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Mucociliary clearance before and after endonasal sinus surgery for chronic rhinosinusitis with and without nasal polyps

Boris R. Haxel, Niki Karaiskaki, Patrick Boessert, Kai Fruth

ABSTRACT

Aims: Mucociliary function is an important protective mechanism of the nasal mucosa that comprises cilia motility and the consistency of the nasal mucus. This study intended to investigate this feature and how it changes following functional sinus surgery (FESS) for chronic rhinosinusitis (CRS) with (CRSwNP) and without (CRSsNP) nasal polyps, in comparison to other parameters associated with this disease. Methods: In 37 patients with CRS±polyps, the saccharin transit time (STT) was measured prior to FESS, as well as two weeks after and six months after. Other parameters like SNOT-20 scores, olfaction, CT and endoscopy scores were also evaluated. Results: There was an insignificant preoperative difference in STT between the CRS subgroups with or without polyps (23.1 and 15.6 minutes respectively). There was also no statistical difference in terms of gender, preoperative CT score or previous surgery, nor was there any correlation with other parameters (like SNOT-20, olfaction and endoscopy score). Two weeks following FESS, a strong trend towards increased STT values (26.4±17.7 minutes, p = 0.051) and a decrease six months later (19.8±14.2 minutes, p = 0.16) were observed. Although other parameters like SNOT-20 scores, olfaction and endoscopy scores showed significant improvement, no correlation with the changes in STT was noticed. Conclusion: In CRS with or without nasal polyps, STT seems to be an inappropriate parameter for estimating the efficacy of FESS. The changes in STT do not correlate with other indicators for successful surgery like increased SNOT-20 or olfaction scores. STT was independent of other factors like gender, CT-score, previous surgery and polyp status. However, CRSwNP patients showed higher STT values.

Keywords: CRS, FESS, polyps, Saccharin Transit Time

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INTRODUCTION

Mucociliary clearance (MCC) plays an important role as a defence mechanism of the nasal mucosa. Bacterial

or viral pathogens can be transported to the pharynx by this mechanism. Two components must be taken into account, these being the consistency of the mucus and ciliary beat frequency. The determination of the saccharin transit time (STT) has been established as a simple means of evaluating MCC [1] in everyday practice. In healthy subjects, STT is considered normal if it falls in the range of between 7 to 15 minutes [2]. Some studies show an improvement in MCC after septal surgery [3] or irrigation therapy [2], while others do not [4]. Chronic rhinosinusitis (CRS) is a multi-factorial disease that can be divided into subgroups: without (CRSsNP) and with polyps (CRSwNP). The treatment can be either medical or surgical. The influence of CRS and the impact of sinus surgery on MCC are still not well analyzed. One former study [5] showed a significantly longer STT in CRS patients compared to control groups and a significant reduction of STT up to a year after surgery. The aim of this study was to investigate MCC in CRS patients with and without polyps, to describe postsurgical changes and to look for correlations with other parameters.

MATERIALS AND METHODS

This study was conducted at the Department of Otolaryngology, Head and Neck Surgery of the Johannes Gutenberg University, Mainz, Germany as a tertiary medical centre. In a prospective clinical study, patients of both genders and over 18 years of age, who were scheduled for FESS because of CRS, were included. Cases of primary and revision surgery were included. All patients had undergone unsuccessful conservative treatment prior to the operation. The diagnosis of CRS was established by the patient's history, nasal endoscopy and computed tomography (CT) scan of the paranasal sinuses according to the EPOS criteria [6]. All patients have signed an informed consent form prior to their participation in the trial.

Exclusion criteria were single-sided CRS, cystic fibrosis, immunodeficiency, primary cilia dysfunction and concomitant medication with drugs interacting with human cilia function.

