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Sinonasal Symptom Outcomes following Endoscopic Anterior Cranial Base Surgery in the Pediatric Population

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Abstract

Objective This study aimed to evaluate the impact of endoscopic anterior cranial base (ACB) surgery on sinonasal symptoms in the pediatric population utilizing the Sino-Nasal Outcome Test (SNOT)-22 questionnaire.
Design This is a retrospective review.
Setting The study was conducted at a tertiary academic medical center.
Participants Thirty-four consecutive patients, age 6 to 17 years, M:F 14:20, who underwent endoscopic ACB surgery from July 2008 to August 2019. Ten patients had baseline and a minimum of two subsequent postoperative SNOT-22 questionnaires available for analysis.
Main Outcome Measures Baseline and postoperative SNOT-22 scores were compared. The mean change from baseline sinonasal symptom scores in the pediatric and historical adult cohorts was compared.
Results The mean baseline SNOT-22 score for our 10 patient cohort was 0.46 out of 5 for each of the first 10 sinonasal-specific questions. This worsened to 1.69 at 1 month and returned to near baseline, 0.7, at 3 months postoperatively. The mean quality-of-life score improved to 0.91 at 1 month and 0.6 at 3 months postoperatively. The mean change from baseline for the following items: need to blow nose, runny nose, postnasal discharge, thick nasal discharge, wake up at night, reduced concentration, and frustrated/restless/irritable were similar to those in our historical adult cohort at 3 months postoperatively.
Conclusion Endoscopic ACB surgery in the pediatric population results in increased sinonasal symptom morbidity in the early postoperative period; however, symptoms return to near baseline by ~3 months, and quality-of-life scores progressively improve in the postoperative period. These trends were similar to those seen in our historic adult cohort.

Keywords
- skull base
- pediatrics
- outcomes

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Introduction

Endoscopic anterior cranial base (ACB) surgery has been performed in the pediatric patient population for the past two decades. In the pediatric population, ACB surgery poses specific challenges: sphenoid pneumatization has not yet occurred in younger children, sinonasal passageways are narrow, and landmarks used in adult ACB surgery are different.[1–3] However, the endoscopic approach provides benefits such as lower morbidity, less blood loss, and seemingly lower rates of recurrence when compared with open resection.[4] As such, most research studies to date have focused on safety outcomes related to this surgical approach as well as the impact on craniofacial development.[1,4–11] Now that this technique has been found to be safe in this cohort of patients, we sought to explore the symptomatic impact of endoscopic ACB surgery on sinonasal quality-of-life outcomes. Most studies addressing outcomes for pediatric ACB patients compare complications and long-term adverse effects. To our knowledge, this is the only study that compares quality-of-life outcomes across time. Our institution has previously evaluated this outcome measure in an adult population undergoing endoscopic ACB surgery. In this study, we also sought to provide a comparison between the adult and pediatric population outcomes.

Materials and Methods

After approval by the Institutional Review Board of the University of California, Los Angeles, we performed a retrospective chart review of sequential pediatric ACB surgeries performed at our tertiary care institution between 2008 and 2019. We included patients younger than 18 years, with at least one postoperative follow-up appointment and without a prior history of sinusitis, totaling 34 patients. From this cohort, we abstracted demographics data (age, gender, sex, diagnosis), and data related to their surgery and postoperative course. Ten of these patients had a complete baseline Sino-Nasal Outcome Test (SNOT)-22 questionnaire and at least two postoperative complete questionnaires. All 10 of these patients underwent postoperative debridement. These patients were included in our primary outcome analysis, comparing baseline and postoperative SNOT-22 scores. To ensure accuracy and sufficient understanding of questions, all surveys were completed by primary caregivers. The SNOT-22 questionnaire is a tool validated in adults and widely used disease-specific health-related quality-of-life measure for rhinosinusitis consisting of 22 items. Each item is measured on an ordinal Likert scale from 0 to 5.[12] Our office routinely provides this questionnaire to patients seen in the rhinology and skull base clinic.

