Outcomes of Endoscopic Sinus Surgery for Chronic Rhinosinusitis in Adults with Primary Ciliary Dyskinesia

Diogo Barreto Plantier[1] Fábio de Rezende Pinna[1] Mary Anne Kowal Olm[2] Rodrigo Athanázio[3] Renata Ribeiro de Mendonça Pilan[1] Richard Louis Voegels[1]

[1] Department of Otorhinolaryngology and Ophthalmology, School of Medicine, Universidade de São Paulo, São Paulo, SP, Brazil
[2] Department of Pathology, School of Medicine, Universidade de São Paulo, São Paulo, SP, Brazil
[3] Pulmonary Division, Instituto do Coração, School of Medicine, Universidade de São Paulo, São Paulo, SP, Brazil

Address for correspondence Diogo Barreto Plantier, MD, Department of Otorhinolaryngology and Ophthalmology, School of Medicine, Universidade of São Paulo, São Paulo 05403-000, Av. Dr. Eneas de Carvalho Aguira, 255, 6th floor, room 6167, SP, Brazil (e-mail: diogoplantier@gmail.com).

Int Arch Otorhinolaryngol 2023;27(3):e423–e427.

Abstract

Introduction Primary ciliary dyskinesia (PCD) is a rare inherited disease associated with impairment of mucociliary transport and, consequently, with a high incidence of chronic rhinosinusitis. For patients with chronic rhinosinusitis who remain symptomatic despite medical treatment, endoscopic sinus surgery is a safe and effective therapeutic option. However, to date, no studies have been found evaluating the effect of surgery on the quality of life associated with the effect on olfaction and nasal endoscopy findings of patients with primary ciliary dyskinesia and chronic rhinosinusitis.

Objective To describe the effect of endoscopic sinus surgery on the quality of life, on olfaction, and on nasal endoscopy findings of adults with PCD and chronic rhinosinusitis.

Methods Four patients who underwent endoscopic sinus surgery were included. The Sinonasal Outcome Test-22 (SNOT-22) score, the Nasal Obstruction Symptom Evaluation (NOSE) questionnaire, and the Lund-Kennedy score were collected preoperatively and at 3 and 6 months postoperatively. The olfaction as assessed with the University of Pennsylvania Smell Identification Test (UPSIT), which was administered preoperatively and 3 months postoperatively.

Results A total of 4 patients with a mean age of 39.3 years old (3 men and 1 woman) completed the study. All patients showed clinically significant improvement in the SNOT-22, NOSE, and Lund-Kennedy scores at 3 months postoperatively, and this improvement was sustained throughout the follow-up period. However, olfaction did not improve after surgery.

Conclusion The endoscopic sinus surgery treatment of chronic rhinosinusitis in adults with PCD was associated with improvement in quality of life and endoscopic findings. However, no improvement in olfaction was demonstrated. Studies with a larger number of patients and control groups should help confirm these findings.

Keywords
- chronic rhinosinusitis
- endoscopic sinus surgery
- hyposmia
- kartagener syndrome
- paranasal sinuses
- primary ciliary dyskinesia

received
November 4, 2021
accepted after revision
March 1, 2022

DOI https://doi.org/10.1055/s-0042-1746193.
ISSN 1809-9777.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Introduction

Primary ciliary dyskinesia (PCD) is a rare hereditary disorder associated with abnormal ciliary function. Impairment of mucociliary transport results in neonatal respiratory distress, recurrent airway infections, and infertility, as well as abnormal laterality of internal organs (situs inversus or ambiguus).[1,2] Thus, these patients experience early impact on physical and emotional quality of life.[3,4]

According to the international PCD (iPCD) cohort, patients with a clinical picture suggestive of PCD can be classified as having "definite PCD" if they are found to have transmission electron microscopy findings or a biallelic genetic mutation known to be associated with PCD. Patients can be classified as having "probable PCD" if they present abnormal findings on high-frequency video microscopy or low nasal nitric oxide levels. Finally, they can be classified as having a "clinical diagnosis of PCD" if the results of the aforementioned tests are negative or ambiguous, or if they have not been tested.[5]

