



Association of severity of chronic rhinosinusitis with degree of comorbid asthma control

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ARTICLE INFO

Article history:

Received for publication July 2, 2016.

Received in revised form August 12, 2016.

Accepted for publication September 23, 2016.

ABSTRACT

Background: Comorbid chronic rhinosinusitis (CRS) is associated with worse asthma control. However, no study has investigated whether CRS severity affects the degree of asthma control.

Objective: To determine the effect size of an association between CRS severity and asthma control.

Methods: A pilot study with a prospective cross-sectional design. Adult patients with CRS and asthma were recruited. CRS severity was measured using the 22-item Sinonasal Outcomes Test (SNOT-22), and asthma control was measured using the Asthma Control Test (ACT). Poor asthma control was defined as an ACT score of 19 or less. In addition to age and sex, we also assessed the participants' history of smoking, aeroallergen hypersensitivity, the presence of polyps, and current use of a corticosteroid-containing asthma inhaler. The association between SNOT-22 and ACT was assessed using univariate and multivariable linear regression.

Results: A total of 40 patients were recruited. The mean (SD) SNOT-22 score was 43.6 (23.6), and the mean (SD) ACT score was 20.6 (4.8). We found that the SNOT-22 score was associated with the ACT score (adjusted $\beta = -0.07$; 95% confidence interval [CI], -0.13 to -0.02 ; $P = .02$) and with having poor asthma control (adjusted odds ratio, 1.06; 95% CI, 1.01–1.11; $P = .02$). A SNOT-22 cutoff score of 45 or higher had the greatest association with uncontrolled asthma (adjusted odds ratio, 14.96; 95% CI, 1.93–115.89; $P = .01$).

Conclusion: CRS severity is negatively associated with asthma control in patients with asthma and CRS. On the basis of this pilot study, further study is warranted to elucidate the effect of CRS severity on asthma control and to determine whether reduction in CRS severity translates to improvement in asthma control.

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Introduction

Chronic rhinosinusitis (CRS) is an inflammatory condition of the sinonasal mucosa that leads to chronic symptoms, such as nasal obstruction, mucopurulent nasal drainage, facial pressure, and hyposmia.^{1,2} It is now recognized that CRS is a heterogeneous disease, and multiple pathophysiologic mechanisms^{3,4} likely exist to culminate in the final clinical phenotype defined by consensus guideline criteria.^{1,2} Possible mechanisms for the development of CRS include genetic predisposition, impaired mucociliary clearance, infectious origins, and inflammatory conditions, such as atopy, autoimmunity, and aspirin sensitivity.^{5–11}

Epidemiologic studies have found strong associations between the prevalence of CRS and other inflammatory conditions of the upper and lower airways.^{12,13} One recent epidemiologic study

found a prevalence of asthma of almost 50% in adults with CRS and nasal polyps.¹⁴ Conversely, the prevalence of CRS in adults with asthma may be as high as 40%.¹⁵ Asthma has also been identified as a premorbid condition for adults with CRS and is associated with a greater risk for the subsequent development of CRS.^{16,17} Moreover, previous studies have found that comorbid CRS in patients with asthma is associated with more asthma-related emergency department visits, hospitalizations, and systemic corticosteroid use.^{18,19} However, no study has yet reported the extent to which CRS severity may affect asthma control.

The most common and significant effect of CRS is the associated quality-of-life detriment that arises from the severity of sinonasal symptoms²⁰ and successful disease control in CRS is measured by monitoring sinonasal symptoms.²¹ Because no previous study has investigated the quantitative association between adult CRS severity and asthma outcomes a priori, it is unclear what magnitude of effect size CRS severity may have on asthma control. Thus, our objective in this pilot study was to characterize the magnitude of effect that CRS symptoms have on asthma control in adults with asthma and CRS.

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Disclosures: Authors have nothing to disclose.

<http://dx.doi.org/10.1016/j.anai.2016.09.439>

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Methods

Study Participants

This study was approved by the Massachusetts Eye and Ear Infirmary Human Studies Committee. Adult patients (≥ 18 years of age) with CRS and asthma were recruited prospectively and provided verbal and written informed consent for inclusion into this cross-sectional study. All participants met consensus guideline-established criteria for CRS.^{1,2} All patients were referred to us with a previous diagnosis of asthma, which was confirmed based on a previous clinical history and symptoms.²² Exclusion criteria included comorbid vasculitis, comorbid cystic fibrosis, and comorbid sarcoidosis.

