

Real-life study showing uncontrolled rhinosinusitis after sinus surgery in a tertiary referral centre

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Keywords

chronic rhinosinusitis; control; functional endoscopic sinus surgery treatment; nasal polyps; uncontrolled rhinitis.

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Abstract

Rationale: The European Position Paper on Sinusitis (EPOS) guidelines provide composite criteria to evaluate chronic rhinosinusitis (CRS) control, taking into consideration the severity of patients' symptoms, aspect of nasal mucosa and medical intake as parameters of CRS control.

Objectives: To study the degree of CRS control using novel EPOS control criteria at 3–5 years after a functional endoscopic sinus surgery (FESS) and correlate these data to symptoms scores.

Methods: Adult CRS patients ($n = 560$) who had undergone bilateral FESS for chronic inflammatory sinonasal disease 3–5 years prior to the study were included. Patients received a postal questionnaire asking for control items according to EPOS control criteria, visual analogue scale (VAS) scores for total and individual sinonasal symptoms, sinonasal outcome test (SNOT)-22 and Short Form (SF)-36 questionnaires. **Measurements and main results:** About 19.5% of CRS patients were well controlled, with 36.8% of patients being partly controlled and 43.7% uncontrolled. The levels of control corresponded to mean total VAS, SNOT-22 and SF-36 scores. Subgroup analysis revealed that female gender, aspirin intolerance and revision FESS were associated with higher prevalence of uncontrolled CRS, whereas allergy, asthma and smoking status did not alter the percentage of patients in each category of control. In 81 patients attending the outpatient clinic, nasal endoscopy changed classification in only four patients (4.9%).

Conclusions: Based on the novel EPOS control criteria, at least 40% of CRS patients are uncontrolled at 3–5 years after FESS. Therefore, better treatment strategies leading to higher disease control are warranted in CRS care.

Chronic rhinosinusitis (CRS) is defined as inflammation of the nose and the paranasal sinuses characterized by two or more symptoms, one of which should be either nasal blockage or nasal discharge in addition to facial pain/pressure

Abbreviations

APA, aspirin intolerance, polyposis and asthma triad; AR, allergic rhinitis; CRS, chronic rhinosinusitis; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; EPOS, European position paper on rhinosinusitis; FESS, endoscopic sinus surgery; PND, postnasal drip; SCUAD, severe upper airway disease; SF-36, Short Form (36) health survey; SNOT-22, sinonasal outcome test-22; VAS, visual analogue scale.

and/or reduction of smell, lasting for at least 12 weeks (1). The latter symptoms should be supported by endoscopic findings or computed tomography (CT) scan changes (1). Within the 2012 European Position Paper on Sinusitis (EPOS) document, clinicians are provided with evidence-based treatment algorithms for CRS. Treatment is advocated according to evidence-based guidelines, with adaptation of treatment according to the response to treatment. Control of disease is defined as a disease state in which the symptoms are not considered bothersome anymore to the patient (1). The 2012 EPOS expert committee proposed an assessment of clinical control of CRS (Table 1), following the concept of the validated asthma control test (2). The proposed CRS

control test takes into account the presence and severity of the four major sinonasal symptoms, sleep disturbance and/or fatigue, nasal endoscopic evaluation and need for oral medication. Based on the presence of none, one or more items of this list, patients are divided into those with well controlled, partly controlled and uncontrolled rhinosinusitis. So far, clinical studies validating this tool are lacking. In this retrospective study, we used the proposed 2012 EPOS criteria to divide patients into the three groups of control and also compared patients with (CRS_{NP}) and without nasal polyps (CRS_{NP}).

Symptoms associated with CRS can be alleviated with medical therapy and functional endoscopic sinus surgery (FESS). However, a considerable percentage of patients continue to suffer from CRS symptoms despite medical or surgical treatment. This group with so-called severe chronic upper airway disease (SCUAD) represents a therapeutic challenge (3, 4, 5), mainly related to the fact that the underlying pathophysiology with different endotypes are not well characterized. Several exogenous and endogenous factors may underlay the pathophysiology of SCUAD (6) and give rise to the variable degree of response to treatment.

This study aimed at applying the recently proposed 2012 EPOS criteria for control of CRS into a well-defined population of CRS patients that had undergone FESS between 3 and 5 years prior to the evaluation. Correlations between the degree of control of CRS and the current standards of evaluation of symptom control, that is visual analogue scale (VAS) scores for total and individual sinonasal symptoms, sinonasal outcome test (SNOT-22) scores and Short Form (SF)-36 questionnaire scores were made. Secondly, we aimed at evaluating the necessity of nasal endoscopy for defining control in CRS, as nasal endoscopy is not always available in non-ear–nose–throat (ENT) practice. To this extent, a subgroup of patients was evaluated for nasal endoscopic

abnormalities and evaluated for a shift in control category following nasal endoscopy.