We analyzed our data using analysis of variance (ANOVA) and paired *t*-tests to determine statistically significant changes in scores over time. To further identify trends, we also performed analyses in two groups: Group 1 consisted of the first 10 sinonasal symptom-specific (rhinologic, extranasal rhinologic, and ear/facial) questions and Group 2 included the last 12 quality-of-life (psychological and sleep dysfunction) questions.

We then compared the outcomes of our pediatric cohort to historical data previously published by our institution on SNOT-20 and SNOT-22 outcomes in the adult population following ACB surgery.[13] Those items available for comparison only included specific questions within the SNOT questionnaire as raw data from this study were not available for review.

Results

We reviewed our pediatric ACB surgery database and 34 patients met our inclusion criteria as described earlier. Most patients were female ($n = 21$, 59.0%) with mean age of 14 years (range: 6–17 years). The most common surgical pathologies included: pituitary adenoma ($n = 12$, 35.3%), craniopharyngioma ($n = 7$, 20.6%), and Rathke's cleft cyst ($n = 6$, 17.6%). Other rarer pathologies included: juvenile xanthogranuloma, leiomyoma, germinoma, mucocele, juvenile angioneurofibroma, esthesioneuroblastoma, pituitary hyperplasia, and encephalocele (see ►**Table 1**).

The following complications occurred: two patients developed a postoperative cerebrospinal fluid (CSF) leak (5.9%), seven developed new postoperative diabetes insipidus (DI) (20.6%), six developed postoperative pituitary dysfunction (17.6%), one patient suffered deep vein thrombosis and pulmonary embolism (2.9%), and one patient experienced fat graft site hematoma (2.9%). Two patients (5.9%) experienced recurrence of disease treated with revision surgical resection that occurred after our study end point. Among our entire cohort, only two patients did not undergo postoperative sinonasal debridement in clinic; neither of these patients was included in our quality-of-life analyses. Average follow-up for first debridement occurred 17 ± 10.0 days after surgery (range: 5–55 days).

Of the 34 patients, 10 had a baseline and 2 postoperative SNOT questionnaires and were thus included in our primary outcome analysis. All 10 patients underwent postoperative debridement. Of the 10 patients, 3 experienced intraoperative CSF leak and underwent nasoseptal flap reconstruction. All other patients underwent free mucosal graft. One patient had preexisting DI, and one patient experienced temporary postoperative DI.

Overall, the mean total SNOT-22 at baseline was a score of 17.6 ± 18.1. Mean first follow-up score was 27.8 ± 17.4, and mean second follow-up score was 13.6 ± 7.5 (see ►**Table 2**). Between patients who experienced intraoperative CSF leak and underwent nasoseptal flap reconstruction and patients who did not, there was no significant difference in baseline or postoperative SNOT-22 scores ($p > 0.1$). The patient with temporary postoperative DI had the highest first postoperative SNOT-22 score, while the patient with preexisting DI had a postoperative SNOT-22 score of 0 (►**Fig. 1**).

Mean time to first follow-up SNOT-22 was 36.6 days ± 19.0. Average time to follow-up for second postoperative SNOT-22 was 82.1 days ± 18.1. Analysis comparing baseline and postoperative SNOT-22 scores was done by one-way