Patients were examined prior to surgery, as well as two weeks following and six months following. To evaluate the nasal ciliary clearance, measurement of the STT was performed as described earlier [7, 8]. This method uses a small particle of saccharine that is placed unilaterally on the head of the inferior nasal turbinate. The time between placement and the patient first reporting the perception of sweetness is recorded. If more than 60 minutes elapsed without the patient indicating a sweet taste, the measurement was stopped and 60 minutes were recorded as the STT. Additionally, before and after surgery the sino-nasal outcome test (SNOT-20) was used to evaluate disease-specific quality of life [9]. This score comprises a list of 20 problems and patients are asked to rate each problem between 0 (no problem) and 5 (as bad as it can be) points. The entire score can reach values between 0 to 100 points. The German-adapted version was used in this trial [10]. The subjective severity of nasal disease (SSND) was also sought. According to the international guidelines, the patients were asked "How troublesome are your symptoms of rhinosinusitis?" and, using a visual analogue scale (VAS) 10 centimetres in length, they then had to mark the extent of their overall nasal condition with scores between 0 (representing "not troublesome") and 10 ("worst thinkable"). The SSND score was adapted to the 2012 EPOS guideline and the complaints could then be divided into mild, moderate or severe. Olfaction was evaluated before and after surgery by the 16-item Sniffin' Sticks identification test. This test consists of 16 odors that are stored in a pen-like device. After placing each pen under the patient's nose for one second, they must then choose one of four presented answers in a forced choice manner [11]. The endoscopy score before and after surgery was classified after rigid nasal endoscopic assessment based on three different scores: mucosal swelling (0=no swelling, 1=mild swelling, 2=severe swelling), mucosa color (0= pale, 1= red), secretion (0=normal, 1=watery, 2=mucoid, 3=purulent) and the appearance of polyps (0=absent, 1=present) for each side separately. The average of both sides was documented and the maximum possible score was seven. Finally, the Lund-Mackay CT score [12] was determined for each patient by reviewing the preoperative CT scan. After the surgery, all patients used nasal irrigation with saline at least twice a day. Two weeks after surgery, treatment with a topical nasal steroid (fluticasone furoate) once a day (27.5 µg) was continued for the entire study period.

STATISTICAL ANALYSIS

All analyses were performed using version 12.0 of the Statistical Package for the Social Sciences software system (SPSS Inc., Chicago, Illinois). The mean values are shown ± standard deviation. To evaluate changes in STT between different time points, the Wilcoxon signed-rank test was used. Influences of different parameters on STT preoperatively were evaluated using the Mann-Whitney U test. The level of significance was set at $p<0.05$. To test for correlations, ordinal scale relationships using Spearman's rank correlation coefficient were employed.

RESULTS

Thirty-seven patients were recruited; their mean age was 50.7 years. The gender distribution was 20 male and 17 female patients. Fourteen patients suffered from CRSsNP and 23 from CRSwNP. Twenty-one patients were sinus revision cases and 16 underwent primary sinus surgery (Table 1).

Alteration of STT

Before the operation, the mean STT was 20.3±15.7 minutes, 26.4±17.7 minutes two weeks following and 19.8±14.2 minutes six months following FESS. The increase in STT after two weeks was almost significant (p = 0.051). There was no statistical difference between the CRSwNP and CRSsNP group (p>0.16) (Table 2). The differences between the time points also showed no significance (p>0.1). Prior to surgery, there were no significant correlations between STT and other parameters in the whole CRS group (age, gender, SNOT-20, CT score). In the CRS ± polyps subgroups, STT before surgery in the CRSwNP group was 23.1 minutes and 15.6 minutes in CRSsNP patients, but this difference was not significant (p=0.28). Interestingly, STT showed a good correlation with SNOT-20 in the CRSsNP subgroup, but not in the CRSwNP subgroup (correlation coefficient 0.70, p=0.01), (Figure 1). The mean increase in STT two weeks after surgery was 6.01 ± 19.2 minutes, which was followed by a decrease of 6.5±23.8 minutes after six months. These changes showed no differences between the subgroups with or without polyps, low or high CT score, gender or previous surgery.

Table 1: Demographics of the study cohort

	Patient group
Total number	37
Female	17 (46%)
Male	20 (54%)
Age range	25–67 years
Mean age	50.7±11.2
Previous sinus operation	21 (57%)
Lund-Mackay-Score ≤ 12	13
Lund-Mackay-Score > 12	24
CRSsNP	14
CRSwNP	23
Mean STT	20.3±15.7

Abbreviations: STT: Sacharin Transtit Time, CRSsNP: chronic rhinosinusitis without polyps, CRSwNP: Chronic Rhinosinusitis with Polyps. Values are indicated ± standard deviation.

