital bed capacity, and rural or nonteaching hospitals as independent risk factors for postoperative complications and/or hospital costs in pediatric patients who underwent surgery for craniopharyngioma. Further clinical studies are warranted to investigate the impact of these variables on complications and hospital costs.

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Disclosures

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

Author Contributions

Conception and design: Zada, Bakhsheshian, Jin. Acquisition of data: Bakhsheshian, Jin. Analysis and interpretation of data: Zada, Bakhsheshian, Jin, Chang. Drafting the article: Bakhsheshian, Jin. Critically revising the article: Zada, Bakhsheshian, Chang, Strickland, Cen, Mack, Attenello, Christian. Reviewed submitted version of manuscript: all authors. Statistical analysis: Bakhsheshian, Jin, Cen. Administrative/technical/material support: Bakhsheshian, Cen. Study supervision: Zada.

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