Discordance of chronic rhinosinusitis disease control between EPOS guidelines and patient perspectives identifies utility of patient-rated control assessment*

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Abstract

Background: The objective of this study was to determine concordance of patient-reported chronic rhinosinusitis (CRS) disease control with CRS disease control assessed according to European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) criteria.

Methods: In 421 participants, CRS disease control was determined using EPOS criteria which include the burden of 5 symptoms measured on a binary scale, use of rescue medications in the prior 6 months and presence of diseased mucosa on nasal endoscopy. Symptom severity was also assessed using a visual analogue scale (VAS). Participants rated their CRS disease control as "controlled", "partly controlled" or "uncontrolled".

Results: Patient-reported and EPOS-based CRS disease control ratings agreed for 49.6% of participants. Amongst cases of disagreement, EPOS guidelines assessed worse CRS disease control relative to 92.9% of patients. Facial pain/pressure and impaired sense of smell distinctly associated with patient agreement with EPOS guidelines on having "uncontrolled" CRS. Higher VAS symptom scores were associated with worse patient-reported CRS disease control (i.e., agreeing with EPOS guidelines). Removal of the nasal endoscopy criterion improved agreement between patients' and EPOS control assessments, and replacement of this criterion with patient-reported control further aligned EPOS guidelines with patient perspectives.

Conclusions: EPOS guidelines regularly assess worse CRS control than assessed by patients. The lack of more gradated symptom severity criteria and inclusion of nasal endoscopy may contribute to discordance of EPOS guidelines with patient-reported CRS control. Replacement of nasal endoscopy findings with a measure of patient-reported CRS disease control better aligns EPOS CRS disease control guidelines with patients' perspectives.

Key words: chronic rhinosinusitis, disease control, patient-reported outcome measure, EPOS, nasal endoscopy

Introduction

Disease control serves as an important goal of treatment for chronic diseases for which no cure may be possible, such as chronic rhinosinusitis (CRS) [1]. The concept of control - which can be defined as the extent to which manifestations of a disease are within acceptable limits - reflects a global assessment of a disease, encompassing all the clinically significant ways in which it may impact a patient. However, defining control in concrete terms can be challenging and diverse criteria may be required to judge disease control for a multifaceted disease such as CRS [2]. For example, although the primary impact of CRS is a diminished quality of life (QOL), CRS may do so through not only its associated nasal symptoms, but also extranasal symptoms related to poor sleep quality and craniofacial discomfort [3-5], the frequency of acute exacerbations of CRS [6,7], as well as the exacerbation of lower airway disease [8-10]. Beyond the direct effects of symptoms felt by patients, active CRS also manifests itself objectively in the sinonasal cavity as mucosal inflammation and clinically through the need for rescue medications or endoscopic sinus surgery [11-13]. As a global reflection of disease status, any definition of CRS disease control would ideally incorporate the perspectives of the primary stakeholders - patients and

healthcare providers [14]. To date, the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) is the only major guideline to describe criteria for assessment of CRS disease control [2,15]. The EPOS CRS disease control guidelines were an important advancement in the comprehensive approach to CRS outcomes [15]. At present, it is unknown how well patients' perspectives of their CRS disease control are reflected by the EPOS CRS disease control criteria. If the EPOS guidelines for CRS disease control are to be used to measure patient outcomes, an understanding of how they align with patients' perspectives is necessary.
On its own, patient-reported CRS disease control has been shown to be a valid measure of CRS disease burden and QOL [16]. Moreover, patients' perspectives about their CRS control may vary significantly from healthcare providers' perspectives [17], so it cannot be taken for granted that the EPOS CRS disease control guidelines - which were developed from the opinions of healthcare providers - would necessarily be reflective of patients' perspectives of their own CRS disease control. Beyond gaining a greater understanding of the EPOS CRS disease control guidelines' utility as an outcome measure, identification of their concordance or discordance with patients' assessments of their own CRS disease control may inform the future evolution of the EPOS criteria [18]. The objective of this study was therefore to determine the extent of agreement between patient-reported CRS disease control and EPOS assessment of CRS disease control, and to identify the determinants of their discordance as a means for informing opportunities to align EPOS CRS disease control guidelines with patients' perceptions of their disease.

Materials and methods

Study participants

This was a prospective study of patients aged 18 or older meeting diagnostic criteria and consensus guidelines for CRS [19] who visited the Department of Otolaryngology – Head and Neck Surgery, University of Cincinnati College of Medicine and who provided informed consent to participate. Participants were recruited from patients who were seen in our rhinology clinic, which is open to the general population but also serves as a tertiary referral center. This study was approved by the University of Cincinnati Institutional Review Board. Patients with comorbid diagnoses of vasculitis, cystic fibrosis, sarcoidosis, and immunodeficiency were excluded. Patients with evidence of unilateral CRS were also excluded. To remove the confounding effect of recent endoscopic sinus surgery, patients who had a history of endoscopic sinus surgery within the prior 6 months were also excluded.