Table 2: STT in the subgroup of CRSsNP and CRSwNP patients at the different time points (mean values ± standard deviation)

Subgroup	CRSsNP	CRSwNP
Number of patients	14	23
STT prior sinus surgery	15.6±8.3	23.1±18.5
STT 2 weeks after sinus surgery	20.7±14.5	29.8±18.8
STT 6 months after sinus surgery	16.9±7.4	21.6±17.0

Abbreviations: STT: Sacharin Transtit Time, CRSsNP: Chronic Rhinosinusitis without Polyps, CRSwNP: Chronic Rhinosinusitis with Polyps

Development of other parameters

The mean SNOT-20 scores decreased significantly from the period prior to surgery (27.5±15.7) to the periods of two weeks (20.7±12.2, p<0.01) and six months after surgery (14.9±14.1, p < 0.01) (Figure 2A). The CRS subgroups with or without polyps showed similar significant results (data not shown). The SSND score decreased from 7.64±2.0, to 3.87±2.6, to 2.56±2.1 over time. These changes were all significant (0.0001 < p < 0.024) and this was true for both subgroups, with or without polyps. In the CRSsNP and CRSwNP subgroups, these values were also significantly reduced at all-time points, except for two weeks after surgery in the CRSsNP subgroup (Figure 2B). The Sniffin´ Sticks scores increased from 8.88±4.2, to 10.31±3.6 and to 10.83±3.4 six months after surgery. These findings were significant for the changes between the period prior to surgery and the results after six months (p=0.008). Concerning the polyp status, this was only true for the CRSwNP subgroup after six months (p=0.032) (Figure 2C). The endoscopy score of the overall group decreased from 3.19±1.2, to 2.43±1.4 and to 1.86±1.6; the differences reached significance after two weeks (p=0.018) and six months (p=0.03). With regard to the subgroups, this could only be confirmed for CRSwNP patients (Figure 2D).

Reasonable correlations were found for SNOT-20 and SSND-Scores at two weeks postoperative (correlation coefficient = 0.49, p=0.002) and the six-month postoperative assessment (correlation coefficient = 0.74, p<0.001), but not prior to surgery (correlation coefficient = 0.30, p = 0.09) (Figure 3).

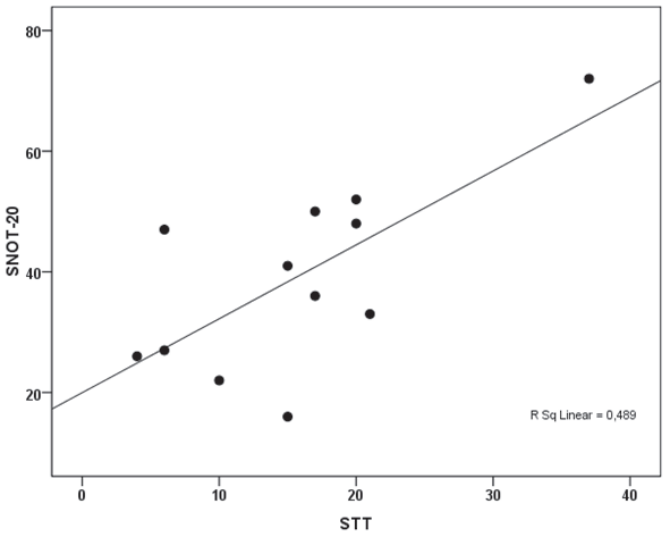

Figure 1: Correlation of saccharin transit time (STT) and SNOT-20 score before surgery in the CRSsNP-group.