In PCD, a malfunction of sinonasal mucociliary clearance leads to stasis of secretions and inflammation of the mucosal lining. Thus, up to 94.8% of adults and 45% of children with PCD have chronic rhinosinusitis (CRS), and up to 56.4% of adults have nasal polyps.[6,7] Chronic rhinosinusitis can have a greater impact on quality of life than many other chronic diseases, including angina, congestive heart failure, and chronic obstructive pulmonary disease.[8]

Endoscopic sinus surgery (ESS) is a safe treatment modality capable of relieving symptoms and improving the quality of life of patients with CRS who do not respond to conservative therapy.[9]

To the best of our knowledge, no studies have yet evaluated the impact of ESS on the quality of life and on the olfaction in adult patients with PCD and CRS refractory to conservative treatment. Furthermore, studies on the treatment of CRS usually exclude patients with PCD, which makes a targeted assessment of these patients even more relevant.

Within this context, the primary objective of the present study is to evaluate the impact of ESS on the quality of life of adults with PCD and CRS. As a secondary objective, we assessed the impact of ESS on olfaction and on nasal endoscopy findings in these patients.

Methods

Patient Recruitment

We carried out a prospective exploratory study of patients recruited from the Outpatient Rhinology Clinic of the Department of Otorhinolaryngology of a tertiary hospital. Patients >18 years old with PCD and indications for ESS for CRS, alone or combined with septoplasty and turbinate surgery, were included in the study.

Access to specific tests for diagnostic confirmation of PCD is very limited in Brazil, and there is no referral center for diagnosis anywhere in the country. Thus, patients with a confirmed, probable, or clinical diagnosis of PCD were eligible for inclusion.[5] The confirmation of the diagnosis of PCD was based on leading published guidelines.[10,11] The diagnosis of CRS was based on the European Position Paper on Rhinosinusitis and Nasal Polyps.[12] Finally, we defined the appropriate medical therapy (AMT) of CRS to be the use of topical nasal corticosteroids and nasal irrigation with saline solution; a short trial of oral corticosteroids and antibiotics may be attempted. The AMT was considered to have failed when uncomfortable symptoms remained in combination with computed tomography (CT) or endoscopic evidence of CRS.[13] For patients in whom AMT failed after at least 8 weeks of treatment, ESS was indicated.

Patients unfit to undergo surgery, those who did not wish to undergo the surgery, and those who had undergone previous sinus surgery were excluded from the study.

All patients underwent ESS under general anesthesia. In accordance with institutional protocols, the surgical technique adopted was based on the wide opening of the paranasal sinuses to facilitate drainage of the sinuses by gravity and access of saline solution and medications to the sinuses. However, we did not perform more radical surgeries such as mega-antrostomy or Draf III in the first surgery. All patients were discharged the day after surgery on a 7-day course of antibiotics and prednisolone, in addition to continuous large-volume, low-pressure nasal irrigation with 0.9% saline solution. The choice of antibiotic used took into account the result of the most recent culture of the patient (sputum or nasal) and the use of prednisolone was to reduce mucosal edema and discomfort, considering that the topical

Table 1 Clinical, demographic, and surgical characteristics of patients.

	Patient 1	Patient 2	Patient 3	Patient 4
Age	34	53	38	32
Gender	M	M	F	M
PCD diagnosis	Clinical PCD	Definite PCD	Definite PCD	Definite PCD
Situs inversus	No	Yes	Yes	Yes
Pulmonary surgery	LL	LT	No	LT
Nasal polyps	No	Yes	Yes	Yes
Septal deviation	No	Yes	Yes	Yes
Lund-Mackay	13	17	16	18

Abbreviations: F, female; LL, lung lobectomy; LT, lung transplant; M, male; PCD, primary ciliary dyskinesia.

Table 2 Lund-Kennedy, SNOT-22, and NOSE scores in each patient in the preoperative period and 3 and 6 months after surgery.

	Endoscopy and quality of life scores			
Variable	**Patient 1**	**Patient 2**	**Patient 3**	**Patient 4**
Lund-Kennedy score				
Preoperative	5	10	14	6
3 months	5	4	4	2
6 months	0	2	1	2
SNOT-22				
Preoperative	93	26	59	49
3 months	40	10	23	15
6 months	27	8	21	25
NOSE				
Preoperative	15	11	17	15
3 months	2	0	0	2
6 months	1	0	0	1

Abbreviations: NOSE, Nasal Obstruction Symptom Evaluation questionnaire; SNOT-22, Sinonasal Outcome Test-22.

corticosteroid had not yet been reintroduced. Patients were evaluated weekly at the clinic until the mucosa of the nasal cavities was completely healed, with no crusting. At this point, topical nasal budesonide 50 mcg was resumed in all patients.

