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RHINOLOGY

Seasonal variations in chronic rhinosinusitis symptom burden may be explained by changes in mood

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Abstract

Purpose There are many year-round modifiers of chronic rhinosinusitis (CRS). However, it is unknown whether there are seasonal variations in the sinonasal symptom burden of CRS.

Methods This was a retrospective cross-sectional study of sinonasal symptom burden measured using the 22-item Sinonasal Outcome Test (SNOT-22) and its four associated nasal, sleep, ear/facial discomfort and emotional subdomains in 1028 individuals with CRS. The season (winter, spring, summer or fall) when the SNOT-22 was completed was recorded. Regressions, controlling for clinical and demographic characteristics, were performed to seek association between season of the year and SNOT-22 total and subdomain scores.

Results The mean SNOT-22 scores were 37.4 for those individuals completing their SNOT-22 in the fall, 40.5 in the winter, 37.4 in the spring and 36.0 in the summer. There was a statistically significant association between higher SNOT-22 scores and completing the SNOT-22 in the wintertime (adjusted $\beta = 4.08$, 95% CI 0.74–7.42, $p = 0.017$). When seeking association between season and SNOT-22 subdomain scores, wintertime was associated only with higher emotional (adjusted $\beta = 0.48$, 95% CI 0.14–0.81, $p = 0.006$) and sleep (adjusted $\beta = 2.23$, 95% CI 0.54–3.91, $p = 0.010$) subdomain scores. Examining individual SNOT-22 items, these associations were due to more symptoms related to depressed mood ("sad") and psychomotor retardation.

Conclusion There are seasonal variations in symptom burden of CRS patients, independent of aeroallergen hypersensitivity, with the greatest increase in baseline CRS symptomatology during the winter. This finding was most strongly associated with increased emotional symptomatology and depressed mood.

Keywords Chronic rhinosinusitis · Seasonal variations · SNOT-22 · Winter · Exacerbation

Introduction

Background and rationale

Chronic rhinosinusitis (CRS) is an inflammatory disease of the sinonasal cavity that takes a tremendous toll on patients by decreasing quality of life (QOL), exacerbating lower airway disease, and diminishing one's ability to work [1–3]. The CRS disease course is characterized by both chronic baseline symptomatology as well as intermittent acute exacerbations of those symptoms, each of which may have independent downstream effects related to the above-mentioned morbidity [4–6]. While acute exacerbations may have a significant impact on CRS patients, the chronic baseline symptomatology associated with CRS is likely the primary driver of the deleterious disease effects.

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Highlighting its importance, assessment of the chronic sinonasal symptomatology associated with CRS rather than serological testing or imaging is the primary outcome measure upon which clinical decision making is often based. One the most common and recommended tools for assessment of CRS symptom burden is the 22-item Sinonasal Outcome Test (SNOT-22) [7, 8], which assesses nasal symptoms as well as symptoms related to poor sleep, ear/facial discomfort, and mood/emotional disturbance [9]. While patients are most focused on the associated nasal symptoms of the disease, extra-nasal symptoms related to poor sleep, discomfort and mood have the greatest impact on functional consequences of the disease such as QOL and lost productivity [10–12].

Previous research has shown that atopic and inflammatory airway diseases may have seasonal variations in severity and burden [13, 14]. The underlying reasons for seasonal variations in disease burden have been attributed in the past to seasonal variations in exposures to infectious agents, such as viruses, and environmental triggers, such as allergens or pollution [15, 16]. CRS may also have seasonal variations in the disease burden felt by patients although any such phenomenon has not been well characterized.

Objectives

The burden of CRS symptoms felt by patients is a complex synthesis of the effects of a baseline level of sinonasal inflammation, which may be modified by environmental and infectious agents, and subjective patient-specific factors such as mood [17]. In this study, we sought to determine whether CRS symptom burden, as measured using the SNOT-22, would demonstrate seasonal variations at the population level through the cross-sectional study of a large group of CRS patients. We further sought to characterize any such seasonal variations in CRS symptom burden as a consequence of nasal or extra-nasal symptomatology.