Study design

This was a cross-sectional study of patients meeting clinical consensus diagnostic criteria for CRS [19]. All data was collected at enrollment. Demographic information, including age and gender, was obtained. A smoker was defined as any participant who currently smoked or reported a history of tobacco use [20]. At enrollment, participants were assessed by the evaluating physician for a history of asthma, diagnosed based on consensus guidelines, as well as a history of allergy which was determined through formal skin or serological testing. Participants were interviewed to identify a history of previous sinus surgery or a history of aspirin sensitivity. The presence of nasal polyps and the history of prior sinus surgery were confirmed on nasal endoscopy. A modified Lund-Kennedy endoscopy score was also determined based on nasal endoscopy [21]. All participants completed a 22-item Sinonasal Outcome Test (SNOT-22) questionnaire [22]. Finally, all participants were also asked to rate their level of CRS disease control with the question "how controlled would you describe your chronic rhinosinusitis/sinus problems over the last month" and given response options of "controlled", "partly controlled" or "uncontrolled" - a scale which corresponds to how disease control is graded in the EPOS guidelines [2].

EPOS disease control assessment

EPOS guidelines recommend assessment of CRS disease control based on 7 criteria: the severity of 5 symptoms (nasal blockage, rhinorrhea/post-nasal drip, facial pain/pressure, impaired sense of smell, and sleep disturbance) reported using a binary descriptive scale with a recall period of over the prior 1 month, the need for rescue medication (antibiotics or oral corticosteroids) over the prior 6 months, and the presence of diseased mucosa on nasal endoscopy [2]. Consistent with EPOS CRS disease control guidelines, the severity of 5 individual CRS symptoms over the prior month was assessed in all study participants using descriptive binary scales for: nasal blockage ("not present or not bothersome" vs. "present on most days of the week"), rhinorrhea/postnasal drip ("little and mucous" vs. "mucopurulent on most days of the week"), facial pain/pressure ("not present or not bothersome" vs. "present on most days of the week", sense of smell ("normal or only slightly impaired" vs. "impaired"), and sleep disturbance or fatigue ("not present" vs. "present"). The severity of each of these 5 symptoms over the prior month was also assessed using a visual analogue scale (VAS), ranging in score from 0 (no burden at all) to 10 (worst possible burden), measured in 0.1 increments. The need for antibiotics and oral corticosteroids within the prior 6 months was assessed by directly querying the participant, while evidence of diseased mucosa was assessed using nasal endoscopy. Although the 2020 EPOS guidelines provide the option of using VAS symptom severity scores to evaluate symptom criteria for CRS disease control, how to do so remains an area of investigation [18] so we chose to use the descriptive binary symptom scales for assessing symptom criteria for CRS disease control. When none of these 7 criteria are met, patients are deemed to have controlled CRS. When one or two criteria are met, patients are deemed to have partly controlled

Table 1. Characteristics of study participants.

	All participants (N =421)
Demographics	
Age, mean in years, (SD)	50.1 (15.3)
Gender	
Male, % (N)	56.5% (238)
Female, % (N)	43.5% (183)
Smoking, % (N)	24.2% (102)
Comorbidities	
Aeroallergen hypersensitivity, % (N)	65.3% (275)
Asthma, % (N)	29.0% (122)
Aspirin sensitivity, % (N)	3.6% (15)
CRS characteristics	
Nasal polyps, % (N)	25.7% (108)
Previous endoscopic sinus surgery, % (N)	28.0% (118)
SNOT-22 score, mean (SD)	42.3 (23.4)
Lund-Kennedy endoscopy score, mean (SD)	3.4 (3.3)

CRS. When three or more criteria are met, patients are deemed to have uncontrolled CRS [2].

Statistical analysis

All statistics were performed using the statistical software R (R Development Core Team, 2008; R Foundation for Statistical Computing, Vienna, Austria) [23]. The sample size was determined based on the goal of having at least 80% power at significance level of 0.05 of identifying weak correlation between control ratings ($\rho \geq 0.3$) and identifying predictors of disparate control ratings (assuming balanced distribution and 2/3rds vs. 1/3rds probability of disagreement vs. agreement for each predictor) on logistic regression. Correlation was performed using Spearman's method, from which a correlation coefficient (ρ) and p-value were calculated. Agreement between CRS disease control ratings (EPOS criteria-based vs. patient-reported) was calculated as the percentage of exact matches. Concordance between CRS disease control ratings (as an ordinal variable) was calculated using a weighted Kappa (κ_w) [24], with weights calculated as the squared distance between differing ratings. Logistic regression was performed for binary dependent variables, from which a log odds ratio (OR) and p-value were determined.

Results

Participants

Baseline characteristics of the entire cohort of 421 participants are presented in Table 1. The mean SNOT-22 score for participants was 42.3 (standard deviation [SD]: 23.4, median: 41, range: 0 – 109) and the mean modified Lund-Kennedy endoscopy

