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Impact of nasal symptoms on the evaluation of asthma control

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Abstract

The united airways concept suggests that patients with asthma typically exhibit parallel inflammation in the upper airway. The resulting nasal symptoms should reduce quality of life and substantially affect the evaluation of asthma control among these patients. This study aimed to assess the association of nasal symptoms with the evaluation of asthma control.

Fifty-eight patients with asthma and persistent nasal symptoms were prospectively recruited for evaluations of their sinonasal symptoms and asthma control in a cross-sectional study from August 2013 to June 2016. Participants underwent thorough nasal endoscopy, sinus computed tomography, pulmonary function testing, the asthma control test (ACT), and the Sino-Nasal Outcome Test-22 (SNOT-22) questionnaires to evaluate their asthma control and sinonasal symptoms.

There was a significant association between ACT and SNOT-22 scores. Among patients with asthma and chronic rhinosinusitis, ACT scores were closely related to the symptoms of cough, post-nasal discharge, dizziness, waking up at night, absence of a good night's sleep, and waking up tired. Among patients with asthma and chronic rhinitis, the forced expiratory volume in 1 second was closely related to the symptoms of needing to blow nose, runny nose, and cough. Patients with emergency clinic visits during the previous 3 months had relatively high SNOT-22 scores, especially for the symptoms of sneezing, runny nose, nasal blockage, cough, and dizziness.

Sinonasal symptom severity was closely associated with measured asthma control status among patients with asthma and persistent nasal symptoms. Therefore, upper and lower airway inflammations should be considered and treated simultaneously.

Abbreviations: ACT = Asthma Control Test, CR = chronic rhinitis, CRS = chronic rhinosinusitis, CRSsNP = chronic rhinosinusitis without nasal polyps, CRSwNP = chronic rhinosinusitis with nasal polyps, CT = computed tomography, FEV1 = forced expiratory volume in 1 s, FVC = forced vital capacity, GINA = Global Initiative for Asthma, IgE = immunoglobulin E, QoL = quality of life, SNOT-22 = Sino-Nasal Outcome Test-22.

Keywords: airway, allergy, asthma, chronic rhinitis, chronic rhinosinusitis

1. Introduction

Asthma is a common, chronic, and inflammatory disease of the lower airway, which currently affects 235 million people throughout the world.[1] The global prevalence of asthma and its related complications have created significant burdens on patients, employers, and socioeconomic systems.[2] During recent decades, disease status has been evaluated using patient-reported outcomes, such as the patient's self-perceived experience of their symptoms and the effects of their illness.[3,4] Thus, the concept of asthma control has replaced the concept of asthma severity, and asthma control is now considered the main outcome during asthma treatment.[5] Furthermore, the Global Initiative for Asthma (GINA) Guidelines suggest that asthma control includes 2 domains: symptom control and future risk of adverse outcomes. In this context, periodic assessments of the patient's asthma control and risk factors are an essential part of asthma management[5]. The asthma control test (ACT) is one of the most commonly used instruments for evaluating asthma control, and this tool includes 4 symptom/relief questions and a self-assessment of asthma control.[6,7] A low forced expiratory volume in 1 second (FEV_1) is the most important risk factor for poor asthma outcomes[5] and has been added to other tools for evaluating asthma control, such as the asthma control questionnaire.[8]

Patients with asthma have a higher incidence of allergic or nonallergic chronic rhinitis (CR)[9–11] and chronic rhinosinusitis (CRS).[11–13] Moreover, based on the united airways concept, these conditions exhibit associations with sinonasal inflammation and related nasal symptoms.[11,14] In this context, nasal symptoms are expected to reduce quality of life (QoL) and substantially affect the evaluation of asthma control among patients with asthma. However, to the best of our knowledge, no studies have investigated the effect of nasal symptoms on the evaluation of asthma control. Therefore, the present study aimed

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to assess the correlations between questionnaire-based nasal symptom scores and asthma control outcomes (e.g., the ACT score, FEV_1, and acute exacerbation) among patients with asthma and persistent nasal symptoms.