Study Design and Data Collection

This is a pilot study with a prospective, cross-sectional design to obtain an estimate for the magnitude of effect that CRS symptoms have on asthma control. All data were collected at enrollment. Data collected directly from all participants included CRS-related symptoms as measured by the validated 22-item Sinonasal Outcomes Test (SNOT-22) survey.²³ Asthma control was assessed using the Asthma Control Test (ACT).^{24,25} We assessed cigarette smoking by asking participants whether they were current or former smokers. We also asked participants if they used a corticosteroid-containing inhaler for asthma and/or intranasal corticosteroid spray for CRS. Data collected from the evaluating physician included whether the patient had a history of aeroallergen hypersensitivity based on formal allergy testing, asthma, nasal polyps, and aspirin sensitivity.

Statistical Analysis

All analysis was performed using the statistical software package R (www.r-project.org). The correlation between SNOT-22 score and ACT score was made with Spearman correlation. Association between SNOT-22 score (as the independent variable) and ACT score (as the dependent variable) was calculated using linear regression. Association between SNOT-22 score and poor asthma control, defined by an ACT score of 19 or less, as the dependent variable was assessed using logistic regression. Multivariable regression models controlled for age, sex, having at least 1 aeroallergen sensitivity, having nasal polyps, smoking status, and use of an asthma controller inhaler.

Results

Study Participants

A total of 40 patients (35.0% males and 65.0% females; mean [SD] age, 49.7 [16.5] years) with CRS and asthma were recruited, and their characteristics are summarized in Table 1. Study participants mostly described themselves as white (85.0%), with only 2.5% of participants describing themselves as black or African American and 12.5% of participants declining to indicate what race they considered themselves. Of these study participants, 27.5% were current or former cigarette smokers, 62.5% had at least 1 aeroallergen hypersensitivity, 50.0% had nasal polyps, 42.5% reported prior sinus surgery for their CRS, and 15.0% had a history of aspirin sensitivity. The mean (SD) SNOT-22 score, reflecting CRS symptom severity, was 43.6 (23.6), and the mean (SD) ACT score was 20.6 (4.8). Of all study participants, 67.5% reported using a steroid-containing inhaler for asthma management, and 72.5% reported using an intranasal corticosteroid medication for CRS management.

Association of CRS Symptoms and Control With Asthma Control

We initially evaluated the association between ACT and SNOT-22 scores (Fig 1) and found a statistically significant negative

Table 1

Characteristics of the Study Participants^a

Characteristic	Finding
Demographics	
Age, mean (SD), y	49.7 (16.5)
Sex	
Male	35
Female	65
Race	
White	85
Black or African American	2.5
Declined to answer	12.5
History of cigarette smoking	27.5
Clinical comorbidities	
Aeroallergen sensitivity	62.5
Aspirin sensitivity	15
CRS characteristics	
Nasal polyps	50
Prior sinus surgery	42.5
SNOT-22 score, mean (SD)	43.6 (23.6)
Intranasal corticosteroid use	72.5
Asthma characteristics	
ACT score, mean (SD)	20.6 (4.8)
Inhaled corticosteroid use	67.5

Abbreviations: ACT, Asthma Control Test; CRS, chronic rhinosinusitis; SNOT-22, 22-item Sinonasal Outcomes Test.

^aData are presented as percentage of patients unless otherwise indicated.

correlation between SNOT-22 and ACT scores ($\rho = -0.52$, $P = .001$), which reflects a large effect size.²⁶ We additionally sought formal associations between CRS symptom severity and ACT score. SNOT-22 score was associated with ACT score on univariate analysis ($\beta = -0.12$; 95% confidence interval [CI], -0.17 to -0.06 ; $P < .001$). This association between SNOT-22 and ACT scores remained statistically significant even after controlling for age, sex, having at least 1 aeroallergen sensitivity, having nasal polyps, smoking status, and the use of an asthma controller inhaler ($\beta = -0.07$; 95% CI, -0.13 to -0.02 ; $P = .02$). SNOT-22 score was also associated with poor asthma control (defined as ACT score ≤ 19) (odds ratio [OR], 1.06; 95% CI, 1.02–1.11; $P = .006$), and this association also remained statistically significant after controlling for the above confounders (OR, 1.06; 95% CI, 1.01–1.11; $P = .02$).