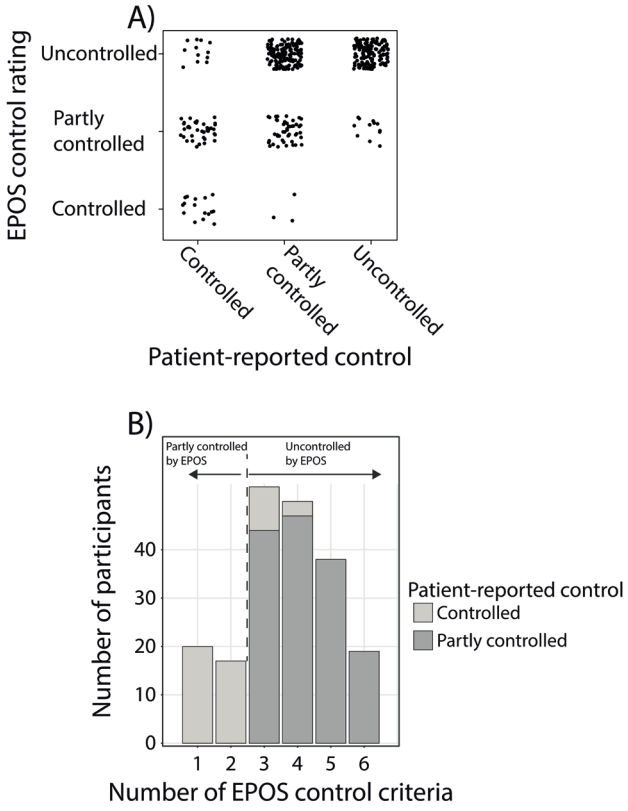

Figure 1. (A) Scatterplot of EPOS criteria-based vs. patient-reported CRS disease control. (B) Stacked barplot representing participants who rated their CRS as more controlled than based on EPOS criteria showing how many participants who met each number of EPOS control criteria and how they rated their own CRS disease control.

score was 3.4 (SD: 3.3, median: 2, range: 0 – 12). Using EPOS criteria, participants' CRS was deemed be controlled in 4.5% (N=19), partly controlled in 22.6% (N=95) and uncontrolled in 72.9% (N=307). In comparison, participants' rating of their own CRS was controlled in 15.4% (N=65), partly controlled in 46.8% (N=197) and uncontrolled in 37.8% (N=159).

Patients rate their CRS as better controlled than assessment by EPOS guidelines

To better understand the concordance between patient-rated CRS disease control and EPOS CRS disease control guidelines, we first plotted and compared how participants judged their CRS disease control in comparison to the assessment of EPOS guidelines (Figure 1A). We found that patient-rated CRS disease control and disease control determined by EPOS criteria were moderately correlated ($\rho = 0.50$, $p < 0.001$) and we found only 49.6% agreement (i.e., with 50.4% disagreement) between CRS disease control assessed in these two manners, with minimal to weak concordance [24] ($\kappa_w = 0.411$, $p<0.001$). Of the 50.4% (N=212) of participants who rated their CRS disease control differently than EPOS, 7.1% (N=15, 3.6% of the entire cohort)

Table 2. Associations of EPOS control symptom criteria with patients reporting controlled CRS in the setting of EPOS-assessed partly controlled CRS.

Descriptive EPOS control criteria	OR (95% CI)	P-value
Nasal blockage		
Not present or not bothersome	Ref	—
Present on most days	0.22 (0.07 – 0.67)	0.008
Rhinorrhea/postnasal drip		
Little and mucous	Ref	—
Mucopurulent on most days of the week	0.60 (0.10 – 3.47)	0.569
Facial pain/pressure		
Not present or not bothersome	Ref	—
Present on most days of the week	0.15 (0.02 – 1.32)	0.088
Sense of smell		
Normal or slightly impaired	Ref	—
Impaired	0.59 (0.14 – 2.53)	0.476
Sleep disturbance or fatigue		
Not present	Ref	—
Present	0.5 (0.19 – 1.30)	0.156
Needed rescue medications		
No	Ref	—
Yes	2.90 (0.80 – 10.52)	0.106
Diseased mucosa on nasal endoscopy		
No	Ref	—
Yes	3.07 (1.23 – 7.67)	0.016
Symptom VAS scores	**OR (95% CI)**	**P-value**
Nasal blockage	0.60 (0.46 – 0.79)	< 0.001
Rhinorrhea/postnasal drip	0.62 (0.50 – 0.78)	< 0.001
Facial pain/pressure	0.40 (0.23 – 0.69)	0.001
Sense of smell	0.82 (0.66 – 1.01)	0.059
Sleep disturbance or fatigue	0.72 (0.58 – 0.89)	0.002