Table 1 Demographics information

Patient	Age	Gender	Diagnosis
1	12	M	Pituitary adenoma
2	10	F	Juvenile xanthogranuloma
3	11	M	Craniopharyngioma
4	17	F	Craniopharyngioma
5	6	F	Juvenile xanthogranuloma
6	17	F	Craniopharyngioma
7	9	M	Craniopharyngioma
8	17	F	Pituitary Adenoma
9	16	F	Pituitary adenoma
10	16	M	Pituitary adenoma
11	15	M	Pituitary adenoma
12	12	F	Rathke's cleft cyst
13	15	F	Leiomyoma
14	15	M	Pituitary adenoma
15	16	F	Rathke's cleft cyst
16	17	F	Pituitary adenoma
17	15	M	Craniopharyngioma
18	15	F	Germinoma
19	17	F	Craniopharyngioma
20	14	M	Rathke's cleft cyst
21	16	F	Pituitary adenoma
22	14	M	Rathke's cleft cyst
23	16	F	Pituitary adenoma
24	16	F	Rathke's cleft cyst
25	16	F	Craniopharyngioma
26	15	F	Pituitary adenoma
27	6	F	Mucocele with skull base defect
28	10	M	Juvenile nasopharyngeal angiofibroma
29	12	F	Esthesioneuroblastoma
30	13	M	Pituitary adenoma
31	14	F	Pituitary hyperplasia
32	15	F	Encephalocele
33	15	M	Rathke's cleft cyst
34	16	M	Pituitary adenoma

Table 2 SNOT-22 totals at various time points

	Mean	Median	Standard deviation
Baseline	17.6	12	18.1
First follow-up	27.8	31	17.4
Second follow-up	13.6	13.8	7.5

Abbreviation: SNOT, Sino-Nasal Outcome Test.

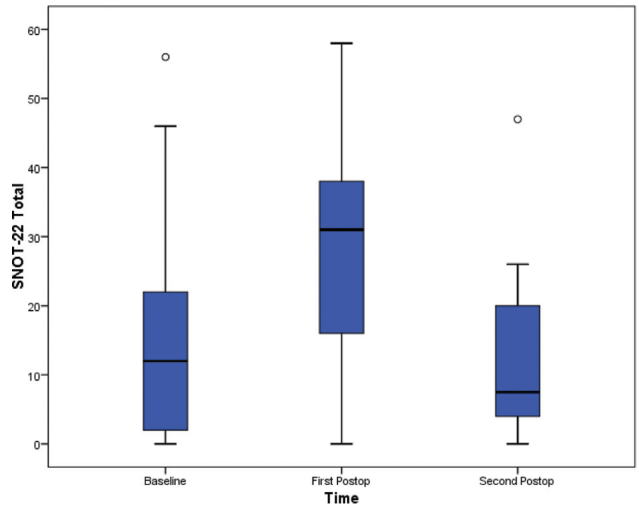

Fig. 1 Box and whisker plot of Sino-Nasal Outcome Test (SNOT)-22 total scores.

repeated measured ANOVA to evaluate whether there were significant changes in SNOT-22 scores from baseline compared with the first and second postoperative appointments. There was a significant effect of time on SNOT-22 scores, Wilks' lambda = 0.275, $F(2,8) = 10.524$, $p = 0.006$. Three paired sample *t*-tests were used to make post hoc comparisons between conditions. Although the average baseline scores were not shown to be significantly different from the first or second postoperative scores ($p = 0.163$ and $p = 0.381$, respectively), there was a significant difference shown between the first and second postoperative scores ($p = 0.003$).

To further explore trends of patients' recoveries, we separated questions into two groups as described in the Materials and Methods section. Group 1 (sinonasal symptoms) mean of baseline individual question scores for our 10-patient cohort was 0.46 ± 0.96 and 1.08 ± 1.74 for Group 2 (quality-of-life measures) questions. Group 1 mean of first postoperative responses was 1.69 ± 1.75 and Group 2 mean was 0.91 ± 1.48. Finally, the mean second postoperative responses for Group 1 was 0.66 ± 1.10 and Group 2 mean was 0.59 ± 1.25. When comparing the postoperative Group 1 scores to baseline scores, there was a significant difference between baseline and first postoperative scores ($p < 0.001$) and a nonsignificant trend toward difference when comparing baseline and second postoperative scores ($p = 0.10$). When comparing Group 2 (quality-of-life measures) scores, there was no significant difference between baseline and first postoperative scores ($p = 0.26$), but a significant difference was shown between baseline and second postoperative scores ($p < 0.01$) (►**Table 3**).