On the basis of the distribution of our participants' SNOT-22 scores (Fig 2A), we evaluated the point estimate for association between various SNOT-22 score cutoffs and having poor asthma

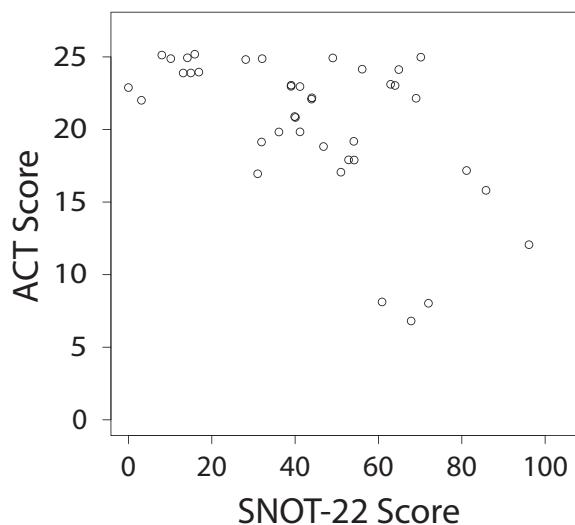


Figure 1. Plot of Asthma Control Test (ACT) score vs 22-item Sinonasal Outcomes Test (SNOT-22) score for the 40 patients with asthma and CRS.

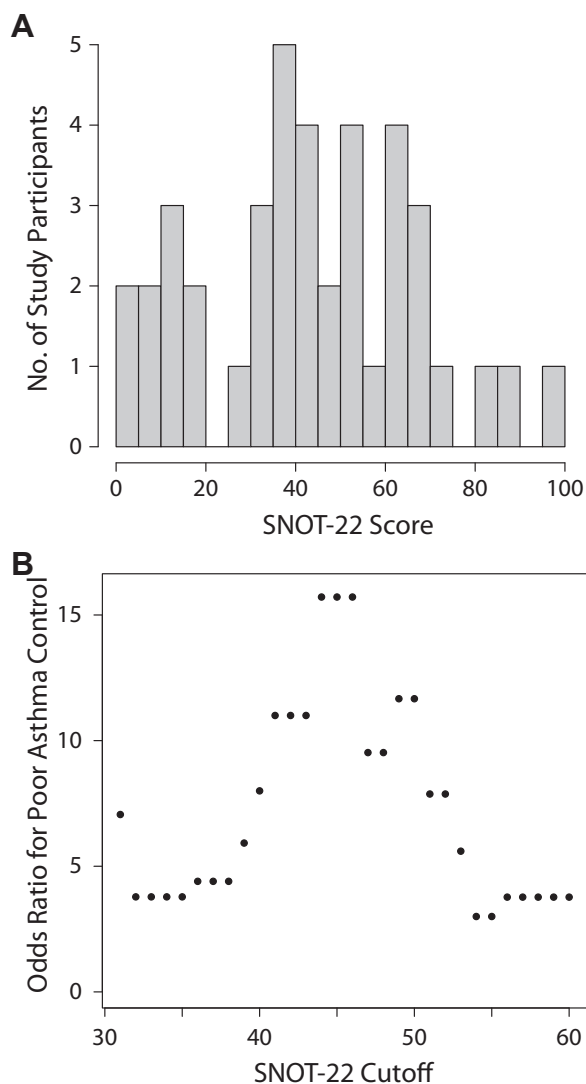


Figure 2. Histogram plot of the 22-item Sinusnasal Outcomes Test (SNOT-22) scores of all study participants (A) and the plot of odds ratio point estimates for having poorly controlled asthma for each minimum SNOT-22 cutoff (B).

control (Fig 2B). We found that a SNOT-22 score in the range of 44 to 46 had the largest point estimate of association with having poor asthma control. A SNOT-22 score of 45 or greater was significantly associated with having poor asthma control (OR, 15.66; 95% CI, 2.76–88.77; $P = .002$). This association between SNOT-22 score and poor asthma control remained statistically significant even after controlling for the above-described confounders (OR, 14.96; 95% CI, 1.93–115.89; $P = .01$).

Discussion

CRS is a common disease that affects 2% to 5% of the population.² CRS is also commonly associated with asthma, which is prevalent in up to 50% of patients with CRS and nasal polyps.¹⁴ Even patients without asthma but with CRS are more likely to have asymptomatic bronchial hyperreactivity.²⁷ The unified airway hypothesis suggests that inflammatory disorders of the upper and lower airways occur through common or overlapping disease processes that allow dynamic interactions between upper and lower airway diseases.²⁸ As an example, CRS exacerbates comorbid lower airway diseases. Although previous studies have established an epidemiologic link between CRS and asthma control, the effect of CRS severity on

asthma outcomes is not well defined. This issue has potential implications for patient care because although CRS cannot be cured, the severity of CRS symptoms can be improved using multiple treatment modalities. If the severity of CRS, rather than its mere comorbidity, can be found to negatively affect asthma outcomes, then treatment of comorbid CRS in patients with asthma may be one avenue for improving asthma control. Because the effect of CRS severity on asthma outcomes has not been well characterized, as a first step toward studying the association between CRS severity and asthma control, we performed this pilot study to determine the effect size of this association. We found that CRS severity, as measured by CRS symptoms, has a large effect on and is negatively associated with asthma control.