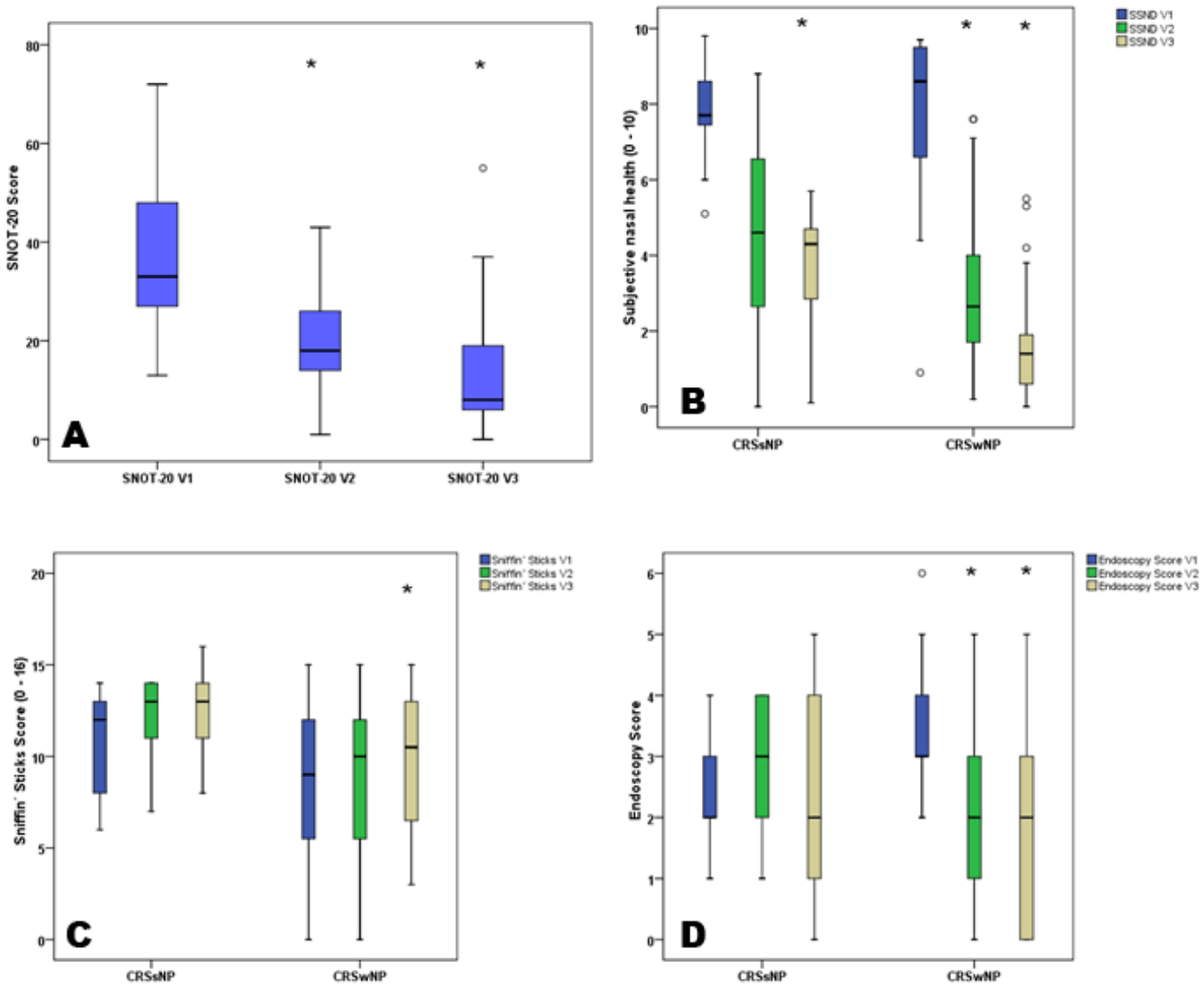

Figure 2: Box plots of the results of (A) SNOT-20 Scores (B) Scores of Severity of nasal disease (SSND) (C) Sniffin' Sticks Scores and (D) Endoscopy Score before surgery (V1), 2 weeks after surgery (V2) and 6 months after surgery (V3) in the whole group (n=37) or in patients with chronic rhinosinusitis without nasal polyps (CRSsNP) and with polyps (CRSwNP). The boxes include 75% of values, the median is indicated and outliers (○). Significant changes are indicated by "*".

DISCUSSION

Mucociliary clearance is an important factor in chronic nasal disease, or may even be a causative factor. The mucociliary clearance was assessed in our cohort by measuring STT. The mean STT in our cohort of patients with CRS was more than 15 minutes which is regarded as the maximum value in normal subjects [7]. Only 11 individuals in our study reached values of less than 15 minutes, indicating a dysfunction of MCC in the majority of patients with CRS. On may speculate that a reduced MCC might be causative or supports the development of CRS in individuals or the chronic inflammatory disease influences MCC by released cytokines.