Outcome Measures

Primary outcomes: Quality of life was assessed with the Sinonasal Outcome Test-22 (SNOT-22) [14] and the Nasal Obstruction Symptom Evaluation (NOSE) questionnaire,[15] both of which have been validated for use in Brazilian Portuguese. The questionnaires were administered preoperatively and 3 and 6 months after ESS.

Secondary Outcome

Olfaction was assessed with the Brazilian version of the University of Pennsylvania Smell Identification Test (UPSIT) [16] at baseline and 3 months after surgery.

The Lund-Kennedy score was used to assess nasal endoscopy findings preoperatively and 3 and 6 months after ESS. Finally, preoperative CT scans were evaluated and classified with the Lund-Mackay score.

Results

The present study included 4 patients with a mean age of 39.3 years old (3 men and 1 woman) who underwent ESS consecutively between 2018 and 2021. Three had a definite diagnosis of PCD, while one had clinical PCD. The clinical diagnosis of PCD had been established on the basis of persistent cough since childhood, recurrent pneumonia and otitis, early-onset CRS, immotile sperm, a history of pulmonary lobectomy and bronchiectasis, consanguineous parents, and negative testing for immunodeficiencies and cystic fibrosis. Two patients had undergone lung transplantation, and one had undergone pulmonary lobectomy (►**Table 1**).

No patient had any intraoperative or postoperative complications.

The primary outcomes and Lund-Kennedy scores are shown in ►**Table 2**. The endonasal endoscopic evaluation showed a mean preoperative Lund-Kennedy score of 8.75. By 3 months postoperatively, the mean score had improved to 3.75 and continued to improve thereafter, reaching 1.25 at 6 months after surgery. Thus, all patients showed improvement in the endoscopic appearance of the nasal cavities.

SNOT-22*:* The mean preoperative SNOT-22 score was 56.8. Three months after surgery, the mean score had declined to 22 and continued to fall thereafter, reaching 20.3 at 6 months. Thus, all patients experienced improvement in quality of life after surgery, persisting throughout the follow-up period.

NOSE*:* Nasal obstruction-related quality of life was quite impaired in the preoperative period, with a mean NOSE score of 14.5. Three months after surgery, the mean score had dropped to 1 and, after 6 months, to 0.5. Thus, all patients achieved relief from the negative impact of nasal obstruction.

UPSIT*:* The subjective assessment of preoperative olfaction ranged between 7 and 30 (mean: 14). Three months postoperatively, the scores ranged from 10 to 25 (mean: 15.8) (►**Table 3**).

According to the UPSIT criteria, 1 patient had mild microsmia (UPSIT score 30–33)[16] and 3 patients had anosmia (UPSIT score 6–18) preoperatively. At 3 months

Table 3 Olfaction outcomes of each patient preoperatively and 3 months after operation.

UPSIT	Patient 1	Patient 2	Patient 3	Patient 4
Preoperative	30	12	7	7
3 months	25	14	14	10

Abbreviation: UPSIT, University of Pennsylvania Smell Identification Test.

Table 4 Results of the evaluation of the Lund-Kennedy, SNOT-22, and NOSE scores until the last patient had completed 6 months of follow-up.

	Endoscopy and quality of life scores		
Patient (months after surgery)	Lund-Kennedy	SNOT-22	NOSE
2 (20 months)	2	9	0
3 (26 months)	1	14	0
4 (33 months)	1	9	0

Abbreviations: NOSE, Nasal Obstruction Symptom Evaluation questionnaire; SNOT-22, Sinonasal Outcome Test-22.

postoperatively, 1 patient had progressed to severe microsmia (UPSIT score 19–25) and the other 3 patients remained anosmatic.

Discussion

In the present study, we found that patients with PCD and CRS who underwent ESS experienced improvement in the SNOT-22 and NOSE scores at the 3rd postoperative month and remained improved until the 6th month. In addition, these patients showed improvement in endonasal endoscopy findings, as measured by the Lund-Kennedy score, throughout the follow-up period. While waiting for all patients to complete 6 months of follow-up after surgery, we continued to assess the SNOT-22, NOSE, and Lund-Kennedy scores in the first 3 patients who underwent surgery (►**Table 4**). We were able to observe that, even after an average of 26.3 months after surgery, these patients continued to show improvement in all 3 scores, confirming the trend observed at the 6-month follow-up.