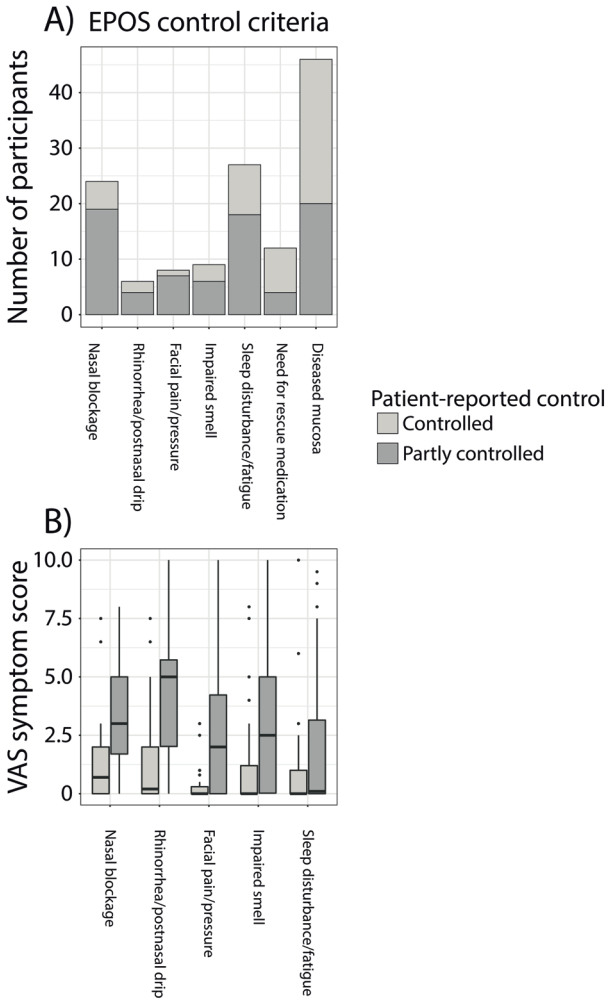

Figure 2. For participants determined to have partly controlled CRS based on EPOS guidelines and who rated their own control as partly controlled or controlled, (A) stacked barplot showing how many participants met each EPOS control criteria based on how participants judged their own CRS disease control and (B) box-and-whisker plot of visual analogue scale symptom scores stratified by how participants judged their own CRS disease control.

rated their CRS as less controlled compared to EPOS criteria while 92.9% (N=197, 46.8% of the entire cohort) rated their CRS as better controlled than as assessed by EPOS guidelines. Of the 307 participants whose CRS was deemed to be uncontrolled by EPOS criteria, 52.1% (N=160) of those participants rated their CRS as more controlled (92.5% [N=148] as partly controlled and 7.5% [N=12] as controlled) relative to the assessment of "uncontrolled" by EPOS criteria. In comparison, of the 95 participants whose CRS was deemed to be partly controlled by EPOS criteria, 38.9% (N=37) rated their CRS as controlled. These results suggest that EPOS CRS disease control guidelines may assess CRS disease control to be worse than patients' perceptions of their CRS disease control, most noticeably in the assessment of uncontrolled disease by the EPOS guidelines. Therefore, we subsequently focused our analyses on the participants who rated their CRS as more controlled compared to EPOS guidelines.

We next examined the number of the seven EPOS CRS control criteria that were met by patients who rated their CRS disease control to be better compared to the assessment of their control by EPOS guidelines (Figure 1B). Amongst the 37 participants who were judged by EPOS criteria as having partly controlled CRS but who rated themselves as having controlled CRS, 54.1% (N=20) met one EPOS control criterion (5% [N=1] nasal obstruction, 0% [N=0] rhinorrhea/post-nasal drip, 5% [N=1] decreased sense of smell, 0.0% [N=0] facial pain/pressure, 10% [N=2] sleep disturbance, 20% [N=4] needing rescue medications, and 60% [N=12] having diseased mucosa on nasal endoscopy) while

Table 3. Associations of EPOS control symptom criteria with patients reporting controlled or partly controlled CRS in the setting of EPOS-assessed uncontrolled CRS

Descriptive EPOS control criteria	OR (95% CI)	P-value
Nasal blockage		
Not present or not bothersome	Ref	—
Present on most days	0.36 (0.17 – 0.77)	0.009
Rhinorrhea/postnasal drip		
Little and mucous	Ref	—
Mucopurulent on most days of the week	0.63 (0.40 – 0.99)	0.046
Facial pain/pressure		
Not present or not bothersome	Ref	—
Present on most days of the week	0.40 (0.25 – 0.65)	< 0.001
Sense of smell		
Normal or slightly impaired	Ref	—
Impaired	0.39 (0.24 – 0.62)	< 0.001
Sleep disturbance or fatigue		
Not present	Ref	—
Present	0.84 (0.48 – 1.47)	0.540
Needed rescue medications		
No	Ref	—
Yes	0.97 (0.62 – 1.52)	0.890
Diseased mucosa on nasal endoscopy		
No	Ref	—
Yes	0.62 (0.36 – 1.06)	0.082
Symptom VAS scores	**OR (95% CI)**	**P-value**
Nasal blockage	0.82 (0.75 – 0.90)	< 0.001
Rhinorrhea/postnasal drip	0.87 (0.80 – 0.95)	0.001
Facial pain/pressure	0.86 (0.80 – 0.93)	< 0.001
Sense of smell	0.91 (0.85 – 0.97)	0.005
Sleep disturbance or fatigue	0.91 (0.85 – 0.98)	0.013