Methods

Study design and setting

This study was approved by our institution's Human Studies Committee. The study design was a retrospective, cross-sectional investigation. All patients were seen and evaluated in a tertiary rhinology clinic.

Study participants

A consecutive series of adult patients (with age of 18 years or older) with CRS based on clinical consensus guideline criteria [18] by the authors between April 2016 and December 2018 was identified and studied. The only other mandatory criteria for inclusion were availability of medical records and completion of a 22-item Sinonasal Outcome Test (SNOT-22) questionnaire, which every patient to the clinic receives. Only the first completed SNOT-22 questionnaire was used for patients with multiple clinic visits in the study period.

Patients with comorbid diagnosis of vasculitis, cystic fibrosis, sarcoidosis, or immunodeficiency were excluded from the study due to possible confounding effects of systemic disease. To remove the confounding effects of heterogeneous treatments, a documented history of endoscopic sinus surgery within the prior 6 months was also an exclusion criterion. Additionally, to remove the confounding effect of transient (and possibly season specific) CRS symptom burden, we excluded any patient documented to be in the midst of an acute exacerbation of their CRS—including active acute rhinosinusitis both as a bacterial infection or in the setting of a viral/upper respiratory tract infection—when the SNOT-22 form was completed.

Variables and data collection

Demographic and clinical characteristics of patients were collected, including age, sex, and smoking history. Any patient who was an active smoker or reported a history of being a tobacco smoker in the past was considered to be a smoker for this study [19–21]. For each patient (1) a diagnosis of asthma based on clinical history and a prior established diagnosis, (2) aeroallergen hypersensitivity based on formal allergy testing, (3) utilization of intranasal corticosteroids (spray or irrigation), (4) a history of aspirin sensitivity, and (5) the presence of nasal polyps on the basis of nasal endoscopy were determined based on the assessment of the rhinologist who evaluated the patient at the time. All patients completed the 22-item Sinonasal Outcome Test (SNOT-22), as a measure of CRS symptom burden, for inclusion [7, 8]. Nasal, sleep, ear/facial discomfort, and emotional SNOT-22 subdomain scores were calculated as previously described [9, 22]. The season was determined as winter if the SNOT-22 was completed in December, January or February; spring if in March, April or May; summer if in June, July or August; and fall if in September, October, or November.

Statistical analysis

All analysis was performed using the statistical software package R (https://www.r-project.org) [23] Associations with SNOT-22 (total or subdomain) scores as dependent variables were performed using linear regression. Associations with SNOT-22 item scores were performed with negative binomial regression.

Results

Study participants and descriptive statistics

A total of 1028 patients were included, and their clinical and demographic characteristics are summarized in Table 1. The mean SNOT-22 score of these patients was 37.6 (standard deviation [SD] 22.6). Mean SNOT-22 subdomain scores were 16.3 (SD 8.9) for the nasal subdomain, 14.3 (SD 11.1) for the sleep subdomain, 5.5 (SD 4.8) for the ear/facial discomfort subdomain, and 1.5 (SD 2.2) for the emotional subdomain. Of all SNOT-22 questionnaires included, 20.8% were completed in the winter, 24.0% were completed in the spring, 30.0% were completed in the summer and 25.2% were in the fall.

Seasonal variations of sinonasal symptom burden in CRS patients

The mean SNOT-22 scores of patients in each season was calculated as 37.4 in the spring, 36.0 in the summer, 37.4 in the fall and 40.5 in the winter (Fig. 1). We checked for association between SNOT-22 being completed in the wintertime compared to other seasons and found a positive association with increased SNOT-22 scores ($\beta = 3.60$, 95% CI 0.19–7.00, $p = 0.039$) on univariate association. On multivariable association, wintertime was also associated with higher SNOT-22 score ($\beta = 4.08$, 95% CI 0.74–7.42, $p = 0.017$) after controlling for age, gender, aeroallergen hypersensitivity, asthma, polyps, history of smoking and use of nasal steroids.