The improvement in quality of life observed in the present study coincides with that previously described by Parsons et al., who reported the cases of three children with PCD who underwent ESS for CRS. The authors identified improvement in upper and lower airway symptoms in all 3 children, but did not use questionnaires for evaluation.[17] Likewise, Tang et al. reported the case of a patient with Kartagener syndrome who underwent ESS for the treatment of CRS and experienced improvement in upper and lower airway symptoms, but they also did not administer quality of life questionnaires.[18] Finally, Alanin et al. identified improvement in quality of life measured by SNOT-22 in 24 patients (adults and children) with PCD who underwent ESS either to identify a possible focus of infection or to treat CRS with symptoms refractory to medical treatment.[19] According to the authors, the patients showed significant improvement from baseline at the 3rd month postoperatively, and this improvement was maintained throughout the 12-month period of assessment.

In the version of the SNOT-22 validated for Brazilian Portuguese, a change $\geq$14 points is necessary to be perceived as improvement or worsening by the patient. The authors consider 10 as the upper limit of normal for the score.[14] Thus, all patients in the present study showed a noticeable improvement between the preoperative period and the 3rd month after surgery. Between the 3rd and the 6th months after surgery, scores changed by values $<$ 14 points. The patient who experienced a 10-point increase in score between the 3rd and the 6th months was re-evaluated 33 months after surgery and, again, had experienced a reduction in the score, to 9 (within normal range). Finally, although all patients showed significant improvement in CRS-related quality of life, only one patient had reached normal range (that is, a score $\leq$ 10) at the 3-month follow-up. We also reassessed this patient 22 months after surgery, and his score remained within the normal range (9 points). The mean preoperative SNOT-22 score reported by Alanin et al. was 39, reducing to 23 by the 3rd postoperative month.[19] In our study, the mean SNOT-22 decreased from 56.8 preoperatively to 22 on the 3rd month after surgery. Despite our small sample size, we believe that patients with a higher preoperative score may experience a more marked improvement in the postoperative period. Furthermore, 3 (75%) of our patients had polyps and, according to Kosugi et al., patients with CRS with nasal polyps show a greater variation between preoperative and postoperative scores.[14]

Assessing olfaction through the Sniffin Sticks extended test, Pifferi et al. found that hyposmia and anosmia were more common in patients with PCD than in patients with CRS without PCD and in a control group. Likewise, the authors found that patients with PCD and worse Lund-Mackay scores or lower nasal nitric oxide levels have a worse sense of smell.[20] In the present study, the patient with the best Lund-Mackay score also performed best on the preoperative and postoperative assessments of olfaction. According to the results of the UPSIT performed preoperatively and at 3 months after surgery, no patient experienced enough improvement in scores to achieve normosmia or even improve in classification.

The limitations of the present study include the small sample size; the fact that some patients had undergone surgery before the publication of a PCD-specific quality of life questionnaire (QOL-PCD),[21] which precluded the use of this instrument; and the absence of a control group.

Conclusions

The present study showed that ESS can lead to improvement in quality of life in patients with PCD, as measured by the SNOT-22 and NOSE instruments. However, the ESS was not able to improve olfaction during the follow-up period. We believe that further research with a larger sample and a control group is warranted to confirm these findings.

Conflict of Interests
The authors have no conflict of interests to declare.

Funding
The author(s) did not receive financial support for the research. The author Diogo Barreto Plantier was a CNPQ doctoral scholarship holder.