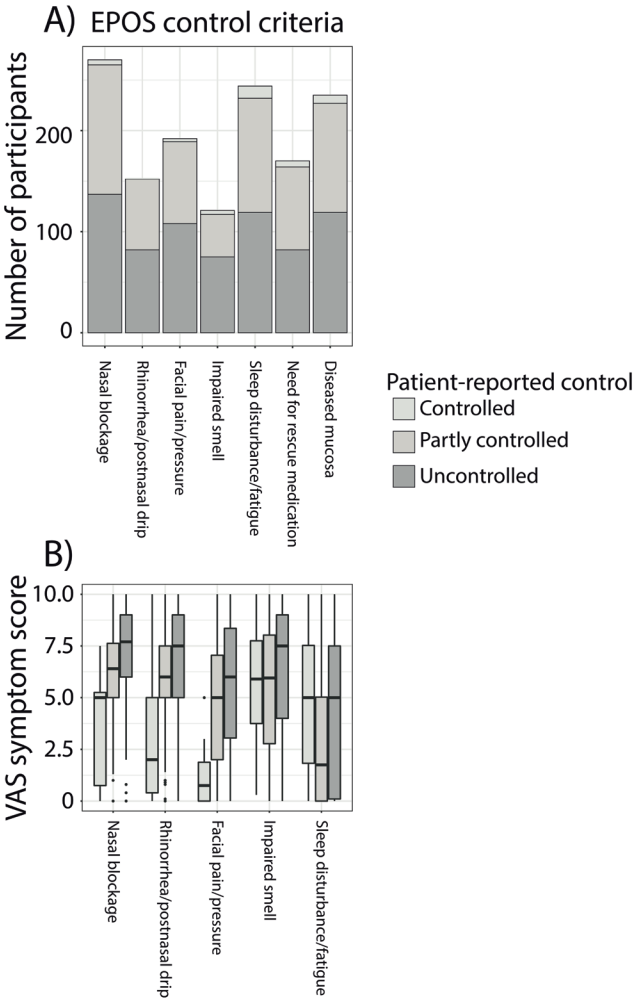

Figure 3. For participants determined to have uncontrolled CRS based on EPOS guidelines, (A) stacked barplot showing how many participants met each EPOS control criteria based on how participants judged their own CRS disease control and (B) box-and-whisker plot of visual analogue scale symptom scores stratified by how participants judged their own CRS disease control.

45.9% (N=17) met two EPOS control criteria. Amongst participants who were judged by EPOS guidelines to have uncontrolled CRS, 3.9% (N=12) of participants reported controlled CRS (75% [N=9] meeting three EPOS control criteria and 25% [N=3] meeting four EPOS control criteria) while 48.2% (N=148) of participants reported partly controlled CRS (29.7% [N=44] meeting three EPOS control criteria, 31.8% [N=47] meeting four EPOS control criteria, 25.7% [N=38] meeting five EPOS control criteria, and 12.8% [N=19] meeting six EPOS criteria).

Discordance between EPOS-based partly controlled CRS and patient-reported controlled CRS

We next focused on the participants whose CRS was assessed to be partly controlled by EPOS criteria, comparing those participants who rated their own CRS as controlled (N=37) to those participants who rated their own CRS as partly controlled (N=46). We first determined whether the presence of any specific EPOS control criteria would be associated with participants rating their CRS as being controlled despite the EPOS guideline-based assessment of partly controlled CRS (Figure 2A and Table 2, top). Participants who reported having nasal blockage that was "present on most days" were less likely (OR=0.22, 95%CI: 0.07 – 0.67, p=0.008) to report controlled CRS (Figure 2A and Table 2, top). In contrast and unexpectedly, however, the presence of diseased mucosa was associated with a higher likelihood (OR=3.07, 95%CI: 1.23 – 7.67, p=0.016) of participants reporting controlled CRS despite EPOS criteria indicating partly controlled CRS.

We next sought to determine whether VAS symptom severity scores were associated with how participants with partly controlled CRS according to EPOS guidelines rated their own control (Figure 2B and Table 2, bottom). We found that increasing severity of nasal blockage, rhinorrhea/postnasal drainage, facial pain/pressure and sleep disturbance were all associated with lower likelihood of reporting controlled CRS ($p \leq 0.002$ in all cases) while the association with severity of smell loss did not reach statistical significance ($p=0.059$). These results suggest that beyond the presence or absence of an uncontrolled symptom according to the descriptive binary EPOS symptom scale (e.g. nasal blockage that is "not present or not bothersome" vs. "present on most days"), the quantitative severities of symptoms may impact how patients view their CRS in relation to controlled or partly controlled disease.

Discordance between EPOS-assessed uncontrolled CRS and patient-reported CRS control

We next focused on the patients who were judged by EPOS guidelines to have uncontrolled CRS (N=307) and of whom 3.9% (N=12) reported controlled CRS, 48.2% (N=148) reported partly controlled CRS and 47.9% (N=147) reported uncontrolled CRS. We sought to identify whether the presence of any of the EPOS CRS control criteria would be associated with participants rating their CRS as more controlled than the EPOS-based assessment of uncontrolled CRS (Figure 3A and Table 3, top). Participants were less likely to report their CRS as more controlled (i.e. controlled or partly controlled) than the EPOS-based assessment of uncontrolled CRS if they reported having facial pain that was "present on most days of the week" (OR=0.40, 95%CI: 0.25 – 0.65, $p<0.001$), a sense of smell that was "impaired" (OR=0.39, 95%CI: 0.24 – 0.62, $p<0.001$) as well as nasal blockage that was "present on most days" (OR=0.36, 95%CI: 0.17 – 0.77, $p=0.009$) and rhinorrhea/postnasal drip that was "mucopurulent on most days of the week" (OR=0.63, 95%CI: 0.40 – 0.99, $p=0.046$). We next investigated VAS symptom scores (Figure 3B and Table 3, bottom) and found that greater severity of nasal blockage, rhinorrhea/postnasal drip, facial pain/pressure, decreased smell and sleep disturbance were all associated with lower likelihood of participants reporting their CRS to be more controlled than the EPOS-based assessment of uncontrolled CRS ($p \leq 0.013$ in all cases).