Materials and methods

Study population

This observational study was conducted at the Department of Otorhinolaryngology of the University Hospitals of Leuven, Belgium, from September 2013 until February 2014. All patients with or without nasal polyps between 18 and 75 years of age who had undergone a bilateral FESS for bilateral inflammatory disease between January 2008 and December 2010 were sent a questionnaire.

Exclusion criteria were revision surgery between 2010 and 2013, a unilateral FESS, benign or malignant tumours, patients with a psychiatric, addictive or other disorder, which would compromise their ability to give truly informed consent and/or fill out the questionnaire, and patients with lack of knowledge of the Dutch language. Patients with cystic fibrosis, known immunodeficiencies, congenital mucociliary dysfunction, fungal balls, systemic vasculitis and granulomatous diseases were also excluded.

Diagnosis of CRS and indication of FESS

The diagnosis of CRS was made by ENT specialists at the University Hospitals Leuven, combining the presence of two or more sinonasal symptoms and consistent sinonasal endoscopic abnormalities. The indication for FESS was made by the authors (P. H. and M. J.) on the base of failure of second-line treatment (douching and nasal corticosteroids, with one or more courses of short-term or long-term oral corticosteroids and/or antibiotics), as recommended by the EPOS treatment algorithms.

Table 1 Proposed criteria for defining controlled, partly controlled and uncontrolled CRS, taken from the EPOS update 2012

Assessment of current clinical control of CRS (in the last month)			
Characteristic	Controlled (all of the following)	Partly controlled (at least 1)	Uncontrolled (≥ 3 features of partly controlled)
Nasal blockage	Not present or not bothersome	Present on most days of the week	
Rhinorrhoea/postnasal drip	Little and mucous	Mucopurulent on most days of the week	
Facial pain/headache	Not present or not bothersome	Present	
Loss of sense of smell	Not present or not bothersome	Present	
Sleep disturbance/fatigue	Not/slightly present	Present	
Nasal endoscopy	Healthy or almost healthy mucosa	Diseased mucosa	
Systemic medication needed to control disease	Not needed	A course of antibiotics/systemic corticosteroids in the last 3 months	Long-term antibiotics/systemic corticosteroids in the last month

The EPOS expert committee proposed to combine the severity of patients' symptoms, aspect of nasal mucosa and medical intake as parameters of control. The proposed CRS control test takes into account the presence and severity of the four major sinonasal symptoms, sleep disturbance and/or fatigue, nasal endoscopic evaluation and need for oral medication. Based on the presence of none, one or more items of this list, patients are divided into those with controlled, partly controlled and uncontrolled rhinosinusitis.

Questionnaires

The questionnaires were sent to the home address of all patients, involving the following specific items:

- 1 The symptoms proposed in the control evaluation diagram of EPOS (Table 1) were asked for, that is nasal obstruction, rhinorrhoea or postnasal drip, facial pain or headache and loss of sense of smell, and sleep disturbance or fatigue in the past month. Each of the symptoms was scored as being absent, not bothersome, or present. In addition, patients were asked whether systemic medication was needed to control the symptoms, including a course of antibiotics or corticosteroids in the last 3 months, or a need of long-term antibiotics or corticosteroids in the last month. Based on the scheme in the update on EPOS in 2012, CRS patients were defined as well, partly or not controlled (1).
- 2 The SNOT-22 questionnaire is a validated 22-item questionnaire, which is a disease-specific, health-related quality-of-life measure for rhinosinusitis (7). The SNOT-22 questionnaire is based on the SNOT-20 questionnaire containing 20 nasal, sinus and general items that are scored by the individual patient. In the SNOT-22 questionnaire, two additional items are measured, namely nasal blockage and sense of taste and smell.
- 3 VAS scores for total sinonasal as well as individual sinonasal symptoms were marked by the patients on a 10-cm scale with 0 meaning total absence of symptom and 10 being the worst thinkable severity. Patients were asked to score each individual symptom (global rhinosinusitis complaints, rhinorrhoea, sneezing, nasal obstruction, reduction in sense of smell, headache, postnasal drip, fatigue and facial pain and pressure) on a scale from 0 to 10. Finally, a total symptom score was assessed (8).
- 4 The 36-item Short Form (SF-36) reflects the perceived general health status. This is a health status measurement tool designed to be applied to all health conditions and to assess general health concepts, such as functional status and wellbeing (9). It consists of 36 items covering eight domains: physical functioning, role limitations due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems and mental health.
- 5 General questions were asked regarding inhalant allergies (documented by blood analysis or skin prick test), asthma, aspirin intolerance, smoking habits, medication use, number of sinus operations and occupation.