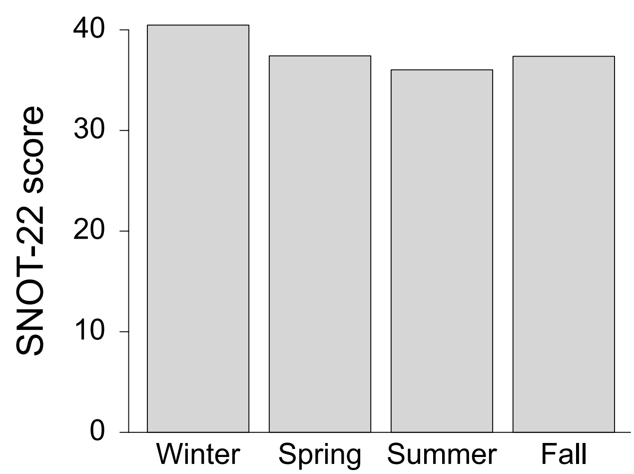

Fig. 1 Bar plot of mean SNOT-22 scores by season (refer to Table 1 for standard deviations of scores by season)

Table 1 Characteristics of patients

Demographics	All patients ($N = 1028$)	Winter patients ($N = 213$)	Spring patients ($N = 246$)	Summer patients ($N = 311$)	Fall patients ($N = 258$)
Age, mean in years (SD)	51.7 (15.9)	51.6 (16.5)	53.0 (15.7)	50.7 (15.6)	51.7 (15.9)
Gender					
Male	48.8%	52.6%	48,8%	45.3%	46.5%
Female	51.2%	47.4%	51.2%	54.7%	53.5%
Smoking	29.3%	29.1%	28.0%	27.3%	32.9%
Comorbidities					
Asthma	32.0%	31.0%	30.9%	30.9%	35.3%
Aspirin sensitivity	4.5%	5.6%	4.9%	4.2%	3.5%
Aeroallergen hypersensitivity	44.5%	46.5%	44.7%	42.1%	45.3%
CRS characteristics					
Nasal polyps	38.6%	39.4%	37.4%	38.3%	39.5%
Previous sinus surgery	37.1%	39.9%	39.0%	30.2%	41.1%
Intranasal corticosteroid use	43.4%	46.5%	43.9%	44.1%	39.5%
SNOT-22 score, mean (SD)	37.6 (22.6)	40.5 (23.9)	37.4 (22.4)	36.0 (23.1)	37.4 (21.0)
SNOT-22 subdomain score, mean (SD)					
Nasal	16.3 (8.9)	17.0 (9.1)	16.4 (9.2)	15.8 (9.1)	16.3 (8.4)
Sleep	14.3 (11.1)	15.9 (11.7)	14.3 (10.5)	13.2 (11.4)	14.2 (10.8)
Ear/facial discomfort	5.5 (4.8)	5.8 (5.0)	5.3 (4.7)	5.5 (4.8)	5.4 (4.7)
Emotional	1.5 (2.2)	1.8 (2.4)	1.4 (2.2)	1.4 (2.2)	1.4 (2.1)

Table 2 Association between wintertime and SNOT-22 subdomain scores

	Univariate analysis		Multivariable analysis[a]	
	β (95% CI)	p value	β (95% CI)	p value
SNOT-22 subdomain score				
Nasal	0.80 (– 0.55 to 2.15)	0.245	1.00 (– 0.32 to 2.32)	0.138
Sleep	2.01 (0.33–3.68)	0.019	2.23 (0.54 to 3.91)	0.010
Ear/facial discomfort	0.38 (– 0.34 to 1.11)	0.300	0.37 (– 0.33 to 1.08)	0.296
Emotional	0.40 (0.07–0.74)	0.018	0.48 (0.14 to 0.81)	0.006

[a]Controlling for age, gender, aeroallergen hypersensitivity, asthma, polyps, history of smoking and use of intranasal corticosteroids