Nasal endoscopy versus patient-rated control as a criterion in the EPOS CRS disease control guidelines

Because previous study has suggested that the inclusion of nasal endoscopy findings may not be necessary in the assessment of CRS disease control [25] and the 2020 EPOS guidelines also do not universally require nasal endoscopy as a criterion for CRS disease control [2], as well as our own findings that EPOS guidelines under-estimate CRS disease control compared to patients' perspectives, we next studied the role and necessity of nasal endoscopy findings in the determination of CRS disease control. First, we found that nasal endoscopy findings were a necessary determinant of the EPOS guideline-based CRS disease control rating in 14.5% of participants. In other words, 14.5% of participants' CRS disease control rating based on EPOS guidelines would change by excluding nasal endoscopy from EPOS CRS disease control criteria. However, excluding nasal endoscopy findings from the EPOS CRS disease control criteria improved the degree of agreement between patient-rated control and EPOS-based control ratings from 49.6% to 55.1% (with κ_w significantly improving from 0.411 to 0.509, $p=0.017$).

We next explored how EPOS-based control ratings would change if nasal endoscopy findings were replaced by a measure of patient-reported control. Specifically, we considered a patient's CRS disease control rating of "controlled" to contribute 0 criteria towards uncontrolled disease, "partly controlled" to contribute 0.5 criteria and "uncontrolled" to contribute 1 criterion. Like the standard EPOS CRS disease control guidelines, we then considered "controlled" disease to be determined by having 0 control criteria met, "partly controlled" CRS to be determined by having >0 but < 3 control criteria met and "uncontrolled" CRS to be determined by having ≥3 control criteria met. This modified EPOS control criteria expectedly led to significant improvement in the degree of agreement between patient-rated control and criteria-based control ratings from 49.6% to 61.0% (with κ_w significantly improving from 0.411 to 0.566, $p<0.001$).

Discussion

Criteria for the assessment of CRS disease control described in the 2012 EPOS guidelines represented a major advancement in establishing comprehensive goals of treatment for CRS [15]. However, without an understanding of how EPOS CRS disease control guidelines align with patients' perspectives of their own CRS disease control, application of these control criteria to assess patient outcomes - and to tailor treatments based on them - is limited. In this study, we found that EPOS disease control guidelines generally underestimate the degree of CRS disease control that patients perceive, with approximately half of our study participants reporting their CRS disease control to be better than what EPOS guidelines specified while less than 5% of participants felt that their CRS was less controlled than what EPOS guidelines specified. We found that the determinants of patients' perceptions of controlled vs. partly controlled CRS and partly controlled CRS vs. uncontrolled CRS were dominated by different symptoms although patients' perceptions of worsening CRS disease control at all levels were significantly associated with the quantitative severities of symptoms that patients were experiencing. Finally, we found that the criterion of diseased mucosa on nasal endoscopy is a source of discordance between

EPOS guidelines and patients' perceptions of their own CRS disease control but that replacement of the nasal endoscopy criterion with an explicit measure of patient-reported CRS disease control may be one means of significantly improving the agreement between patients' perceptions of their CRS control and EPOS CRS disease control guidelines.

Previous work has shown that the extent of CRS disease control judged by EPOS criteria is associated with, and a reflection of, disease-specific QOL [18,25,26]. Independently, patient-reported CRS disease control has also been shown to be a valid, reliable and responsive measure of the QOL burden experienced by CRS patients [16]. Moreover, patient-reported CRS disease control has been shown to be reflective of not only disease-specific [27] and general health-related [28] QOL but also downstream consequences of CRS such as productivity loss [29]. To date, however, the agreement between patient-reported CRS disease control and EPOS CRS disease control guidelines has not been studied.

Our results very interestingly showed that EPOS CRS disease control guidelines almost never over-estimate patient-reported CRS disease control. While approximately half of CRS patients may agree with the assessment of CRS disease control determined by EPOS criteria, approximately half of CRS patients viewed their CRS to be more controlled compared to the assessment of the EPOS guidelines. These findings are important in not only showing such a stark discordance but also the direction of the discordance. That most participants, who disagreed with the EPOS criteria-based assessment of their CRS, rated their CRS as more controlled elicits two interpretations. First, and most conspicuously - the EPOS disease control criteria are more aggressive in identifying uncontrolled CRS compared to how patients judge their own CRS disease control. This is expected given that EPOS criteria were developed using healthcare providers' perspectives on CRS disease control, which include factors such as use of rescue medication (antibiotics and systemic corticosteroids) and nasal endoscopy findings that patients do not consider in their judgement of CRS disease control [17]. Second, our results may be interpreted as indicating that the EPOS CRS control criteria are - for the most part - fully comprehensive in capturing all of the CRS disease manifestations that patients may consider in judging their own CRS control. In other words, very few patients (less than 5%, at most) may have considered factors extrinsic to the EPOS criteria in judging their CRS to be less controlled than the EPOS guidelines' determination.

