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Reversibility of mucociliary clearance and olfaction impairment following endoscopic sinus surgery: a prospective observational study

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Abstract

Objective. Chronic rhinosinusitis is associated with altered mucociliary clearance and olfaction. The study aimed to analyse the reversibility of impairment and endoscopic factors predicting changes in mucociliary clearance and olfactory parameters.

Methods. This prospective study included patients undergoing functional endoscopic sinus surgery for medically refractory chronic rhinosinusitis. Pre- and post-operative measurements of mucociliary clearance, olfactory thresholds, and identification scores were recorded.

Results. Of the 96 patients, 65.6 per cent had polyposis and 80.2 per cent underwent primary surgery. Improvements in mucociliary clearance and olfaction scores were seen in all patients, with greater reversibility of impairment in patients with polyposis and in those who underwent revision surgery. The presence of polyps correlated significantly with changes in mucociliary clearance and olfaction.

Conclusion. The study highlights improvements in mucociliary clearance, olfactory thresholds and identification scores after functional endoscopic sinus surgery in chronic rhinosinusitis with or without nasal polyposis, as well as for primary and revision surgeries. Adequate post-operative care and prevention of polyps recurrence help to improve mucociliary clearance and olfaction scores.

Main Article

Dr R Kurien takes responsibility for the integrity of the content of the paper

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Introduction

Mucociliary clearance and olfaction are two of the most important physiological attributes of the nose and paranasal sinuses. The nasal mucosa, being a delicate structure, requires prime functioning of the mucociliary mechanism, playing a vital role in the host defence mechanism, and thus maintaining its structural and functional integrity.[1] Olfaction, yet another important function of nasal mucosa, is highly dependent on a healthy sinonasal environment, and any alteration in this milieu, be it due to internal or external factors, can have deleterious effects on its optimal functioning.

Chronic rhinosinusitis, both with and without nasal polyposis, causes prolongation of mucociliary clearance and a reduction in sense of smell.[2,3] Multiple mechanisms cause the dysfunction of mucociliary clearance. These could be obstructive, secondary to oedema and polypoidal mucosal changes within the ostiomeatal complex, or structural anatomical abnormalities that cause impediment to the natural drainage pathway of the paranasal sinus. Direct insult to the sinonasal mucosa via inflammatory mediators like cytokines and toxins from various bacteria causes disruption of sodium channels and damages the integrity of the ciliated epithelium, resulting in a slow and disorganised ciliary beat.[4–6] In addition, alterations in the viscoelastic properties of the mucous blanket and impaired mechanical mucociliary coupling cause blunting of effective mucociliary transport.[7]

Olfactory dysfunction is a common symptom affecting 65–80 per cent of patients with chronic rhinosinusitis.[8] Mechanical obstruction from oedematous mucosa or polyposis, combined with injury to the olfactory neuroepithelium secondary to bipolar neuron damage with impairment in neurogenesis, has been postulated to be a causative factor.[9]

Functional endoscopic sinus surgery (FESS) is the recommended treatment for medically refractory chronic rhinosinusitis. The goal of surgery is to remove the obstructive pathology, provide access for topical medical therapy and facilitate the return of normal physiological functions. The reversible nature of chronic rhinosinusitis is dependent on how quickly the mucociliary clearance regains its ultrastructural function, thus improving the dynamics of sinus ventilation. Studies in the literature have shown a slower rate of mucociliary clearance in patients with chronic rhinosinusitis, with reversibility of impairment following FESS.[10,11] Moreover, the return of olfactory function can be quite challenging, with conflicting reports in the literature.[3,12–14] Although studies show an improvement of mucociliary clearance and olfaction following FESS, analysis of objective improvement within the various subgroups, such as chronic rhinosinusitis

with or without polyps subgroups, and especially in those undergoing primary versus revision surgery, is lacking.

This study aimed to assess whether FESS would help restore mucociliary clearance and olfactory function of the nose. We also wanted to examine the role of any predictive factors and assess the difference in restoration patterns of these physiological functions, in patients with or without nasal polyps, and in those undergoing primary or revision surgery. Furthermore, changes in olfactory discrimination and threshold were also analysed in these subgroups.

Materials and methods

This prospective observational study evaluated the changes in mucociliary clearance and olfaction following FESS. The study was conducted in the Department of ENT over a period of seven months, after obtaining approval from the institutional review board. All patients diagnosed as having chronic rhinosinusitis, with or without nasal polyps, based on the European position paper on rhinosinusitis and nasal polyps 2012 guidelines,[15] and who were scheduled to undergo elective FESS after failure of maximal medical therapy, were included in the study. Patients aged less than 18 years, those diagnosed as having ciliary motility disorders, choanal atresia, sinonasal malignancies or invasive fungal sinusitis, and smokers, were excluded from the study.