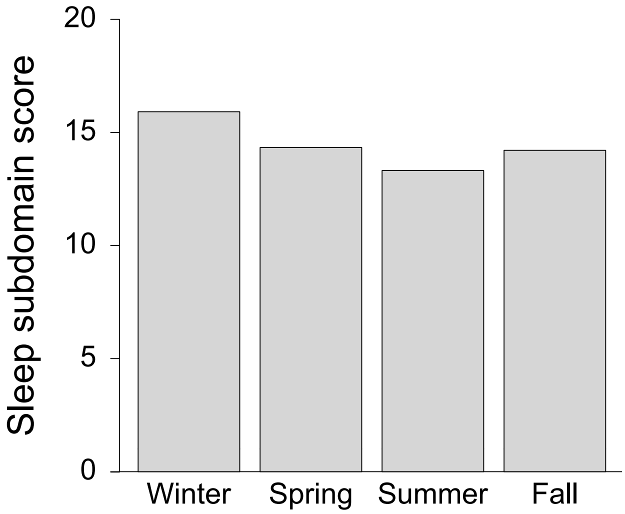

Fig. 2 Bar plot of mean SNOT-22 sleep subdomain scores by season (refer to Table 1 for standard deviations of scores by season)

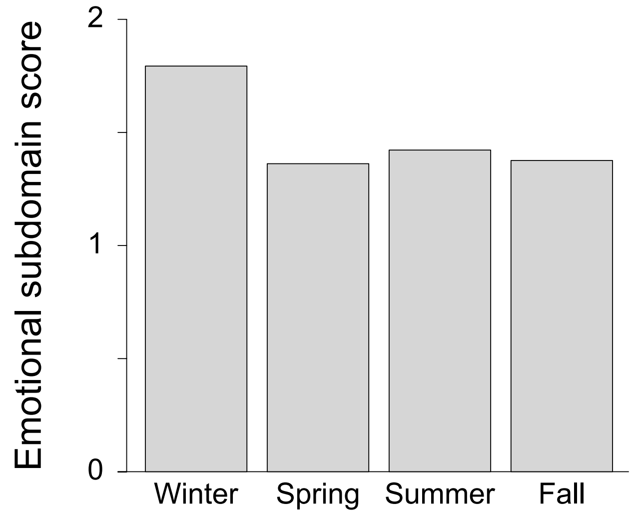

Fig. 3 Bar plot of mean SNOT-22 emotional subdomain scores by season (refer to Table 1 for standard deviations of scores by season)

Relationship between seasonal elevation of the SNOT-22 score and depressed mood

We next sought associations between completion of the SNOT-22 in the winter and scores on each of the SNOT-22 subdomains (Table 2). Wintertime was not associated with higher nasal ($\beta = 0.80$, 95% CI − 0.55 to 2.15, $p = 0.245$) or ear/facial discomfort ($\beta = 0.38$, 95% CI − 0.34 to 1.11, $p = 0.300$) subdomain scores on univariate analysis and these results were confirmed on multivariable analysis as well. In contrast, wintertime was associated with higher sleep ($\beta = 2.01$, 95% CI 0.33–3.68, $p = 0.019$) and emotional ($\beta = 0.40$, 95% CI 0.07–0.74, $p = 0.018$) subdomain scores on univariate analysis (Figs. 2, 3). Wintertime was associated with higher sleep ($\beta = 2.23$, 95% CI 0.54–3.91, $p = 0.010$) and emotional ($\beta = 0.48$, 95% CI 0.14–0.81, $p = 0.006$) subdomain scores on multivariable analysis as well, after controlling for age, gender, aeroallergen hypersensitivity, asthma, polyps, history of smoking and use of intranasal corticosteroids.