Our results also indicated that specific symptoms and overall quantitative symptom severity act as dominant determinants of discordance between different levels of patient-reported CRS disease control and the algorithmic determination of CRS disease control based on the seven, binary EPOS criteria. That we found facial pain/pressure and impaired sense of smell to be important in patients' disagreement with EPOS guidelines between partly controlled and uncontrolled CRS is consistent with prior studies of CRS-specific patient reported outcome measures that have shown craniofacial and smell loss items to be most informative at higher disease severities [30,31]. Our finding that the magnitude of symptom severities is also associated with discordance between patients' perceptions of their CRS control and EPOS guidelines raises the interesting question of whether the EPOS control criteria should have a more quantitative categorization of patients' symptom severities rather than the current binary options. Although VAS symptom severity scores were introduced in the 2020 EPOS guidelines as one means of judging symptom-based control criteria, these VAS are nevertheless recommended to be interpreted in a binary fashion as either above or below a threshold value [2], which we have recently calculated to be 3.5 out of 10 [18]. However, it is possible that a more gradated accounting of symptom severities in the determination of CRS control may have better aligned EPOS guidelines with patient-reported control. Finally, our results also indicate that nasal endoscopy findings in the EPOS CRS disease control criteria represents one source of discordance between EPOS guidelines and patient-reported CRS disease control. The role of nasal endoscopy findings or objective burden of disease in assessing CRS disease control has been controversial, with previous studies both identifying it [32] and excluding it [17] as a determinant of healthcare providers' perceptions of their patients' CRS control. Moreover, there is conflicting evidence as to whether endoscopic findings are generally reflective or predictive of any meaningful CRS outcomes or goals of treatment, such as QOL [33-36]. The EPOS guidelines have even suggested the non-critical nature of this control criterion by recommending that nasal endoscopy findings be used "when available" [2,15]. Although it follows naturally that incorporation of patient-reported CRS control into the EPOS control guidelines would lead to greater agreement with patients' perceptions of their own CRS control, we show that replacement of nasal endoscopy findings - a potentially unnecessary criterion for CRS control - with a measure of patient-reported CRS control provides one means to significantly improve alignment of the EPOS disease control criteria with patients' perceptions of their disease while still incorporating the perspectives of healthcare providers, e.g. through inclusion of rescue medication usage or the number and breadth of symptoms assessed.

Conclusions

Our study should be interpreted within the constraints of its limitations. Although our study is monocentric in nature, including patients from primarily one geographic location, we believe that our study has revealed novel insights that will aid in the interpretation of EPOS CRS disease control guidelines with

respect to patient outcomes and inform strategies developing greater alignment between the EPOS CRS disease control guidelines and patients' perspectives. We nevertheless hope that this study will serve to motivate future confirmatory studies, as well as studies of this topic in general, at other centers and geographic locales. It is also possible that the length of time that the patient has been affected by CRS may influence how they judge their CRS disease control. However, this may reflect even more reason why inclusion of patients' perspectives of their control could be important in a global measure of CRS disease control, such as the EPOS guidelines, as it accounts for how acceptable the current CRS disease state is for the patient and would therefore directly inform treatment decisions for this patient-centric disease.

Authorship contribution

ARS: concept of study, collection of data, analysis of results, write up of manuscript, critical review of all contents; KWS: collection of data, write up of manuscript, critical review of all contents; KMP: concept of study, collection of data, analysis of results, write up of manuscript, critical review of all contents.

Conflict of interest

The authors declare that there are no conflicts of interests regarding the publication of this paper.