Pre-operatively, all patients underwent nasal endoscopy, computed tomography (CT) of the paranasal sinuses without contrast, and measurement of mucociliary clearance and olfaction.

Nasal endoscopy

All recruited patients underwent a rigid nasal endoscopy in the out-patient clinic. Each patient was scored based on the Lund–Kennedy endoscopic scoring system, wherein each parameter, including scarring, crusting, oedema, polyps and discharge, was assessed.[16]

Computed tomography of paranasal sinuses

All patients underwent a CT scan of the paranasal sinuses. The images were scored based on the Lund–Mackay staging system and a total score was assigned for each side.[17]

Mucociliary clearance measurement

Mucociliary clearance was evaluated using the saccharin method.[2,18] The procedure was explained to patients. No mucolytic agents or topical preparations were used prior to the commencement of the test. The patients were asked to blow their nose to remove any excessive secretions. Saccharin powder (5 mg) was placed over the anterior end of the inferior turbinate. The time from the placement of the particles to the perception of a sweet taste sensation by the patient was recorded in minutes and taken as the clearance time.

Olfaction measurement

The procedure was explained to the patients, who provided consent. The measurement of olfaction consisted of two parts, as described by the Connecticut Chemosensory Clinical Research Center:[19] olfactory threshold testing and odour identification.

Olfactory threshold test

The threshold test employed aqueous dilutions of 1-butanol differing by a factor of 3, with the highest dilution being 4 per cent. Two bottles were presented to the patient, one containing 1-butanol at a particular concentration and the other being water (blank). The test started with the lowest concentration. The patient was asked to identify the bottle that had a stronger smell. If incorrect, the participant received another blank paired with the next highest concentration. Errors by the patient triggered increments in concentration, whereas correct choices led to another presentation of the same concentration and a blank. Four correct choices in a row led to the cessation of testing, and the concentration at which this occurred was taken as the olfactory threshold. The final threshold scores were documented, ranging from 0 to 6.

Olfactory identification test

The odour identification test was performed using seven odorants (cinnamon, asafoetida, coffee, tea, pepper, clove and Johnson's powder), which were presented in an irregular order. Patients were asked to identify the odorant from a list of items. The score for the test was calculated based on the number of olfactory items identified correctly.

The composite score for olfaction was the average of the odour threshold and the odour identification scores in each nostril, and was graded as normosmia = score of 6 or more, mild hyposmia = 5–5.75, moderate hyposmia = 4–4.75, severe hyposmia = 2–3.75 and anosmia = 2 or less.

Procedure

The endoscopic, CT scan, mucociliary clearance and olfaction scores were recorded for the involved side in patients with unilateral disease. In patients with bilateral disease, the more affected side based on endoscopy was used for assessment.

Following FESS, all patients were given standard instructions to use saline nasal douching along with intranasal corticosteroid sprays, and were reviewed from three to six months post-operatively. During each follow-up visit, the patients underwent rigid nasal endoscopy with the Lund–Kennedy endoscopic scoring, to assess the cavity post-operatively. Post-operative mucociliary clearance and olfaction testing were performed. The individual pre- and post-operative scores for each of these parameters were recorded in the proforma and stored in the database for further evaluation.

Statistical methods

Categorical variables were summarised using frequencies and percentages. Quantitative variables were summarised using means and standard deviations (SDs). The Pearson correlation test was used to investigate the relationship between the quantitative variables. The paired samples *t*-test was used to assess the pre- and post-intervention outcome measures. The independent sample *t*-test and Mann–Whitney U test were used to compare the change in score between the groups based on the normality assumption. The chi-square test was used to compare the association between the groups. For all the analyses, $p < 0.05$ was considered to be significant.

Results

A total of 96 patients were recruited into the study, consisting of 57 males and 39 females, with ages ranging from 20 to 66

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years. Chronic rhinosinusitis with polyposis was seen in 63 patients (65 per cent), while 33 (34 per cent) had chronic rhinosinusitis without polyposis. Around 50 per cent of the patients fell into the 20–35-year age group in both types of chronic rhinosinusitis. Unilateral disease was seen in 42 patients, while 54 patients had bilateral disease. Primary surgery was performed in 77 patients (80 per cent), whereas 19 (19 per cent) were scheduled for a revision surgery having undergone primary surgery elsewhere. Co-morbid illness was seen in 32 patients in the cohort, of which diabetes mellitus (14 per cent) and bronchial asthma (11 per cent) were the most common.