The study protocol was approved by the medical ethical committee of the University Hospitals of Leuven.

Doctor's clinical evaluation

The EPOS expert panel suggests to incorporate nasal endoscopic evaluation of the sinonasal mucosa into the criteria for defining control of CRS.

All patients who received a letter and accompanying questionnaire were invited for a clinical examination free of charge during the month of December 2012. Nasal endoscopy was

performed by M. T. and P. H., and the presence or absence of the following features was noted:

- oedema/mucosal obstruction, primarily in the middle meatus;
- mucopurulent discharge from the middle meatus; and
- nasal polyps: presence and grading according to Davos' score. Size of nasal polyps was scored from 0–3: 0 = no polyps, 1 = polyps posterior to the middle nasal turbinate, 2 = polyps inferior to the middle nasal turbinate, 3 = massive polyposis (1).

Statistical analysis

SPSS (IBM, Armonk, New York, US) software was used for statistical analysis. Descriptive statistics included frequencies and means and were used to calculate the percentage of patients with CRS who were well, partly or not controlled according to the EPOS definitions. VAS, SNOT-22 and SF-36 scores were analysed between three groups of patients (by disease control) by use of one-way ANOVA or between two groups of patients (patient characteristics) by use of Student's *t*-test. Proportion of patients was compared by Pearson's chi-squared test. A significance level of $P < 0.05$ was used.

Results

Study population

Of the 560 patients included in the study, 389 returned a filled questionnaire (69.0% response rate). Twenty patients were not able to respond to the questionnaire because the mailing address was incorrect, they did not speak Dutch or because they had passed away. After taking this into consideration, the response rate was 72%. Of the responders, 53.2% were men and the mean age was 47.3 years old (SD: 14.1 years). About 33.4% of patients had known allergy, 17.7% asthma, 4.1% aspirin intolerance and 15.4% were current smokers. About 29.0% of patients had two or more sinus surgeries, and 54.5% of all patients had a history of nasal polyps (Table 2). For all of these variables, except smoking, a significantly higher percentage was found in patients with a history of nasal polyps. Patients with a history of nasal polyps were also significantly older ($P < 0.05$).

Among patients who responded, 81 (20.8%) accepted the invitation for a voluntary outpatient visit where nasal endoscopy was performed by an ENT specialist. About 43.2% of these patients had signs of relapse on nasal endoscopy and 16.0% of all examined patients had recurrent nasal polyps.

Twenty-one patients were called in January 2016 and asked the EPOS control criteria to evaluate whether there was a response bias explaining the results. There were 10 men and 11 women. Six patients had a history of nasal polyps. The results will be discussed below.

Clinical characteristics of uncontrolled and partly controlled CRS at 3–5 years after FESS

Using the current EPOS control criteria for defining the level of control, 389 patients were divided into those with well

Table 2 Population characteristics

	Total (n = 389)	CRSsNP (n = 177, 45.5%)	CRSwNP (n = 212, 54.5%)	P-value
Age (mean ± SD)	47.3 ± 14.1	45.7 ± 15.0	49.3 ± 12.7	
Gender (% male)	53.2	42.5	66.1	<0.0001
Atopy (%)	33.4	28.8	39.0	0.034
Aspirin intolerance (%)	4.1	0.0	9.0	<0.0001
Asthma (%)	17.7	12.3	24.3	0.002
Smoking (%)	15.4	17.9	12.4	0.135
Revision FESS (%)	29.0	23.6	35.6	0.009

Of the 560 patients included in the study, 389 returned a filled questionnaire (69.0% response rate). The proportion of patients with CRSsNP and CRSwNP were compared by Pearson's chi-squared test.

controlled (76 patients, 19.5%), partly controlled (143 patients, 36.8%) and uncontrolled CRS (170 patients, 43.7%). Comparing CRSsNP and CRSwNP, similar percentages of well controlled, partly controlled and uncontrolled were found ($P = 0.787$, Fig. 1).

In the uncontrolled CRS group, blocked nose was reported by 146 patients (85.9%), followed by headache by 133 patients (78.2%), sleep disturbance by 128 patients (75.3%), with postnasal drip/secretions and smell disorder being reported by 90 patients (52.9%) and 85 patients (50.0%), respectively. There was a significant difference in control of CRS between men and women, with more women (90 women, 49.5%) than men (80 men, 38.6%) being uncontrolled ($P = 0.032$; Table 3). Aspirin intolerance is also associated with a significantly higher percentage of uncontrolled CRS ($P = 0.039$), which was not the case for asthma or allergy. Primary FESS was associated with a higher percentage of controlled patients than revision FESS ($P = 0.002$).

