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# Risk factors for cerebrospinal fluid leak in pediatric patients undergoing endoscopic endonasal skull base surgery☆

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ABSTRACT

*Objectives:* To determine the risk factors associated with cerebrospinal fluid (CSF) leak following endoscopic endonasal surgery (EES) for pediatric skull base lesions.
*Methods:* Retrospective chart review of pediatric patients (ages 1 month to 18 years) treated for skull base lesions with EES from 1999 to 2014. Five pathologies were reviewed: craniopharyngioma, clival chordoma, pituitary adenoma, pituitary carcinoma, and Rathke's cleft cyst. Fisher's exact tests were used to evaluate the different factors to determine which had a statistically higher risk of leading to a post-operative CSF leak.
*Results:* 55 pediatric patients were identified who underwent 70 EES's for tumor resection. Of the 70 surgeries, 47 surgeries had intraoperative CSF leaks that were repaired at the time of surgery. 11 of 47 (23%) surgeries had post-operative CSF leaks that required secondary operative repair. Clival chordomas had the highest CSF leak rate at 36%. There was no statistical difference in leak rate based on the type of reconstruction, although 28% of cases that used a vascularized flap had a post-operative leak, whereas only 9% of those cases not using a vascularized flap had a leak. Post-operative hydrocephalus and perioperative use of a lumbar drain were not significant risk factors.
*Conclusions:* Pediatric patients with an intra-operative CSF leak during EES of the skull base have a high rate of post-operative CSF leaks. Clival chordomas appear to be a particularly high-risk group. The use of vascularized flaps and perioperative lumbar drains did not statistically decrease the rate of post-operative CSF leak.



## 1. Introduction

Pediatric patients who undergo endoscopic endonasal surgery (EES) for skull base tumors have unique pre-operative, intra-operative, and post-operative challenges in comparison to adult patients with similar lesions. As the indications for endonasal resection of pediatric skull base tumors widens, so do the reconstructive challenges. A post-operative cerebrospinal fluid (CSF) leak can place the patient at risk for significant complications including pneumocephalus, mental status changes, and meningitis. Our 15-year history of treating pediatric skull base tumors using the endoscopic endonasal approach (EEA) has given us a unique perspective on the surgical and post-operative challenges that these patients face.

Tatreau et al. [1] in 2010 evaluated the anatomic considerations in pediatric patients undergoing EES. They found three areas of limitation in the pediatric patient as compared to adults. The nasal pyriform aperture, sphenoid sinus pneumatization and sphenoid bone thickness, and intercarotid distance within the sphenoid sinus were all areas where anatomic limitations could influence surgical outcomes. All of these factors can effect surgical outcomes and the reconstructive options available to the pediatric skull base surgeon.

The adult literature on the use of reconstructive materials including bio-synthetic products and local vascularized flaps to repair intra-operative CSF leaks has been a recent area of intense

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**Table 1**
Demographic information for surgical cohort.

| | Pathology | Age (yrs.) | # Resections | # Staged tumor resections |
|---|---|---|---|---|
| Clival chordoma | 11 | 10.23 | 15 | 4 |
| Pituitary adenoma | 14 | 16.72 | 17 | 1 |
| Rathke's cleft cyst | 9 | 15.43 | 10 | 0 |
| Craniopharyngioma | 20 | 8.46 | 27 | 0 |
| Pituitary carcinoma | 1 | 17.80 | 1 | 0 |
| **Totals:** | 55 | 13.7 | 70 | 5 |

review. A systematic review of the adult literature evaluated 22 studies looking to create an evidence-based algorithm for skull base reconstruction techniques. However, due to the wide variety of reconstructive techniques used, inconsistent reporting of high or low flow intra-operative CSF leaks, and lack of uniform post-operative outcomes reporting, a true algorithm could not be created. They focused on two factors: location of skull base defect and degree of intraoperative CSF flow. They concluded that repair of high-flow intraoperative CSF leaks with pedicled vascularized flaps was superior to non-vascularized flaps and that location of the defect did not matter, with the exception of the clivus[2].

There are case series in the literature addressing the feasibility of nasoseptal flap repair of skull base defects after undergoing EES in the pediatric population [3–5]. However, the objective of this study was to determine the risk factors associated with post-operative CSF leaks in pediatric patients undergoing EES.