We have only seen a trend towards higher preoperative STT values in CRSwNP patients in comparison to the CRSsNP subgroup. Sigh et al. described an increasing STT for more severe forms of CRS (single-sided versus bilateral and CRSsNP/CRSwNP [13]) and we have also seen maximum preoperative STT values of 40 minutes in the CRSsNP subgroup, whereas in the CRSwNP subgroup, four patients reached a value of 60 minutes.

The increased STT prior to operation was accompanied by a high impairment in the SNOT-20 score in the patients without polyps, indicating a close correlation between reduced MCC and subjective complaints in this subgroup.

Two weeks after surgery, we found a non-significant increase in STT in both subgroups (CRSsNP and CRSwNP), which is similar to the results of Gelardi et al. after four weeks in the group rinsing with saline after FESS [14]. This increase in STT could be the result of the acute surgical trauma. Six months after surgery, the

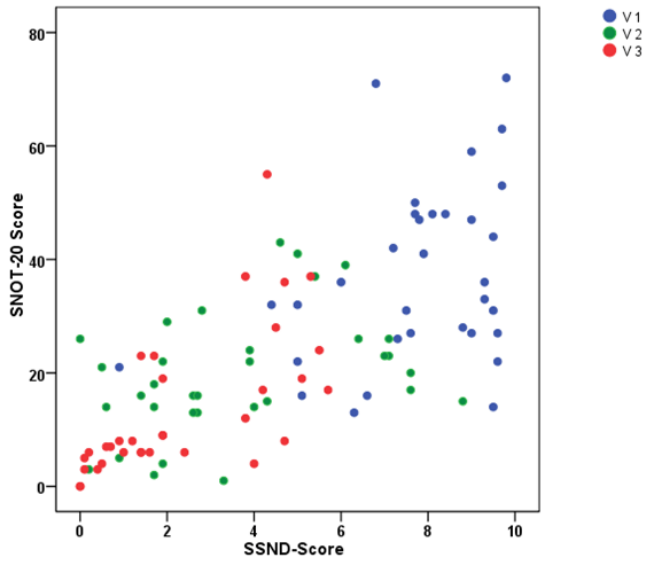

Figure 3: Correlation of SNOT-20 scores and the score of the "Severity of Nasal Disease" (SSND) before surgery (blue), 2 weeks after surgery (green) and 6 months after surgery (red).

patients in our cohort returned to their preoperative STT levels and it can be stated that neither surgery nor medical treatment with nasal topical steroid had a positive effect on STT. Maybe rinsing with sodium hyaluronate or using dexpanthenol spray after FESS might show better results as described in earlier publications [5, 14, 15].

If the activity of cilia is regarded, and not STT, other studies have found decreased cilia beat frequencies (CBF) in CRSsNP patients and could measure an increase of CBF after FESS to normal values after six months (from 7 to 11.5 Hz) [16]. In another study that investigated CBF and STT in patients with extensive CRS [17], an improvement of STT to 13.8 minutes was measured seven months after sinus surgery in those without recurrent disease, in comparison to those experiencing relapse (20.6 minutes). CBF, on the other hand, remained reduced (8.3 ± 1.2 Hz) compared to normal controls (9.5 ± 1.7 Hz). It is therefore unclear whether a positive effect of surgery in CRS is due to improved cilia activity or improved mucus (composition) drainage.

In our study, patients with polyps showed a trend towards prolonged STT values compared to patients with CRS without polyps; this is comparable to the results of Singh *et al.* [13], but in our study the changes between the time points did not differ between the subgroups. The statistically unchanged STT before, two weeks and six months after surgery was independent of other quality of life parameters, like SNOT-20, VAS or olfaction, which all showed significant improvements.

CONCLUSION

Although most parameters after functional sinus surgery (FESS) for chronic rhinosinusitis (CRS) showed improvement after two weeks or at least six months after surgery, saccharin transit time (STT) showed stable values over the entire study period after a non-significant increase at the two-week time point. Although the CRSwNP subgroup showed a trend towards longer STT at all time points, the changes reached no statistical significance. It is therefore doubtful whether STT is a reliable parameter for postsurgical follow-up after FESS.

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Author Contributions

Boris R. Haxel – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Niki Karaiskaki – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Patrick Boessert – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Kai Fruth – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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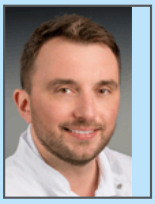

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