2. Methods

2.1. Patients

Between August 2013 and June 2016, we prospectively recruited patients with asthma and persistent nasal symptoms who were being treated at our Thoracic Medicine Department. Figure 1 shows the study flow chart. The inclusion criteria were patients with asthma who fulfilled the diagnostic criteria from the GINA guidelines[5] and had failed 3 months of medical treatment for their nasal symptoms. Participants received initial medical therapy including: at least either 3 months course of topical corticosteroids or 1 week course of oral corticosteroids, and at least 2 weeks of culture-directed or broad spectrum antibiotics per the standard of care. The failed medical therapy was based upon persistent symptoms reported by participants and/or physical examination. All patients' asthma had been treated based on the GINA guidelines for $\geq$6 months and the antiasthma medication was showed on Table 1. We excluded patients with major medical disorders, such as diabetes, nephrotic diseases, autoimmune disorders, immunodeficiency, malignancy, and other chronic illnesses. The institutional review board of Chang Gung Memorial Hospital approved this study's design ((IRB number: 103-7085B), and all patients provided their informed consent.

2.2. Objective and subjective measurements

All patients were referred to the Otolaryngology Department and underwent thorough nasal endoscopy and sinus computed tomography (CT). The findings from these examinations were interpreted using the Lund–Kennedy endoscopy score[15] and the Lund–Mackay CT score,[16] respectively. Pulmonary function testing includes the evaluation of forced vital capacity (FVC), FEV_1, and the FEV_1/FVC ratio. Percentages of the predicted values for these tests can be calculated according to age, sex, height, and ethnicity.[17] Participants completed the ACT and the Sino-Nasal Outcome Test-22 (SNOT-22) questionnaires[18] at the same time to evaluate their asthma control and sinonasal symptoms. Additional data regarding the patients' clinical characteristics were collected from their medical records.

The ACT includes 5 items regarding asthma control: activity limitations, shortness of breath, waking up because of asthma symptoms, use of asthma relief medication, and a global evaluation of asthma control. The ACT items evaluate symptoms that were experienced during the last 4 weeks and are scored from 1 to 5, with a maximum score of 25 indicating perfectly controlled asthma.[7]

The SNOT-22 questionnaire is the most widely used and validated self-reported measure of nasal symptom severity and health-related QoL among patients with sinonasal conditions. The SNOT-22 questionnaire evaluates various symptoms, physical problems, functional limitations, and emotional consequences of having a sinonasal disorder.[18]

Table 1

Clinical characteristics of the study groups.

	CR	CRS	*P*
Cases, n	28	30	
Age, y	54.3±2.7	57.3±2.2	0.409
Male:female, n	20:8	11:19	0.008*
Atopy, n	11	14	0.571
CT score	0.6±0.2	12.0±1.0	<0.001†
Endoscopy score	0.4±0.1	6.2±0.5	<0.001†
Serum IgE, IU/mL	235.9±83.8	538.1±195.9	0.063
SNOT-22 score	54.2±5.1	59.5±5.0	0.597
ACT score	20.2±1.1	20.5±0.7	0.396
FVC (%) predicted	80.0±3.6	72.3±3.0	0.186
FEV_1 (%) predicted	69.4±4.1	63.5±3.2	0.191
FEV_1/FVC (%) predicted	84.1±3.5	80.6±3.0	0.396
Antiasthma medication, n			0.174
Step 1, as-needed SABA	2	1	
Step 2, low-dose ICS	10	6	
Step 3, low-dose ICS + LABA	8	12	
Step 4, medium/high-dose ICS + LABA	5	2	
Step 5, anti-IgE or OCS	3	9	

ACT = asthma control test, CR = chronic rhinitis, CRS = chronic rhinosinusitis, CT = computed tomography, E = SNOT-22, FEV_1 = forced expiratory volume in 1 s, FVC = forced vital capacity, ICS = inhaled corticosteroid, IgE = immunoglobulin, LABA = long-acting beta2-agonist, OCS = oral corticosteroid, SABA = short-acting beta2-agonist, Sino-nasal Outcome Test-22.
Data are reported as mean ± standard error or number.
* $P < 0.05$ using the chi-Square test.
† $P < 0.05$ using the Mann–Whitney *U* test.