The previously published means and changes in means of adult responses for SNOT-22 questions 1, 3, 5, 6, 12, 17, and 18 were used to compare responses from our pediatric cohort.[13] As described in the Materials and Methods section, only these specific questions were available for analysis. There was a statistically significant difference of $p < 0.01$ in changes in response between the baseline and first

Table 3 Comparisons between baseline and postoperative scores for sinonasal (Q1–10) and quality-of-life symptoms (Q11–22)

Group	Pairs "a and b"	Mean difference (a − b)	Standard deviation	Lower[a]	Upper[a]	Significance
Sinonasal	Baseline and postoperative 1	−1.23	0.20	−1.62	−0.84	<0.0001[b]
	Baseline and postoperative 2	−0.19	0.12	−0.42	0.03	0.10
Quality of life	Baseline and postoperative 1	0.18	0.15	−0.43	0.48	0.26
	Baseline and postoperative 2	0.49	0.11	0.26	0.72	<0.001[b]

[a]Lower and upper bounds of the 95% confidence interval.
[b]Statistical significance.

Table 4 Comparison between pediatric and adult changes in SNOT-22 scores over time

SNOT item	Baseline		First follow-up			Second follow-up		
	Adult, mean	Pediatric, mean	Adult, mean	Pediatric, mean	*p*-Value	Adult, mean	Pediatric, mean	*p*-Value
Q1: need to blow nose	1.07	0.8	0	0.9	0.20	−0.36	−0.5	0.69
Q3: runny nose	1.19	0.3	−0.27	1.9	<0.01[a]	−0.64	−1.0	0.26
Q5: postnasal discharge	1.20	0.1	−0.34	2.1	<0.01[a]	−0.30	−0.5	0.53
Q6: thick nasal discharge	0.51	0.4	0.17	0.5	0.40	0.28	0.30	0.94
Q12: wake up at night	1.71	0.9	−0.69	−0.1	0.46	0.18	0.60	0.27
Q17: reduced concentration	1.51	1.7	−0.59	0.1	0.269	−0.38	0.50	0.152
Q18: frustrated/irritable	1.46	1.1	−0.56	0.1	0.258	−0.37	0.60	**0.04[a]**

Abbreviation: SNOT, Sino-Nasal Outcome Test.
[a]Statistical significance.

postoperative response for questions 3 and 5 pertaining to runny nose and postnasal discharge, respectively. When comparing changes from second postoperative appointment compared with the baseline responses, a statistically significant difference was seen in question 18 pertaining to frustration and irritability ($p = 0.04$). No other differences between the adult and pediatric cohort were statistically significant (►**Table 4**).

Discussion

Although ACB surgery has been used to treat the pediatric population for many years, most studies to date have explored safety of the procedure or evaluated outcomes by examining postoperative complications. Many case series are small due to the rare nature of pediatric ACB tumors and range from single to double digit cohorts. To our knowledge, our study is the first study that attempts to explore the postoperative outcomes of patients based on quality-of-life measures.

Our group's experience with ACB surgery in the pediatric population spans over a decade of patient care. Our experiences with adult ACB surgery have informed our standardized pediatric protocols, which we believe contribute to our high success rates and improved quality of life. Preoperatively, all patients undergo preoperative assessments, discussion, and counseling about surgery and postoperative care. Intraoperatively, our team uses various algorithms for surgical approach, tumor dissection, and reconstruction. As mentioned earlier, all patients with CSF leak undergo nasoseptal flap reconstruction, while patients without leaks undergo free mucosal graft reconstruction. Nasopore packing (Stryker) is used in each patient. Postoperatively, all patients undergo endocrinological monitoring, encouragement of frequent saline sprays and irrigations by patient or caregiver, and outpatient clinic visits with sinus debridements.