References

1 Horani A, Ferkol TW, Dutcher SK, Brody SL. Genetics and biology of primary ciliary dyskinesia. Paediatr Respir Rev 2016;18:18–24
2 Goutaki M, Meier AB, Halbeisen FS, et al. Clinical manifestations in primary ciliary dyskinesia: systematic review and meta-analysis. Eur Respir J 2016;48(04):1081–1095
3 Behan L, Rubbo B, Lucas JS, Dunn Galvin A. The patient's experience of primary ciliary dyskinesia: a systematic review. Qual Life Res 2017;26(09):2265–2285
4 Behan L, Leigh MW, Dell SD, Dunn Galvin A, Quittner AL, Lucas JS. Validation of a health-related quality of life instrument for primary ciliary dyskinesia (QOL-PCD). Thorax 2017;72(09): 832–839
5 Goutaki M, Maurer E, Halbeisen FS, et al;PCD Italian Consortium Swiss PCD Group French Reference Centre for Rare Lung Diseases Genetic Disorders of Mucociliary Clearance Consortium. The international primary ciliary dyskinesia cohort (iPCD Cohort): methods and first results. Eur Respir J 2017;49(01):1601181
6 Frija-Masson J, Bassinet L, Honoré I, et al. Clinical characteristics, functional respiratory decline and follow-up in adult patients with primary ciliary dyskinesia. Thorax 2017;72(02):154–160
7 Bhatt JM, Muhonen EG, Meier M, Sagel SD, Chan KH. Rhinosinusitis in Pediatric Primary Ciliary Dyskinesia: Impact of Disease. Otolaryngol Head Neck Surg 2019;161(05):877–880
8 Gliklich RE, Metson R. The health impact of chronic sinusitis in patients seeking otolaryngologic care. Otolaryngol Head Neck Surg 1995;113(01):104–109
9 Bezerra TFP, Piccirillo JF, Fornazieri MA, et al. Assessment of quality of life after endoscopic sinus surgery for chronic rhinosinusitis. Braz J Otorhinolaryngol (Engl Ed) 2012;78(02):96–102
10 Shapiro AJ, Davis SD, Polineni D, et al; Diagnosis of Primary Ciliary Dyskinesia. An Official American Thoracic Society Clinical Practice Guideline Am J Respir Crit Care Med 2018;197(12):e24–e39
11 Lucas JS, Barbato A, Collins SA, et al. European Respiratory Society guidelines for the diagnosis of primary ciliary dyskinesia. Eur Respir J 2017;49(01):1–25
12 Fokkens WJ, Lund VJ, Mullol J, et al. EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. Rhinology 2012;50(01):1–12
13 Orlandi RR, Kingdom TT, Hwang PH, Smith TL, Alt JA, Baroody FM, et al. International Consensus Statement on Allergy and Rhinology: Rhinosinusitis. Int Forum Allergy Rhinol 2016 Feb;6 (Suppl 1):S22–S209
14 Kosugi EM, Chen VG, Fonseca VM, Cursino MM, Mendes Neto JA, Gregório LC. Translation, cross-cultural adaptation and validation of SinoNasal Outcome Test (SNOT): 22 to Brazilian Portuguese. Braz J Otorhinolaryngol Sep-Oct 2011;77(05):663–669
15 Bezerra TFP, Padua FGM, Pilan RRDM, Stewart MG, Voegels RL. Cross-cultural adaptation and validation of a quality of life questionnaire: the Nasal Obstruction Symptom Evaluation questionnaire. Rhinology 2011;49(02):227–231
16 Fornazieri MA, dos Santos CA, Bezerra TFP, Pinna FdeR, Voegels RL, Doty RL. Development of normative data for the Brazilian adaptation of the University of Pennsylvania Smell Identification Test. Chem Senses 2015;40(02):141–149
17 Parsons DS, Greene BA. A treatment for primary ciliary dyskinesia: efficacy of functional endoscopic sinus surgery. Laryngoscope 1993;103(11 Pt 1):1269–1272
18 Tang X, Zou J, Liu S. Endoscopic sinus surgery for treatment of kartagener syndrome: a case report. Balkan Med J 2013;30(02): 244–247
19 Alanin MC, Aanaes K, Høiby N, et al. Sinus surgery can improve quality of life, lung infections, and lung function in patients with primary ciliary dyskinesia. Int Forum Allergy Rhinol 2017;7(03): 240–247
20 Pifferi M, Bush A, Rizzo M, et al. Olfactory dysfunction is worse in primary ciliary dyskinesia compared with other causes of chronic sinusitis in children. Thorax 2018;73(10):980–982
21 Queiroz APL, Athanazio RA, Olm MAK, et al. Translation of the quality-of-life measure for adults with primary ciliary dyskinesia and its application in patients in Brazil. J Bras Pneumol 2019;45 (03):e20170358