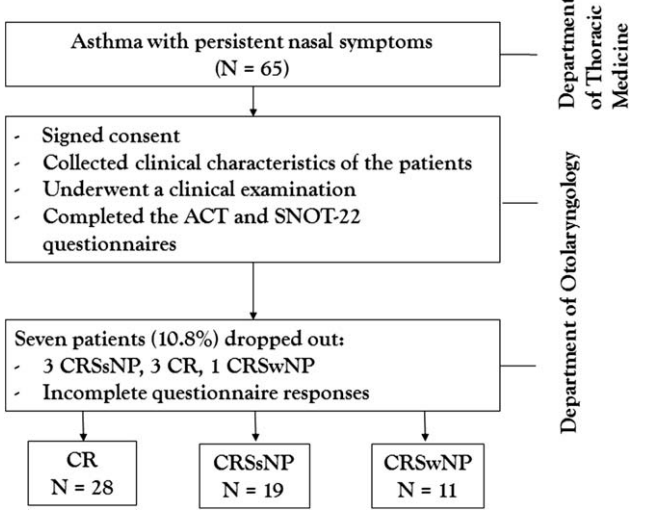

Figure 1. Study flow chart. ACT = asthma control test, CR = chronic rhinitis, CRSsNP = chronic rhinosinusitis without nasal polyps, CRSwNP = chronic rhinosinusitis with nasal polyps, SNOT-22 = Sino-nasal Outcome Test-22.

2.3. Diagnoses of chronic rhinosinusitis, chronic rhinitis, and nasal polyps

Cases of CRS were diagnosed using the criteria from the European position paper,[19] which requires the presence of 2 or more related symptoms for at least 12 weeks, as well as relevant endoscopic signs and/or CT findings. The related symptoms include facial pain/pressure, reduction or loss of smell, nasal blockage, or nasal discharge. At least one of the related symptoms should be nasal blockage/obstruction/congestion or nasal discharge. Cases of CR were defined as non-CRS cases with persistent nasal symptoms. Nasal polyps were identified using nasal endoscopy.

2.4. Statistical analyses

Data were reported as mean ± standard error or number (%), and were analyzed using GraphPad Prism software (version 5; GraphPad Prism Software Inc., San Diego, CA). Categorical

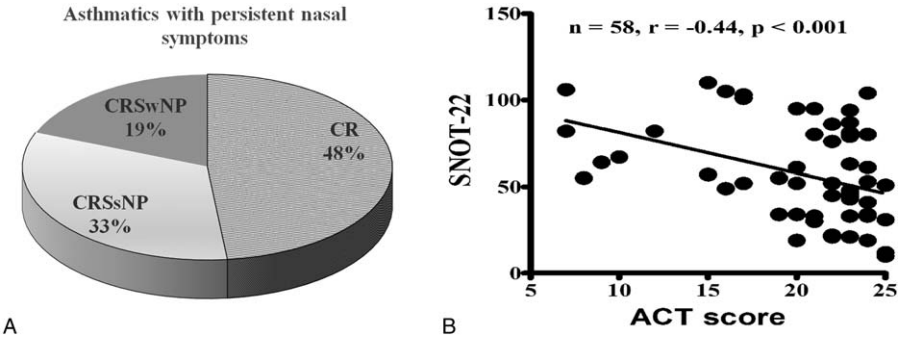

Figure 2. (A) Distribution of the upper airway diseases among patients with asthma and persistent nasal symptoms. (B) A good correlation was observed between the ACT and SNOT-22 scores. ACT = asthma control test, CR = chronic rhinitis, CRSsNP = chronic rhinosinusitis without nasal polyps, CRSwNP = chronic rhinosinusitis with nasal polyps, SNOT-22 = Sino-nasal Outcome Test-22.

variables were analyzed using the chi-square test or Fisher's exact test, as appropriate. Continuous variables were compared between 2 or 3 groups using the Mann–Whitney *U* test or the Kruskal–Wallis test, respectively. Correlations between 2 items were evaluated using Spearman's correlation coefficient. A *P*-value of < 0.05 was considered statistically significant.