There were no significant associations between co-morbid illness and the type of chronic rhinosinusitis or type of surgery (primary *vs* revision cases). There were no significant associations between changes in mucociliary clearance and olfaction scores and age, gender or co-morbid illness.

Out of the 96 patients who were initially enrolled into the study, 68 attended their post-operative follow-up appointments during the six-month period and were tested for all the post-operative variables.

Changes in mucociliary clearance

Entire cohort

The mean pre-operative mucociliary clearance time of the entire cohort was 19.7 minutes (SD = 9.3), while the mean post-operative mucociliary clearance time was 14.5 minutes (SD = 4.1), showing an improvement of 5.1 minutes; this difference was statistically significant ($p < 0.0001$) (Table 1).

Chronic rhinosinusitis with versus without nasal polyps

Patients with chronic rhinosinusitis with nasal polyps had a post-operative improvement in mucociliary clearance time of 7.2 minutes (SD = 8.0). This was statistically significant ($p < 0.0001$) compared with those who had chronic rhinosinusitis without nasal polyps. For the latter group, there was an improvement of only 0.5 minutes (SD = 6.9) and the finding was not statistically significant ($p = 0.750$) (Table 1).

Primary versus revision surgery

In patients who underwent primary surgery, there was a decrease in mean mucociliary clearance time, from 17.5 minutes (SD = 8.6) a preoperative value of 13.9 minutes (SD = 3.6) post-operatively; this difference was statistically significant ($p = 0.002$). Patients who underwent revision surgery showed an improvement of 10.2 minutes, which was statistically significant ($p < 0.0001$) (Table 2).

Changes in olfaction

Entire cohort

On analysing the entire cohort, there were statistically significant post-operative improvements in mean composite olfaction score (difference of 1.4 points) (SD = 1.7) ($p < 0.0001$). There was a mean difference of 1.2 points (SD = 1.6) ($p < 0.0001$) for olfactory thresholds and 1.7 points (SD = 2.2) ($p < 0.0001$) for olfactory identification scores (Table 1).

Chronic rhinosinusitis with versus without nasal polyps

Both groups with chronic rhinosinusitis showed an improvement in olfaction scores. However, the difference was statistically significant in patients with chronic rhinosinusitis with nasal polyps (1.5 points) (SD = 1.6) ($p < 0.0001$), compared with the difference in patients with chronic rhinosinusitis without nasal polyps (1.0 points) (SD = 2.03), which was just approaching significance ($p = 0.053$).

The olfactory threshold scores also showed a significant improvement in both the groups. However, the olfactory identification scores showed a significant improvement (1.9 points) (SD = 2.1) in the chronic rhinosinusitis with nasal polyps group ($p < 0.0001$), compared with patients who had chronic rhinosinusitis without nasal polyps (0.9 points) (SD = 2.3), where the improvement was not significant ($p = 0.13$).

Primary versus revision surgery

There was a statistically significant improvement in the mean composite olfaction scores in patients who underwent primary (1.1 points) (SD = 1.8) or revision surgery (2.2 points) (SD = 1.0) ($p < 0.001$). Moreover, a similar significant improvement was seen in both the threshold and identification scores in both the groups ($p < 0.0001$) (Table 2).

Endoscopy, mucociliary clearance and olfaction

There were statistically significant correlations between the pre-operative endoscopy scores and both pre-operative mucociliary clearance time (correlation co-efficient = 0.417, $p < 0.001$) and olfaction scores (correlation co-efficient = 0.465, $p < 0.001$). Significant correlations were also seen between post-operative endoscopic scores and both post-operative mucociliary clearance time (correlation co-efficient = 0.481, $p < 0.001$) and olfaction scores (correlation co-efficient = 0.281, $p = 0.023$).

Computed tomography, mucociliary clearance and olfaction

The mean CT score for the side being assessed, within the cohort, was 7.79. There were statistically significant correlations between the pre-operative CT scores and pre-operative mucociliary clearance time (correlation co-efficient = 0.55, $p < 0.001$) and olfaction scores (correlation co-efficient = 0.65, $p < 0.001$).

Changes in olfactory loss

Pre-operatively, 22 per cent of the patients had anosmia, 68 per cent had hyposmia and 10 per cent had normosmia. Post-operatively, there was a significant decrease in the proportion of patients with anosmia (6 per cent), and a marginal increase in the proportions of patients with hyposmia (80 per cent) or normosmia (14 per cent).