When comparing individual EPOS control criteria, the most frequent complaints in partly controlled patients were sleep disturbance (54 patients, 37.8%) and blocked nose (47 patients, 32.9%). There is a large difference in total medication use, ranging from 7.7% in partly controlled patients and reaching 58.8% in uncontrolled patients.

Association between control of CRS and VAS for total sinonasal symptoms, SNOT-22 and SF-36

Table 4 provides an overview of the total VAS, SNOT-22 and SF-36 scores in the three groups of control of CRS. Mean total VAS scores for global sinonasal symptoms, as well as SNOT-22 scores, increased significantly as level of control decreased ($P < 0.05$). In addition, mean SF-36 scores were significantly higher in patients with a better level of control ($P < 0.05$).

The individual mean VAS scores were compared between groups with different levels of control (Fig. 2A, B, Table 5).

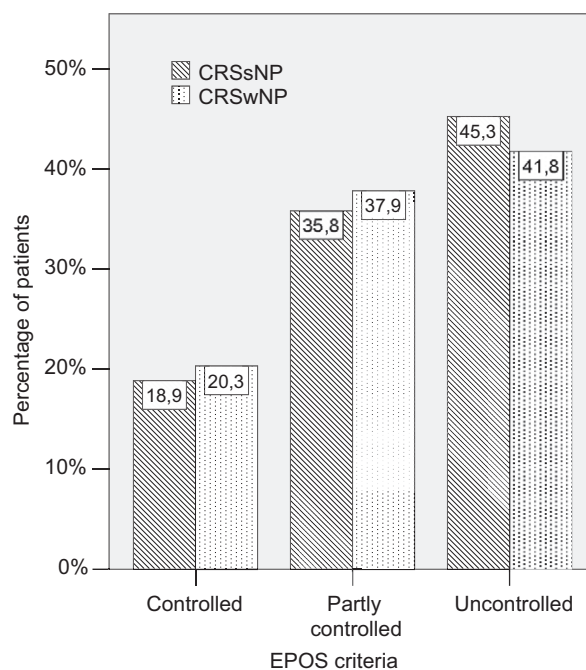


Figure 1 Percentage of patients with CRSsNP compared to CRSwNP stratified by disease control. All CRS patients were divided into two groups; patients without a history of nasal polyps (CRSsNP) and with history of nasal polyps (CRSwNP). They were categorized into three groups using the EPOS control criteria. As seen in this figure, there is a large difference in percentage of controlled and partly controlled patients but a smaller difference between partly controlled and uncontrolled patients.

We found that only uncontrolled patients had scores higher than 5 on a VAS scale of 10. Nasal obstruction had a mean of 5.9 cm and global sinonasal symptoms, rhinorrhoea and postnasal drip (PND) all scored 5.5 cm. Between all the different levels of control, there was a significant difference in mean individual VAS scores for all the factors ($P < 0.05$), except for sneezing. This difference was not significant between the well controlled and partly controlled group. The absence of nasal polyps significantly increases individual VAS scores. As seen in Fig. 2A, there is a significant increase ($P < 0.05$) in PND in CRSsNP patients going from a mean of 1.8 cm (SD 2.1 cm) in the well-controlled group to 4.3 cm (SD 2.9 cm) in the partly controlled group. Except for smell impairment (3.8 cm) and sneezing (3.3 cm), all means exceed 5 cm in uncontrolled patients without nasal polyps. In patients with a history of nasal polyps, smell impairment is more present and exceeds 5 cm in uncontrolled patients, reaching a mean of 5.4 cm. In these patients with a history of nasal polyps, the mean VAS for fatigue, headache, pain and sneezing was less than 5 cm in uncontrolled patients (Fig. 2B).

Nasal endoscopic evaluation in relation to degree of control of CRS

To evaluate the impact of nasal endoscopic findings in defining the level of control of CRS, 81 CRS patients attended

Table 3 The effect of different variables on EPOS level of control

Percentages	Controlled	Partly controlled	Uncontrolled
Mean age (years)	48	48	46
Women	16.5	34.1	49.5
Men	22.2	39.1	38.6
CRSsNP	18.9	35.8	45.3
CRSwNP	20.3	37.9	41.8
No allergy	19.7	39.0	41.3
Allergy	19.2	32.3	48.5
No aspirin intolerance	19.8	37.5	42.6
Aspirin intolerance	12.5	18.8	68.8
No asthma	20.9	36.6	42.5
Asthma	13.0	37.7	49.3
Nonsmoker	19.1	37.1	43.8
Smoker	21.7	35.0	43.3
Primary ESS	23.6	35.5	40.9
Revision ESS	9.7	39.8	50.4
Pearson's chi-square tests: <i>P</i> -value			
Gender	0.154	0.301	0.032
CRSsNP	0.716	0.683	0.491
Allergy	0.914	0.197	0.180
Aspirin intolerance	0.468	0.127	0.039
Asthma	0.134	0.861	0.303
Smoking	0.651	0.758	0.950
Revision ESS	0.002	0.423	0.086