Previous studies have found a negative effect for CRS on comorbid asthma. In patients with asthma, CRS is associated with more asthma-related emergency department visits, hospitalizations, and systemic corticosteroid use.^{18,19} Patients with asthma and CRS also have significantly worse pulmonary function and lower asthma-specific and general health-related quality of life compared with patients with asthma without CRS.²⁹ This effect of CRS on patients with asthma directly translates to greater asthma-related health care costs as well.¹⁹ One previous retrospective study of patients with CRS and asthma, culled from a database of patients who underwent endoscopic sinus surgery for CRS, found that the degree of paranasal sinus opacification on computed tomography was associated with those patients' National Heart, Lung, and Blood Institute (NHLBI) classification of asthma severity.³⁰ Although this study provided evidence that CRS severity may be directly related to asthma severity, this study was limited in several ways. Aside from its retrospective nature, sinus computed tomographic findings were not necessarily obtained at the same time as the assessment of asthma severity. It was also unclear whether the patients were being actively treated for asthma, which would confound assessment of asthma severity by NHLBI guidelines that are recommended for when patients with asthma are not taking controller medication.²² In addition, radiographic measures of CRS correlate poorly with sinonasal symptoms.³¹ By contrast, sinonasal symptoms may not only be reflective of the pathophysiologic processes driving a patient's CRS but also correlate well with important clinical features of CRS control, such as antibiotic and systemic corticosteroid use.^{32,33} Understanding whether CRS symptom severity is associated with asthma control would provide evidence for potential improvement of asthma outcomes through treatment of CRS.

In our prospective, cross-sectional designed pilot study, we found that the severity of CRS symptoms is negatively associated with asthma control, with a large effect size. Moreover, a cutoff SNOT-22 score of 45 and greater revealed the greatest association with poor asthma control. Our findings have several important implications. These findings provide evidence that further investigations into the effect of CRS severity on asthma outcomes are warranted. Elucidation of the role of CRS symptoms and CRS disease control in the setting of comorbid asthma will provide insight into the mechanisms through which CRS may lead to poor asthma outcomes. Our findings also provide further credence for the notion of the unified airway, although the specific mechanisms for the interaction between CRS and asthma remain unknown. It is possible that common inflammatory pathways causing more CRS symptoms or poor CRS control may also negatively affect asthma outcomes. Alternatively, the sequelae of poor CRS control and CRS symptoms, such as mucopurulent postnasal drainage, may also serve to directly exacerbate pulmonary inflammation. Finally, our findings also raise the possibility that treatment of comorbid CRS may be one potential component of asthma treatment that deserves additional study.

Previous studies have generally found a beneficial effect for CRS treatment on asthma outcomes.³⁴ Prospective studies of CRS treatments have revealed that both medical and surgical

management of CRS in patients with asthma may lead to less bronchodilator and oral corticosteroid use, fewer asthma-related hospitalizations, and even improved pulmonary function.^{35,36} In contrast, one recent study found that treatment of chronic sinonasal disease with intranasal corticosteroid spray was ineffective in improving asthma control.³⁷ Extension of this latter study to CRS is limited because its inclusion criteria did not meet established clinical consensus guideline criteria for CRS^{1,2} and because intranasal corticosteroid sprays have less penetration into the paranasal sinuses compared with sinonasal irrigations³⁸ and they may therefore be less efficacious in the treatment of CRS.³⁹ However, none of these previous studies have begun to examine how CRS outcomes, for example, improvement of sinonasal symptoms through better CRS control, may be related to a change in asthma outcomes after CRS treatment.

To our knowledge, our pilot study is the first prospective, cross-sectional investigation into the association of CRS symptoms with asthma control. Our study is currently limited by our cohort size, but our preliminary investigation demonstrates a large effect size in the correlation between our CRS symptom severity and asthma control. In addition, we did not measure pulmonary function, so we cannot draw any conclusions in that regard. The results presented here will nonetheless serve to motivate studies with larger enrollment to estimate the incremental effect of decreasing sinonasal symptoms on asthma control.

Acknowledgments

We gratefully acknowledge the contribution of the patients who participated in this study.

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