Predictive endoscopic factors

Of all the endoscopic parameters used in the Lund–Kennedy endoscopic scoring system, the presence of polyps was the only statistically significant factor correlating with improvement in both mucociliary clearance time (correlation co-efficient = 0.396; $p < 0.001$) and olfaction scores (correlation co-efficient = 0.295; $p = 0.016$) (Table 3).

Discussion

Chronic rhinosinusitis, with or without polyps, is associated with impairment in mucociliary clearance and olfaction, with FESS recommended for medically refractory disease.

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Table 1. Changes in mucociliary clearance and olfaction in entire cohort, and among chronic rhinosinusitis patients with or without nasal polyposis

	Entire cohort*		CRSwNP†		CRSsNP‡	
Parameter	Mean (SD)	*P*-value	Mean (SD)	*P*-value	Mean (SD)	*P*-value
Mucociliary clearance time (minutes)		<0.0001		<0.0001		0.750
– Pre-operative	19.7 (9.3)		21.8 (9.6)		14.5 (6.2)	
– Post-operative	14.5 (4.1)		14.6 (4.3)		14 (3.7)	
Olfaction composite score		<0.0001		<0.0001		0.053
– Pre-operative	3 (1.9)		2.8 (1.9)		3.7 (1.8)	
– Post-operative	4.4 (1.3)		4.3 (1.4)		4.7 (1.1)	
Olfactory threshold score		<0.0001		<0.0001		0.012
– Pre-operative	2.3 (1.7)		2.2 (1.7)		2.7 (1.7)	
– Post-operative	3.5 (1.2)		3.4 (1.3)		4 (1.1)	
Olfactory identification score		<0.0001		<0.0001		0.13
– Pre-operative	3.7 (2.4)		3.4 (2.4)		4.6 (2.2)	
– Post-operative	5.4 (1.5)		5.3 (1.7)		5.5 (1.1)	

*$n = 96$; †$n = 63$; ‡$n = 33$. SD = standard deviation; CRSwNP = chronic rhinosinusitis with nasal polyposis; CRSsNP = chronic rhinosinusitis without nasal polyposis

Table 2. Changes in mucociliary clearance and olfaction among primary and revision surgery patients

	Primary surgery		Revision surgery	
Parameter	Mean (SD)	*P*-value	Mean (SD)	*P*-value
Mucociliary clearance time (minutes)		<0.002		<0.0001
– Pre-operative	17.5 (8.6)		26.5 (8.4)	
– Post-operative	13.9 (3.6)		16.3 (4.3)	
Olfaction composite score		<0.0001		<0.0001
– Pre-operative	3.4 (1.9)		1.9 (1.5)	
– Post-operative	4.5 (1.3)		4.1 (1.2)	
Olfactory threshold score		<0.0001		<0.0001
– Pre-operative	2.7 (1.7)		1.3 (1.1)	
– Post-operative	3.7 (1.2)		3.1 (1.2)	
Olfactory identification score		<0.0001		<0.0001
– Pre-operative	4.1 (2.4)		2.5 (2.3)	
– Post-operative	5.5 (1.5)		5.1 (1.5)	

SD = standard deviation

In our cohort, consisting of 96 patients, there was a minor male preponderance in both subgroups; this finding is in agreement with Asian literature,[20,21] but in discordance with some Caucasian cohort studies where chronic rhinosinusitis without nasal polyposis was associated with a female preponderance.[22,23] Our finding that asthma and diabetes mellitus are common co-morbidities of chronic rhinosinusitis is similar to that seen in the literature.[24,25]

There was a significant improvement in mucociliary clearance times for the entire cohort, as reported in the literature.[1,11–13] Singh *et al.* showed a greater improvement in mucociliary clearance among patients with chronic rhinosinusitis with nasal polyps, a finding also shown in our study.[10] Removal of the obstructive burden secondary to nasal polyps, in patients with chronic rhinosinusitis with nasal polyps, results in a more dramatic improvement in the nasal airway, reflecting a corresponding improvement in mucociliary clearance times in this subgroup.

Revision FESS causes multiple areas of scarring, creating greater impediments to mucociliary transport, the removal of which could account for the greater improvement in mucociliary clearance times seen in our study. This aspect has not been evaluated in the literature, making a comparative analysis difficult.