The effect of different variables on EPOS level of control. There was a significant difference in control of CRS between men and women, with more women (90 women, 49.5%) than men (80 men, 38.6%) being uncontrolled ($P = 0.032$). Aspirin intolerance is also associated with a higher percentage of uncontrolled CRS ($P = 0.039$), which was not the case for asthma or allergy. Primary FESS was associated with a higher percentage of controlled patients than revision FESS ($P = 0.002$).

Table 4 Comparison of mean total VAS, SNOT-22 and SF-36 between patients stratified by disease control

	Controlled	Partly controlled	Uncontrolled	<i>P</i> -value
Total VAS	9.6 ± 7.9	22.8 ± 12.0*	45.2 ± 19.0*†	<0.0001
SNOT-22	10.2 ± 9.7	21.6 ± 12.4*	43.4 ± 19.9*†	<0.0001
SF-36	82.1 ± 14.3	76.5 ± 16.8	61.9 ± 19.6*†	<0.0001

VAS of total symptoms (sum of individual mean VAS scores), SNOT-22 and SF-36 were compared between controlled, partly controlled and uncontrolled CRS patients by ANOVA and Bonferroni's multiple comparison test.

* $P < 0.01$ compared to controlled.

† $P < 0.01$ compared to partly controlled. Data were presented as mean with standard deviation.

the outpatient visit including nasal endoscopy (Table 6). Based on the questionnaire without nasal endoscopy, 9.9% met the criteria of well controlled, 27.1% of partly controlled and 63.0% of uncontrolled CRS. When also taking into consideration the nasal endoscopy findings, only four of 81 patients changed into a different category, with 8.6%, 24.7%

and 66.7% meeting the criteria of well controlled, partly controlled and uncontrolled disease.

Telephonic survey and patients' view on control

Twenty-one patients were telephoned to eliminate the possibility of a response bias and to discard the hypothesis that unhappy patients were more likely to answer the questionnaire, explaining the high percentage of uncontrolled patients. Using the EPOS control criteria, they were divided into well controlled (4 patients, 19.1%), partly controlled (7 patients, 33.3%) and uncontrolled groups (10 patients, 47.6%). These results are similar to the patient group answering the written questionnaire. Therefore, we can conclude that the results from the written questionnaire are a good representation of the entire study population.

We also asked the patients whether they thought their sinusitis symptoms had disappeared after FESS completely, partly or not at all. Ten patients (47.6%) regarded themselves as well controlled, eight patients (38.1%) partly controlled and three patients (14.3%) uncontrolled. Comparison between patients without and with nasal polyps was difficult in this case due to the small patient group and majority having no nasal polyps (15 of 21 patients). However, we did notice that regardless the history of nasal polyps, patients found themselves to be more well controlled than when the EPOS control criteria were used. Three of six patients were found to be partly controlled, and three were uncontrolled. But two found themselves to be well controlled, three partly controlled and one uncontrolled.

Discussion

CRS is an underestimated common condition, affecting 11% of the total European population (1, 10). Although state-of-the-art guidelines provide evidence-based treatment algorithms, a significant portion of patients remain uncontrolled, despite prolonged medical treatment and one or more surgical interventions. The recently proposed criteria for defining control of CRS by the EPOS expert committee were designed following the concept of the asthma control test of the GINA (Global Initiative for Asthma) guidelines (11). However, these criteria should still be validated. Here, we evaluated the proposed EPOS criteria of control in a real-life academic setting and compared them not only to other questionnaires regarding CRS (SNOT-22 and VAS), but also to objective signs of CRS evaluated by nasal endoscopy. We also compared the results to overall quality of life using SF-36 questionnaires.

Our results show that 19.5% of patients meet the criteria of well controlled CRS after FESS, whereas 36.8% have partly controlled and 43.7% have uncontrolled CRS. This finding is surprising as the current perception of success of FESS is higher (1). The success rate seen as symptomatic improvement after FESS can be as high as 80% in patients with and without nasal polyps (12).