3. Results

3.1. The participants' clinical characteristics

Figure 2A shows the final diagnoses of the upper airway inflammation among patients with asthma and persistent nasal symptoms, based on their symptoms, endoscopy findings, and CT findings. Among the 58 participants, 30 patients had CRS (52%), which included 19 cases (33%) of CRS without nasal polyps (CRSsNP) and 11 cases (19%) of CRS with nasal polyps (CRSwNP). Table 1 summarizes the participants' clinical characteristics. The patients with and without CRS did not exhibit any significant differences in the values for age, atopy, serum immunoglobulin E (IgE) levels, SNOT-22 score, ACT score, pulmonary function, and antiasthma medication. However, patients with CRS exhibited significantly higher endoscopy and CT scores, which indicated that these tests were the most reliable for diagnosing CRS.

3.2. Correlations between SNOT-22, ACT, and FEV_1 outcomes

We observed a good correlation between the ACT and SNOT-22 scores (Fig. 2B). The SNOT-22 nasal symptoms score had a crucial effect on asthma evaluation using the ACT question-

Table 2

The associations of SNOT-22 items with ACT score and predicted FEV1 among patients with asthma and persistent nasal symptoms.

	ACT score				Predicted FEV_1			
	CR		CRS		CR		CRS	
Item	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
1. Need to blow nose		0.250		0.391	–0.48	0.010*		0.824
2. Sneezing		0.262		0.838		0.423		0.322
3. Runny nose		0.572		0.619	–0.39	0.038*		0.171
4. Nasal blockage		0.383		0.751		0.101		0.760
5. Decreased sense of smell/taste		0.489		0.867		0.202	–0.47	0.009*
6. Cough	–0.46	0.028*	–0.69	0.001*	–0.42	0.025*		0.276
7. Postnasal discharge		0.959	–0.55	0.013*		0.369		0.243
8. Thick nasal discharge		0.216		0.415		0.057		0.328
9. Ear fullness		0.081		0.072		0.415		0.905
10. Dizziness		0.173	–0.73	<0.001*		0.755		0.837
11. Ear pain		0.607		0.358		0.780		0.402
12. Facial pain/ pressure		0.951		0.053		0.934		0.925
13. Difficulty falling asleep		0.193		0.088		0.198		0.622
14. Waking up at night		0.150	–0.47	0.037*		0.560		0.771
15. Absence of a good night's sleep		0.189	–0.49	0.027*		0.429		0.801
16. Waking up tired		0.235	–0.58	0.007*		0.863		0.235
17. Fatigue		0.616		0.120		0.934		0.503
18. Reduced productivity		0.266		0.209		0.134		0.051
19. Reduced concentration		0.299		0.093		0.344		0.417
20. Frustrated/ restless/irritable		0.560		0.136		0.176		0.290
21. Sad		0.895		0.105		0.871		0.129
22. Embarrassed		0.751		0.140		0.232		0.290
Total		0.178	–0.50	0.025*		0.165		0.595

ACT = asthma control test, CR = chronic rhinitis, CRS = chronic rhinosinusitis, FEV_1 = forced expiratory volume in 1 second, SNOT-22 = Sino-nasal Outcome Test-22.
Correlations were evaluated using Spearman's correlation coefficient.
* Statistical significance was set at $P < 0.05$.