In our study of 34 patients, the most common surgical pathologies were pituitary adenoma, craniopharyngioma, and Rathke's cleft cyst, similar to those in prior studies.[5,9] Our most common postoperative complications include new DI ($n = 7$, 20.6%) and pituitary dysfunction ($n = 6$, 17.6%). Of the cases of new DI, five were transient and eventually resolved; two patients had permanent DI resulting from surgery (5.9%). Although DI is a known complication of sellar tumor resection, reported rates in the literature differ greatly. One 2018 study by Yamada et al showed a postoperative development of DI in 33 of 40 pediatric patients (82.5%) undergoing primary skull base surgery for treatment of craniopharyngioma and development of DI in all four patients undergoing revision surgery.[6] Another 2019 study by Koumas et al reported an occurrence of new DI in 14 of 30 patients in a mixed cohort of craniopharyngiomas, pituitary adenomas, and Rathke's cleft cysts. Of these 14, 9 were transient (30%), and 5 resulted in permanent DI (16.7%).[9] Our postoperative complication rate of DI is well within the published range.

Pituitary dysfunction is also a widely reported adverse outcome of ACB surgery in pediatric patients. A 2018 case series of 11 pediatric patients treated for craniopharyngioma showed new onset of hypopituitarism in 6 of 10 patients without prior endocrinopathies.[10] However, larger studies report a lower rate. The Yamada et al's study reported that 28 of 65 patients experienced partial hypopituitarism (43.1%) and 31 of 65 experienced panhypopituitarism with or without DI (47.7%).[6] A 2019 review of pediatric ACB cases between 1995 and 2017 by Shenouda et al showed a late complication rate of endocrinopathies at 20.7%, a rate that is more similar to ours.[8]

Patients in our cohort rarely experienced other complications including CSF leak, deep vein thrombosis and pulmonary embolism, and graft site hematoma. CSF leak has generally been reported at a rate of 3 to 10%.[6,9,10] Our study reports a frequency well within this range. All patients with intraoperative CSF leak underwent nasoseptal flap reconstruction. Otherwise, a free mucosal graft was used. Among the 10 patients evaluated further for quality-of-life measures, three experienced intraoperative CSF leak and underwent nasoseptal flap reconstruction. There was no significant difference in baseline or postoperative scores between patients who experienced CSF leak and those who did not. Of note, although meningitis is a serious risk with any skull base surgery, no patients in this study experienced postoperative meningitis. This compares to a rate of 4.6% in the Yamada et al's study and 7.3% in a 2019 study of 82 skull base patients.[6,14]

Although recurrence rates are difficult to compare as recurrence is dependent on tumor type as well as surgical approach, it appears that recurrence rates have decreased over the years. A 2013 review of juvenile nasopharyngeal angiofibroma between 1990 and 2012 yielded 345 cases and a 10.8% rate of recurrence.[7] A 2013 single institution study of 104 pediatric cases of mixed diagnoses reported a rate of 15.4%.[4] Some smaller studies have recurrence rates of up to 50%.[6,7] However, as surgical techniques and technology have improved, recurrence rates have decreased. The Yamada et al's study reported similar rate to ours, at 4.6%.[6]

While there are multiple publications detailing rates of recurrence and common adverse events in this population, our study's examination of quality-of-life measures is unique. Although the SNOT-22 has been validated for use in adults with chronic rhinosinusitis,[15] it has not been widely validated for use in pediatric populations. A study by Thamboo et al showed a SNOT-22 score greater than 11 was significantly predictive of nasal polyps in pediatric cystic fibrosis patients.[16] Instead, the Sinus and Nasal Quality of Life Survey (SN-5) is a quality-of-life measure specifically designed for use in the pediatric population, with good test–retest reliability, construct validity, and responsiveness.[17] Still, a systematic review by Morley and Sharp of 15 sinonasal outcomes tests showed the SNOT-22 was superior to other tests, including the SN-5. The survey had better reliability, validity, responsiveness, and ease of use.[12] In our experience, the comprehensive nature of the SNOT-22 allows for accurate assessment of clinical symptoms and postoperative outcomes, regardless of age. This literature and our clinical experience guided use of the SNOT-22 to measure quality of life in this study.