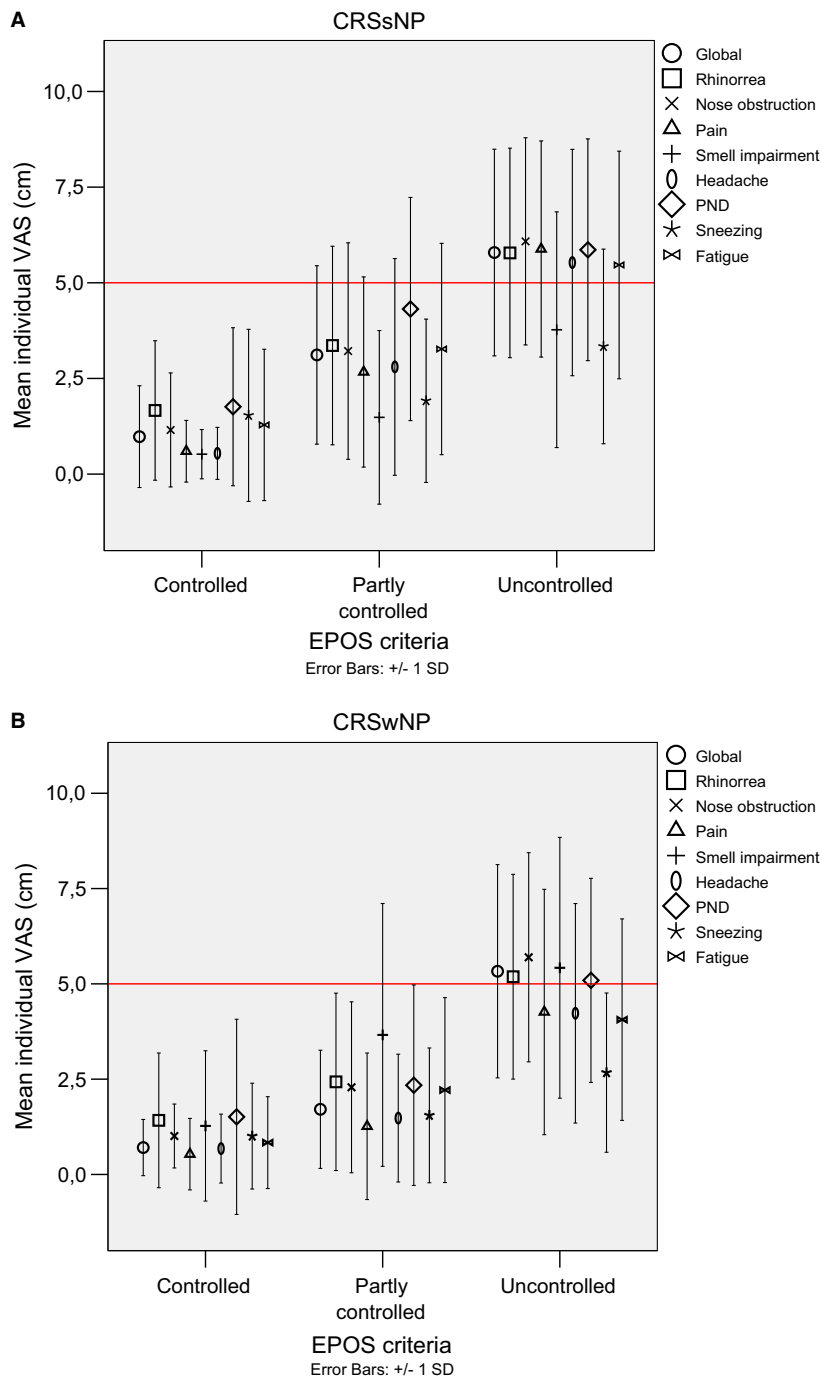


Figure 2 Mean VAS scores of CRS symptoms for CRS patients stratified by disease control. Mean VAS scores of CRS symptoms for patients without (A) a history of nasal polyps (CRSsNP) or with (B) a history of nasal polyps (CRSwNP) were compared for different levels of control according to the EPOS control criteria. Data were presented as mean with standard deviation. [Colour figure can be viewed at wileyonlinelibrary.com]

Only one other study has been carried out to evaluate the EPOS control criteria and it confirms our results as they also found a higher level of uncontrolled patients than expected (13). Although they had a smaller population group, there was a follow-up of 12 years after surgery. The group found

that 18 of 38 patients (47.4%) were uncontrolled according to the EPOS control criteria whereas 10 of 18 (26.3%) were well controlled and the same number were party controlled. In particular, the uncontrolled percentage is very similar to the results we found.