To gain greater understanding of these results, we performed univariate associations between completion of the SNOT-22 in wintertime and the individual SNOT-22 items comprising the emotional and sleep subdomains. For the emotional subdomain-related SNOT-22 items, we found that wintertime was associated with higher scores on item #19 "sad" (relative rate [RR] = 1.38, 95% CI 1.08–1.76, $p = 0.011$) but not with scores on item #20 "embarrassed" (RR 1.19, 95% CI 0.86–1.63, $p = 0.290$). For the sleep subdomain-related SNOT-22 items, we found that wintertime was associated with higher scores on items #14 "waking up tired" (RR 1.13, 95% CI 1.01–1.26, $p = 0.041$), #16 "reduced productivity" (RR 1.19, 95% CI 1.01–1.39, $p = 0.032$), #17 "reduced concentration" (RR 1.20, 95% CI 1.02–1.41, $p = 0.028$), and #18 "frustrated/restless/irritable" (RR 1.22, 95% CI 1.02–1.45, $p = 0.028$). In contrast, wintertime was not associated with scores on sleep-related items #11 "difficulty falling asleep" (RR 1.11, 95% CI 0.92–1.33, $p = 0.280$), #12 "waking up at night" (RR 1.10, 95% CI 0.97–1.26, $p = 0.151$), #13 "lack of a good night's sleep" (RR 1.12, 95% CI 0.99–1.27, $p = 0.066$), and #15 "fatigue during the day" (RR 1.12, 95% CI 0.99–1.26, $p = 0.058$).

Discussion

Key results

CRS has a significant disease burden, leading to decreased QOL and exacerbation of lower airway disease. Amongst CRS disease manifestations, the burden of chronically persistent symptoms is most often utilized for clinical decision making. CRS symptomatology has been previously characterized as nasal and extra-nasal, with extra-nasal symptoms including poor sleep, craniofacial discomfort and mood disturbances. The SNOT-22 is a validated questionnaire that assesses the burden of nasal and extra-nasal symptoms due to CRS and it is used both for research and in the clinic, serving as a useful aid in clinical decision making. As CRS patients are assessed and judgements regarding their treatment are made all throughout the year, it is important to understand whether seasonal variations in symptoms exist and if so, then why. Although the frequency of acute exacerbations of CRS is known to have seasonal variations, it is yet unknown whether the baseline chronic symptoms of CRS exhibit seasonal variations.

To achieve our study objectives of characterizing seasonal variations in CRS symptoms, we took a population level approach by examining SNOT-22 questionnaires completed by over 1000 unique CRS patients throughout the year, specifically focusing on patients who were not in the midst of an acute exacerbation of their CRS. We found that patients with CRS have a higher SNOT-22 score in the winter compared to other seasons and that this wintertime elevation in SNOT-22 score may be due to increased prevalence of depressed mood. While there were no significant associations between wintertime and increases in nasal or ear/facial discomfort symptoms, CRS patients reported significantly worse sleep and emotional scores on their SNOT-22 questionnaires in the wintertime. A more focused examination of these subdomain-level findings suggested that depressed mood may explain our findings. Amongst the SNOT-22 items comprising the emotional subdomain, we found that only "sad" was higher in the winter, but not "embarrassed". Amongst the SNOT-22 items comprising the sleep subdomain, "waking up tired", "reduced productivity", "reduced concentration", and "frustrated/restless/irritable" were higher in the winter, but not "difficulty falling asleep", "waking up at night", "lack of a good night's sleep", or "fatigue during the day". These SNOT-22 items that were higher in the winter are reflective of depressed mood and the psychomotor retardation that is associated with depressed mood [24].

Limitations

Our results should be interpreted in the context of its limitations. Our study is retrospective and subject to the biases inherent to such a study design. Our study is also cross-sectional, which although suited to performing a population-level study does not provide patient-level data on seasonal variations. Furthermore, the increase we found in SNOT-22 score associated with winter was approximately four points, which does not meet any previously reported minimal clinically significant difference of the SNOT-22 [7, 25]. Thus while the general clinical significance of seasonal variations in SNOT-22 due to mood requires further characterization, it may be a factor for some patients [26, 27].