Various studies, including systematic reviews, have shown improvements in olfaction following FESS, as in the current study.[3,12,26,27] The added gains in chronic rhinosinusitis with nasal polyps patients may again be due to the removal of the obstructive pathology. However, reports have also shown a lack of olfactory improvement after FESS,[28] with no predictive correlation to the severity of chronic rhinosinusitis, presence of nasal polyps or allergy status.[8,14,29] Eosinophilic endotype and tissue eosinophilia have predicted a worse olfactory outcome, especially in patients with chronic rhinosinusitis with nasal polyps.[30,31]

The degree of olfactory improvement after revision FESS has not been studied extensively before, with very few articles

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Table 3. Endoscopic parameters predicting recovery of mucociliary clearance and olfaction

Mucociliary clearance & olfaction parameters	Endoscopic parameters				
	Polyp	Discharge	Oedema	Scarring	Crusting
Changes in mucociliary clearance time					
– Correlation co-efficient	0.396	0.090	0.050	0.084	0.126
– *P*-value	<0.001	0.464	0.688	0.494	0.306
Changes in olfaction score					
– Correlation co-efficient	0.295	0.222	0.107	0.129	0.130
– *P*-value	0.016	0.074	0.392	0.300	0.297

in the literature. Our study showed significant improvement in olfactory function after revision FESS, indicating an equal chance of recovery in this subgroup, which is otherwise associated with poor outcomes. Hsu *et al.*[32] and Deconde *et al.*[33] showed a 50 per cent improvement after revision surgery, with opacification of the olfactory cleft on imaging and removal of polyps from this region associated with a better outcome. On the contrary, other studies have shown revision surgery to be associated with poor olfactory outcomes,[34,35] especially in association with aspirin-exacerbated respiratory disease,[36] sinus neo-osteogenesis on CT scan [32,37] and persistence of mucosal oedema.[3,32]

Both olfactory threshold and identification are key components of olfactory evaluation. A decreased threshold is associated with sinonasal causes, while loss of identification is often related to cerebral pathology.[38] However, a recent study by Whitcroft *et al.*[39] showed that in patients with chronic rhinosinusitis, changes in the olfaction scores correlated best with variations in olfactory identification scores. Our study, using the Connecticut Chemosensory Clinical Research Center method of olfactory evaluation, analysed changes in these components and showed improvements in both threshold and identification scores. These changes were seen in all the subgroups, with patients with chronic rhinosinusitis with nasal polyps and those undergoing revision FESS faring better. The identification scores showed a better improvement than the threshold scores in all the subgroups, highlighting the significance of including both components for olfactory evaluation in patients with chronic rhinosinusitis.

The degree of improvement in olfaction was also dependent on the pre-operative severity of olfaction. The current study showed that a number of pre-operative patients with anosmia became hyposmic or normosmic post-operatively, while patients with hyposmia remained relatively the same, similar to other studies.[3,30,33] The main reason for this could be that patients with anosmia often had a mechanical obstruction that was amenable to surgical removal, while hyposmic patients had a more multifactorial cause, secondary to inflammation and neuroepithelial damage.[3] Despite recovery in olfactory function, many patients do not normalise, as seen in our study, and experience some amount of persistent neuroepithelial damage.[8]

On analysis of the endoscopic predictive factors, our study showed a significant correlation between the presence of polyps and changes in both mucociliary clearance and olfaction. None of the other parameters in the Lund–Kennedy endoscopic scoring system were found to be predictive of mucociliary clearance and olfactory changes, highlighting the importance of post-operative intranasal steroid nasal sprays in preventing the recurrence of polyps.

- Chronic rhinosinusitis is often associated with altered mucociliary clearance and olfaction
- The study showed significant improvements in mucociliary clearance, olfactory thresholds and identification scores
- Greater improvements were seen in patients with polyposis and in those who underwent revision surgery
- Presence of polyps correlated significantly with changes in mucociliary clearance and olfaction

The limitations of our study include the lack of a longer post-operative follow-up period, and with some patients lost to follow up. Although many of our patients were followed up for six months, a longer follow-up period might have resulted in more improved results with regard to the recovery of mucociliary clearance and olfaction.

Conclusion

Despite these limitations, the current study, with a level of evidence of 2b, highlights the improvement of both mucociliary clearance and olfaction in all the chronic rhinosinusitis patient subgroups following FESS. Olfactory improvements were seen in both the threshold and identification parameters, in all subgroups. The presence of polyps in the post-operative FESS cavity causes deterioration in mucociliary clearance and olfaction. Hence, meticulous post-operative follow up, with continuation of nasal steroid sprays, can prove effective in the restoration of vital physiological functions of the nose.

Competing interests. None declared

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