Several considerations need to be made when evaluating our data. Firstly, the patients included in our study had been treated in a tertiary referral centre for rhinologic diseases, causing a bias towards the more severe spectrum of disease. Secondly, belonging to the uncontrolled group does not exclude a beneficial effect of surgery. This observational study only allows the evaluation of the disease state after surgery without evaluation of the improvement of the disease

Table 5 Mean VAS scores of CRS symptoms for patients stratified by disease control

	Controlled	Partly controlled	Uncontrolled	P-value
Global	0.8 ± 1.1	2.4 ± 2.1*	5.5 ± 2.8*†	<0.0001
Rhinorrhoea	1.6 ± 1.8	2.9 ± 2.5*	5.5 ± 2.7*†	<0.0001
Nose obstruction	1.1 ± 1.2	2.7 ± 2.6*	5.9 ± 2.7*†	<0.0001
Pain	0.6 ± 0.9	2.0 ± 2.3*	5.1 ± 3.1*†	<0.0001
Smell impairment	0.9 ± 1.5	2.5 ± 3.1*	4.4 ± 3.3*†	<0.0001
Headache	0.6 ± 0.8	2.2 ± 2.4*	4.9 ± 3.0*†	<0.0001
PND	1.7 ± 2.3	3.4 ± 3.0*	5.5 ± 2.8*†	<0.0001
Sneezing	1.3 ± 1.9	1.7 ± 1.9	3.1 ± 2.4*†	<0.0001
Fatigue	1.1 ± 1.7	2.7 ± 2.6*	4.8 ± 2.9*†	<0.0001

Mean VAS scores of CRS symptoms were compared between controlled, partly controlled and uncontrolled CRS patients by ANOVA and Bonferroni's multiple comparison test.

* $P < 0.01$ compared to controlled.

† $P < 0.01$ compared to partly controlled.

Table 6 Effect of nasal endoscopy on degree of control of CRS when using the EPOS control criteria

EPOS control criteria	Without nasal endoscopy		With nasal endoscopy		P-value
	n	%	n	%	
Controlled	8	9.9	7	8.6	0.79
Partly controlled	22	27.1	20	24.7	0.72
Uncontrolled	51	63.0	54	66.7	0.62
Total	81	100	81	100	

Proportion of patients without and with nasal endoscopy were compared by Pearson's chi-squared test.

Table 7 Variables and their effect on mean total VAS, SNOT-22 and SF-36 scores (APA, allergy and smoking had no significant effect and were excluded from this table)

	Women	Men	CRSsNP	CRSwNP	No asthma	Asthma	Primary FESS	Revision FESS
Total VAS	33.6	26.8*	32.8	26.7*	29.2	34	27.9	35.2*
SNOT-22	32.9	25.4*	31.9	25.3*	28.4	31.5	26.8	34.2*
SF-36	65.9	75.9*	67.5	75.7*	72.3	66.2*	72.6	67.9*

Total VAS scores, SNOT-22 scores and SF-36 scores were compared for different variables (gender, history of nasal polyps, asthma and revision FESS) by use of Student's *t*-test (* $P < 0.05$).

by surgery. Thirdly, patients belonging to the uncontrolled group have a mean VAS score for global sinonasal symptoms of 5.5, which is not considered an excessively high score. In view of the latter argument, the authors feel that the EPOS control criteria are relatively strict in defining the group with uncontrolled disease.

Another concern we would like to highlight is that only one factor has to be present for a patient to be considered partly controlled. As mentioned above, in the partly controlled group, the most frequent symptom was sleep disturbance while this can be caused by other comorbidities. Therefore, we would propose to replace the EPOS criterion of sleep disturbance by 'sleep disturbance caused by CRS'. It is also not clear what the meaning of partly controlled CRS is. Do these patients need more treatment or is it simply a way of describing different CRS patient groups? In future studies more attention should be given to the perceived control of CRS by these patients to guide physicians in decision-making. It is also for this reason that we asked the patients who were telephoned how they perceived CRS control after FESS. Ten of 21 patients (47.6%) regarded themselves as having controlled CRS. This is more than double compared to using the EPOS control criteria (4 patients, 19.1%).

When comparing EPOS control criteria scores to other known tests, the three categories of control of CRS showed significantly different values of mean total and individual VAS scores, SNOT-22- and SF-36 scores. Previous studies showed improved SNOT-22 or other quality-of-life questionnaire scores after sinus surgery in a substantial number of patients. However, from these studies, it is not clear what the burden of uncontrolled disease is (14–16). Unfortunately, there are no other studies comparing the EPOS control score with SF-36, VAS scores and SNOT-22 results so far. These are needed to further validate our results.

Interestingly, multivariate analysis showed that history of nasal polyps had no significant effect on level of control of CRS, as the percentages of patients in the three categories of control did not differ between CRSsNP and CRSwNP. However, symptom profiles differed between the two disease phenotypes, with headache and sleep disturbance being more present in CRSsNP while loss of sense of smell was more bothersome in CRSwNP using VAS scores and EPOS control criteria (17),(18).