Interpretation

Prior work on seasonal variations in inflammatory airway diseases has largely focused on variations in environmental triggers like allergens, pollution or infectious agents. For example, seasonal patterns of asthma exacerbations have been attributed to variations in exposure to allergens, respiratory viruses and pollution [28–30]. Similarly, prior research on seasonal variations of CRS disease burden has focused on acute exacerbations. Specifically, acute exacerbations of CRS are more frequently reported by patients in the winter [31] and this is associated with greater intranasal detection of viruses [32, 33]. Other seasonal inflammatory stimuli such as aeroallergens may also lead to seasonal CRS exacerbations depending on a CRS patient's specific environmental triggers [34]. Beyond seasonal variations in acute exacerbations of CRS, little is known about whether seasonal variations exist in CRS patients' baseline symptomatology.

To the best of our knowledge, there are no other studies reported in the literature that show seasonal variations in the baseline symptomatology of CRS. That we specifically excluded patients experiencing an acute exacerbation of CRS allowed us to gain novel insights into the seasonal variability of CRS symptoms. Specifically, beyond seasonal variations in environmental exposures, we find that there may be seasonal variations in mood that may modulate patient-reported outcome measures such as the reporting of sinonasal symptom burden on the SNOT-22. Seasonal affective disorder (SAD) is now a well-established entity, in which affected patients experience sleep disturbances and manifestations of psychomotor retardation such as fatigue, irritability, and diminished ability to concentrate during winter months [35]. Our results indicate that SAD may influence seasonal variations in SNOT-22 score.

CRS patients, in general, have been shown to exhibit a higher prevalence of psychiatric comorbidity including depression compared to healthy controls [36]. Amongst CRS patients, there is a trend for greater prevalence of depression in CRS patients without polyps compared to CRS patients with polyps [36]. Mood disturbance has been shown to be an important modulator of decreased QOL and functional impairment due to CRS (as well as other inflammatory upper airway disease such as allergic rhinitis) [12, 17, 37]. In CRS patients, depressed mood has been shown to be the primary symptom associated with lost productivity [12]. Moreover, in CRS patients with uncontrolled CRS symptoms, depressed mood is a primary determinant of whether the patient reports good or bad QOL [17]. It is, therefore, understandable that known variations in mood, which may occur with SAD, could also modulate patient-reported sinonasal symptom burden. That we did not find a change in nasal symptoms by season may be surprising given that we expect seasonal allergen exposure to have an impact on allergic CRS patients. We, however, propose that the lack of seasonal variations in nasal symptoms is not unexpected because allergens and environmental triggers vary all throughout the year. Given the heterogeneity of CRS pathophysiology from patient to patient, at any time of the year some patients are likely experiencing greater-than-usual symptoms due to exposures (e.g. allergens, etc.). Thus while we might expect to see patient-specific seasonal variations in symptom burden based on allergy season, on the population level, this effect likely diminishes.

Generalizability

SAD is a well-described phenomenon that may occur throughout the world [35], although there is question about geographic effects on its prevalence, with some studies finding that more extreme latitudes are associated with higher prevalence of SAD due to greater seasonal variations in, for example, ambient daylight. While studies have found mixed results with respect to a consistent association between geography and the prevalence of SAD [38–42], it is possible that geographic characteristics—from seasonal variations in climate to differences in maritime or continental climates—may be a factor in the development of SAD. The patients enrolled in the study were from the northeast United States where it is possible that there may be a disparate incidence of SAD in the winter, therefore potentially limiting the general applicability of our study results.

Conclusion

At the population level, a small increase in SNOT-22 score may occur in the wintertime due to an increase in SNOT-22 items that may be affected by SAD. The magnitude of this effect may not be clinically significant in reaching the SNOT-22 minimal clinically important difference but the possible confounding effects of seasonal variations in mood on SNOT-22 score should be considered on a patient-by-patient basis.

Compliance with ethical standards

Conflict of interest There are no potential conflicts or financial relationships.

Ethical approval This study and its design was approved by the institutional human studies committee.

Informed consent Not performed given the retrospective study design.

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