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References

1. Sedaghat A, Hopkins C. Chronic rhinosinusitis disease control as a metric for guiding treatment. Rhinology 2020; 58:193.
2. Fokkens WJ, Lund VJ, Hopkins C, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology Suppl 2020; 58:1-464.
3. Hoehle LP, Phillips KM, Bergmark RW, Caradonna DS, Gray ST, Sedaghat AR. Symptoms of chronic rhinosinusitis differentially impact general health-related quality of life. Rhinology 2016; 54:316-322.
4. Speth MM, Hoehle LP, Phillips KM, Caradonna DS, Gray ST, Sedaghat AR. Changes in chronic rhinosinusitis symptoms differentially associate with improvement in general health-related quality of life. Ann Allergy Asthma Immunol 2018; 121:195-199.
5. Orb Q, Orlandi RR, Alt JA. Sleep dysfunction and its association to chronic rhinosinusitis: Updated review. Laryngoscope Investig Otolaryngol 2017; 2:46-52.
6. Phillips KM, Hoehle LP, Bergmark RW, Caradonna DS, Gray ST, Sedaghat AR. Acute Exacerbations Mediate Quality of Life Impairment in Chronic Rhinosinusitis. J Allergy Clin Immunol Pract 2017; 5:422-426.
7. Kuiper JR, Hirsch AG, Bandeen-Roche Ket al. Prevalence, severity, and risk factors for acute exacerbations of nasal and sinus symptoms by chronic rhinosinusitis status. Allergy 2018; 73:1244-1253.
8. Phillips KM, Talat R, Caradonna DS, Gray ST, Sedaghat AR. Quality of life impairment due to chronic rhinosinusitis in asthmatics is mediated by asthma control. Rhinology. 2019;57(6):430-435.
9. Jarvis D, Newson R, Lotvall Jet al. Asthma in adults and its association with chronic rhinosinusitis: the GA2LEN survey in Europe. Allergy 2012; 67:91-98.
10. Kariyawasam HH, Rotiroti G. Allergic rhinitis, chronic rhinosinusitis and asthma: unravelling a complex relationship. Curr Opin Otolaryngol Head Neck Surg 2013; 21:79-86.
11. Hopkins C, Hettige R, Soni-Jaiswal Aet al. CHronic Rhinosinusitis Outcome MEasures (CHROME), developing a core outcome set for trials of interventions in chronic rhinosinusitis. Rhinology 2018; 56:22-32.
12. Ranford D, Hopkins C. Safety review of current systemic treatments for severe chronic rhinosinusitis with nasal polyps and future directions. Expert Opin Drug Saf 2021; 20:1177-1189.
13. Kennedy JL, Borish L. Chronic rhinosinusitis and antibiotics: The good, the bad, and the ugly. Am J Rhinol Allergy 2013; 27:467-472.
14. Hunter C, Fitzpatrick R, Jenkinson Cet al. Perspectives from health, social care and policy stakeholders on the value of a single self-report outcome measure across long-term conditions: a qualitative study. BMJ Open 2015; 5:e006986.
15. Fokkens WJ, Lund VJ, Mullol Jet al. European Position Paper on Rhinosinusitis and Nasal Polyps 2012. Rhinology Suppl 2012; (23):298.
16. Phillips KM, Houssein FA, Singerman K, Boeckermann LM, Sedaghat AR. Patient-reported chronic rhinosinusitis disease control is a valid measure of disease burden. Rhinology 2021.59:(6),545-551.
17. Sedaghat AR, Hoehle LP, Gray ST. Chronic rhinosinusitis control from the patient and physician perspectives. Laryngoscope Investig Otolaryngol 2018; 3:419-433.
18. Phillips KM, Singerman KW, Sedaghat AR. Individual symptom visual analogue scale severity scores for determining EPOS guideline-based chronic rhinosinusitis disease control. Rhinology 2022.60:3,229-235.
19. 1Rosenfeld RM, Piccirillo JF, Chandrasekhar SSet al. Clinical practice guideline (update): adult sinusitis. Otolaryngol Head Neck Surg 2015; 152:S39.
20. Hoehle LP, Phillips KM, Caradonna DS, Gray ST, Sedaghat AR. A contemporary analysis of clinical and demographic factors of chronic rhinosinusitis patients and their association with disease severity. Ir J Med Sci 2018; 187:215-221.
21. Psaltis AJ, Li G, Vaezeafshar R, Cho KS, Hwang PH. Modification of the Lund-Kennedy endoscopic scoring system improves its reliability and correlation with patient-reported outcome measures. Laryngoscope 2014; 124:2216-2223.
22. Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. Clin Otolaryngol. 2009; 34:447-454.
23. R Development Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing, 2011.
24. McHugh ML. Interrater reliability: the kappa statistic. Biochem Med (Zagreb) 2012; 22:276-282.
25. van der Veen J, Seys SF, Timmermans Met al. Real-life study showing uncontrolled rhinosinusitis after sinus surgery in a tertiary referral centre. Allergy 2017; 72:282-290.
26. Doulaptsi M, Prokopakis E, Seys S, Pugin B, Steelant B, Hellings P. Visual analogue scale for sino-nasal symptoms severity correlates with sino-nasal outcome test 22: paving the way for a simple outcome tool of CRS burden. Clin Transl Allergy 2018; 8:32.
27. Gray ST, Phillips KM, Hoehle LP, Caradonna DS, Sedaghat AR. The 22-item Sino-Nasal Outcome Test accurately reflects patient-reported control of chronic rhinosinusitis symptomatology. Int Forum Allergy Rhinol 2017; 7:945-951.
28. Gray ST, Hoehle LP, Phillips KM, Caradonna DS, Sedaghat AR. Patient-reported control of chronic rhinosinusitis symptoms is positively associated with general health-related quality of life. Clin Otolaryngol 2017; 42:1161-1166.
29. Campbell AP, Hoehle LP, Phillips KM, Caradonna DS, Gray ST, Sedaghat AR. Symptom control in chronic rhinosinusitis is an independent predictor of productivity loss. Eur Ann Otorhinolaryngol Head Neck Dis 2018. 135(4):237-241.
30. Liu DT, Philips KM, Speth MM, Besser G, Mueller CA, Sedaghat AR. Item Response

Theory for Psychometric Properties of the SNOT-22 (22-Item Sinonasal Outcome Test). Otolaryngol Head Neck Surg 2021:1945998211018383.
31. Liu DT, Phillips KM, Speth MM, Besser G, Mueller CA, Sedaghat AR. Exploring possibilities for shortening the 22-item Sino-Nasal Outcome Test (SNOT-22) using item response theory. Int Forum Allergy Rhinol 2022; 12:191-199.
32. Snidvongs K, Heller GZ, Sacks R, Harvey RJ. Validity of European position paper on rhinosinusitis disease control assessment and modifications in chronic rhinosinusitis. Otolaryngol Head Neck Surg 2014; 150:479-486.
33. Epperson MV, Phillips KM, Caradonna DS, Gray ST, Sedaghat AR. Predictors of efficacy for combination oral and topical corticosteroids to treat patients with chronic rhinosinusitis with nasal polyps. Int Forum Allergy Rhinol 2019. 9(12):1436-1442.
34. Soler ZM, Colman S, Velez FF, Schlosser RJ. Exhalation delivery system with fluticasone improves quality of life and health status: pooled analysis of phase 3 trials NAVIGATE I and II. Int Forum Allergy Rhinol 2020; 10:848-855.
35. Speth MM, Gaudin RA, Hoehle LPet al. Reciprocal Predictive Accuracy of Sinonasal Symptom Severity, Nasal Endoscopy, and Frequency of Past Chronic Rhinosinusitis Exacerbations. Otolaryngol Head Neck Surg 2018; 159:766-773.
36. Jeong SS, Chen T, Nguyen SA, Edwards TS, Schlosser RJ. Correlation of polyp grading scales with patient symptom scores and olfaction in chronic rhinosinusitis: a systematic review and meta-analysis. Rhinology 2022. 60(5); 322-334.

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