We took a closer look at patient characteristics and the difference between the different levels of control (Table 3). Surprisingly, there was a significant difference between men and women in the uncontrolled group ($P = 0.032$). The

reason for this finding however is unclear and in the literature we could not find an explanation for this. Primary FESS was associated with a higher percentage of controlled patients than revision FESS. We believe that patients who have to undergo multiple FESS procedures have CRS that is more difficult to control and therefore also score worse using the EPOS control criteria. Aspirin intolerance is associated with a lower level of control and this is also reported in the literature (1, 17, 18).

When taking a closer look at the total mean VAS-, SNOT-22- and SF-36 scores we found that history of nasal polyps had a significant effect, decreasing the first two scores and increasing the latter (Table 7). Thereby, we can conclude that patients with nasal polyps have significantly less symptoms after FESS and have a better perceived health status and quality of life. Also being of the male gender had a significantly positive effect on these scores ($P = 0.001$, $P = 0.0003$ and $P = 0.0001$, respectively) while revision FESS had the opposite effect (Table 7; $P = 0.001$, $P = 0.001$ and $P = 0.035$, respectively).

When looking at the mean individual VAS scores, it is clear that only patients in the uncontrolled group have VAS scores exceeding 5 cm. Interestingly, a VAS score of 5 or more had also been proposed an elegant tool for the evaluation of symptom control in allergic rhinitis (8). The group of patients with uncontrolled rhinitis and rhinosinusitis is nowadays of utmost importance as this patient population is the focus of attention in the design of novel treatment for improved health state.

We evaluated whether nasal endoscopic findings would have a major impact on defining the level of control in CRS patients. Interestingly, we did not discover a major shift in categories of CRS patients based on nasal endoscopic findings (Table 6). In 95.1% of cases, endoscopic investigation did not alter the category of control based on filling out the control questionnaire on the presence of symptoms and medication use. Based on the nasal endoscopic findings, only four of 81 patients (4.9%) moved to a different category of control. However, we have to take into consideration that the majority (63%) of patients who came for nasal endoscopic evaluation were defined as having uncontrolled disease based on history and medication use, with only 9.9% being well controlled. This shows that there was a clear selection bias in this group as more uncontrolled patients came for the endoscopic evaluation. Additional large-scale studies need to be performed for better evaluation of the role of nasal endoscopy in the evaluation of the level of control of CRS.

The strengths of this study relate to the innovative character of the study, the real-life nature of this observational study, the large number of patients and the monocentre nature of the study thereby minimizing differences in surgical therapy and postoperative care. Additional strengths are the comparisons made in this study, not only using the EPOS control criteria to determine level of control, but also comparing it to SNOT-22, VAS and SF-36 results. In addition, the clinical observation of the nasal mucosa by nasal

endoscopy was performed by only two ENT specialists, thereby minimizing interpersonal differences in scoring sino-nasal mucosa according to the EPOS control criteria. Our study also has limitations. One limitation is that patients were asked to answer the questionnaires at home, without the help of an expert. Another limitation is that this was an observational study and that patients were screened for eligibility for the study based on their medical records and that the evaluation of the effect of FESS is not possible. Some might see the monocentre nature of the study as a limitation as results of FESS could be better or worse than other centres, thereby over- or underestimating the rate of control. Lastly, psychometric validation (including internal consistency, responsiveness and known group differences) of the proposed EPOS control criteria is necessary to obtain validated metrics, which will be useful for future prospective studies. These studies are needed to validate our findings.

In conclusion, the percentage of partly and uncontrolled CRS, as defined by the 2012 EPOS control criteria, greatly overshadows the 19.5% of well-controlled CRS patients. We strongly believe that prospective studies are needed where patients are scored before and after surgery with a long enough follow-up. It may also be interesting to ask a larger group of patients how they feel about the status of control of CRS, as we found that many patients experienced a higher level of control after FESS than the results of the EPOS control criteria score suggest. If our results are confirmed, this explorative study highlights the need for better treatment strategies in CRS, as the majority of patients may continue to experience symptoms despite surgery.

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Authors' contributions

Julie van der Veen, Marieke Timmermans, Sven F. Seys and Peter W. Hellings designed the study, conducted the study, analysed the data and wrote the manuscript. Wytse J. Fokkens was leading the EPOS team defining criteria for control of CRS. Wytse J. Fokkens and Patrick Levie have contributed to the design of the study protocol. All patients with CRS had been diagnosed and surgically treated by Peter W. Hellings or Mark Jorissen.

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Conflict of interest

All authors stated that they have no conflict of interest in relation to this study and the results described in the manuscript.

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