## 2. Methods

This is an IRB approved retrospective chart review from January 1999 to September 2014 at Children's Hospital of Pittsburgh of the University of Pittsburgh Medical Center. Inclusion criteria were pediatric patients, ages 1 month to 18 years old, who had EES for surgical resection of five high-risk tumor pathologies Craniopharyngioma, Pituitary Tumors (Adenoma, Carcinoma, Rathke's cleft cyst), and Clival Chordoma. Only patients who had intraoperative CSF leaks were included in the study. These 5 tumor types were included due to their relatively high prevalence and/or a high rate of intraoperative CSF leak.

Indications for surgery included endocrine abnormalities, cranial nerve palsies, vision loss, orbital complications, persistent headaches, hydrocephalus, or other mental status changes. Image-guided navigation was used for all cases. All tumors were removed by the skull base team, which consists of a neurosurgeon and otolaryngologist operating concurrently. Gross total resection was the primary goal in the surgical resection of craniopharyngiomas, pituitary adenomas, pituitary carcinoma, and clival chordomas. Rathke's cleft cysts were opened and drained into the sphenoid sinus. All clival chordomas were referred for proton beam radiation therapy following surgical resection.

The study parameters included: pathologic diagnosis, age, gender, weight, height, growth percentile, surgical corridor approach (transsellar, transclival, transpterygoid, transplanum, transtuberculum), reconstruction technique, intra-operative CSF leak, post-operative complications, tumor recurrence, post-operative CSF leak, hydrocephalus, and lumbar drain use. Fisher's exact test was used to determine which factors had a statistically significant risk ($p < 0.05$) of leading to a post-operative CSF leak.

## 3. Results

170 pediatric patients who underwent EES from January 1999 to September 2014 were identified. Of those, 55 patients met our inclusion criteria.

The pathology included 20 craniopharyngiomas, 14 pituitary adenomas, 11 clival chordomas, 9 Rathke's Cleft cysts, and 1 pituitary carcinoma. The overall average age for the cohort was 13.7 years with craniopharyngiomas being the youngest group averaging 8.43 years old (Table 1). Of the 14 pituitary adenomas, 5 presented with Cushing's Disease, 3 Prolactinomas, 2 Pituitary Apoplexy, 2 with vision loss, 1 Acromegaly, and 1 incidental imaging finding.

Patient size was recorded based upon height, weight, BMI, and growth percentile. The size of the patient was evaluated to determine if this affected the incidence of CSF leak. Pituitary adenomas were our largest patients averaging the 92nd percentile for weight and a BMI of 42. The smallest patients in our group were the craniopharyngiomas, averaging 55th percentile for weight and a BMI of 19. There was no statistical difference in CSF leak rates for the groups based on height, weight, or BMI (Table 2).

Interestingly, age (analyzed by quartiles) did show a statistically significant difference in post-operative leaks, with higher leak rates in the 2nd quartile (ages 5.8–9.6) and 4th quartile (>16.2 years of age) (Table 2).

The 55 patients that were included in the study underwent 70 EES for removal of tumor (Table 1). Five clival chordomas and one

**Table 2**
Risk of post-operative leak based on Age in quartiles, BMI, Site/Pathology, and Vascularized Reconstruction. Fisher's exact test used for statistical analysis.

| | | N | # with post op CSF leak | % with post op CSF leak | p-value |
|---|---|---|---|---|---|
| Age *[quartile]* | *< = 5.7* | 11 | 0 | 0.0 | |
| | *5.8–9.6* | 12 | 6 | 50.0 | |
| | *9.7–16.2* | 12 | 0 | 0.0 | |
| | *>16.2* | 12 | 5 | 41.7 | 0.001 |
| BMI *[quartile]* | *< = 15.8* | 10 | 3 | 30.0 | |
| | *15.9–18.9* | 11 | 1 | 9.1 | |
| | *19.0–28.4* | 10 | 2 | 20.0 | |
| | *>28.4* | 11 | 3 | 27.3 | 0.692 |
| Site/pathology | *sellar/suprasellar* | 36 | 7 | 19.4 | |
| | *posterior fossa* | 11 | 4 | 36.4 | 0.256 |
| Vascularized flap | *no* | 11 | 1 | 9.1 | |
| | *yes* | 36 | 10 | 27.8 | 0.416 |