Using preoperative and postoperative SNOT-22 scores, we found that patients appear to have higher SNOT-22 scores at their first postoperative visit, generally occurring at approximately 1 month postoperatively. This trend is expected given the presence of nasal packing, crusts, and clot that require debridement at the first postoperative visit. The second postoperative SNOT-22 scores, completed at an average of 3 months postoperatively showed that patients returned to a score below baseline, indicating their quality of life improved at least to baseline overall. When comparing the SNOT-22 scores reported in this study, the differences between the baseline and first postoperative scores are not statistically different ($p = 0.163$) and neither are the baseline scores compared with the second postoperative scores ($p = 0.381$) (►**Table 2**). However, when comparing the first postoperative scores with the second postoperative scores, there is a significant difference ($p = 0.006$), likely due to the effects of sinonasal debridement, daily saline irrigations, and resolution of postoperative edema.

For further analysis, we separated questions by topic: Group 1 included questions 1 to 10 addressing sinonasal symptoms, and Group 2 included questions 11 to 22 addressing quality of life. Group 1 mean individual baseline SNOT-22 scores for our 10-patient cohort was 0.46 ± 0.96 and 1.08 ± 1.74 for Group 2 (quality-of-life measures) questions. This suggested that preoperative sinonasal symptoms were not as severe as quality-of-life disturbances, which is expected given the lack of rhinologic disease in our patient cohort. When comparing first postoperative scores to baseline scores in Group 1, the mean significantly increased ($p < 0.001$) indicating increase of sinonasal symptoms soon after surgery. Again, this is likely due to nasal packing, crusts, clot, and edema. Baseline and final postoperative scores for Group 1 showed a nonsignificant trend toward difference ($p < 0.1$), suggesting that long-term postoperative sinonasal symptoms were similar to baseline. This trend is similarly suggested in the literature. A 2018 study by Alalade et al reported that only 3 of 11 patients reported postoperative nasal symptoms: one patient reported transient anosmia that resolved a year after surgery, another complained of epistaxis, and another complained of nasal discharge with hyposmia that resolved a month after surgery.[10]

When comparing Group 2 quality-of-life measures, no significant difference was found to exist between baseline and first postoperative scores, but a significant difference was found when comparing baseline to second postoperative scores ($p < 0.01$), suggesting that quality of life was significantly improved from baseline (►**Table 3**). This may be due to improvement in their preoperative tumor-related symptoms. In conclusion, our data suggest that long-term sinonasal symptoms did not significantly change from baseline, although long-term quality of life improved. Our 2013 study analyzing SNOT-20 and SNOT-22 responses in adults suggested a similar trend. The study also separated questions into symptom and quality-of-life measures, with Factor I describing symptoms and Factor II describing quality of life. Although the study mainly compared changes in factors between surgical approaches, the data also suggest sinonasal symptoms return to baseline over time, although trends for quality of life were not as clear.[13]

When comparing the previously published means and changes in means of adult responses for SNOT-22 1, 3, 5, 6, 12, 17, and 18 were used to compare responses from our pediatric cohort, there were some significant differences. Changes in response between baseline and first postoperative responses for questions 3 and 5 pertaining to runny and postnasal discharge were significant at a level of $p < 0.01$, indicating more development of these symptoms in pediatric patients when compared with adults. When comparing changes from second postoperative to baseline responses, a statistically significant difference was seen between adults and children, with children reporting significantly higher frustration and irritability ($p = 0.04$). No other differences between the adult and pediatric cohort were statistically significant.[13]

Conclusion

Our study confirms endoscopic treatment of pediatric ACB tumors is an effective, safe treatment for the pediatric population. Our findings suggest long-term postoperative sinonasal symptoms are not significantly different from baseline, but there is a significant improvement in quality of life. Trends in our findings were similar to our previously published study in 2013, with generally similar differences between postoperative SNOT-22 scores and baseline. The surgery and postoperative care, including in-office sinus debridement, are well tolerated by pediatric patients.

Conflict of Interest
None declared.

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