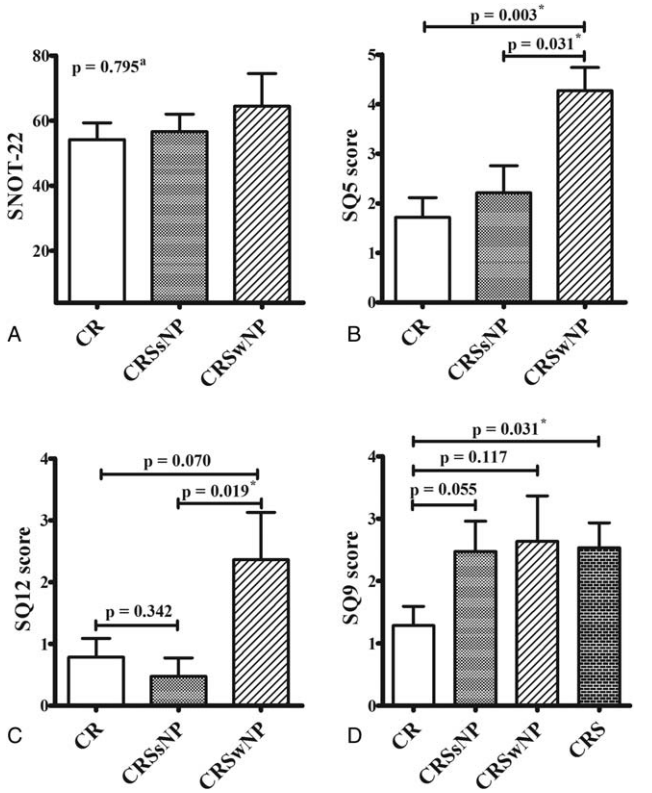

Figure 3. Comparing the SNOT-22 scores from patients with asthma and different sinonasal conditions. There were no significant differences in the total SNOT-22 scores when we compared patients who had asthma and CR, CRSsNP, or CRSwNP (A). Patient with CRSwNP exhibited higher scores for decreased sense of smell/taste (SQ5, B) and facial pain/pressure (SQ12, C), and patients with CRS exhibited higher scores for ear fullness (SQ9), compared to patients without these conditions (D). [a] The Kruskal–Wallis test was used to compare the 3 groups. *Statistical significance was set at $P < 0.05$. ACT, asthma control test, CR = chronic rhinitis, CRS = chronic rhinosinusitis, CRSsNP = chronic rhinosinusitis without nasal polyps, CRSwNP = chronic rhinosinusitis with nasal polyps, SNOT-22 = Sino-nasal Outcome Test-22.

naire. Among patients with asthma and CRS, the ACT score was closely related to the SNOT-22 items regarding cough, postnasal discharge, dizziness, waking up at night, absence of a good night's sleep, and waking up tired. Among patients with asthma and CR, the ACT score was closely related to cough symptoms in the SNOT-22 questionnaire (Table 2). We also evaluate the correlations between the predicted FEV_1 and the SNOT-22 items (Table 2). Among patients with CR, the predicted FEV_1 was closely related to the symptoms of needing to blow nose, runny nose, and cough. Among patients with CRS, the predicted FEV_1 was closely related to a decreased sense of smell/taste.

3.3. Comparing SNOT-22 items among patients with CR, CRSsNP, or CRSwNP

When we compared the SNOT-22 items between patients with asthma and CR, CRSsNP, or CRSwNP, we found that patients with asthma and CRSwNP had higher scores for a decreased sense of smell/taste and facial pain/pressure. In addition, patients with CRS had more severe symptoms for ear fullness, compared to patients without CRS. Nevertheless, the total SNOT-22 scores were not significantly different when we compared the 3 subgroups (Fig. 3).

3.4. Nasal symptoms and emergency clinic visits for acute asthma exacerbation

We retrospectively reviewed the participants' medical records and found that 16 patients had visited an emergency clinic because of acute asthma exacerbation during the previous 3 months. When we compared the patients with and without an emergency clinic visit, we found that patients with an emergency clinic visit had relatively high SNOT-22 scores, especially for the symptoms of sneezing, runny nose, nasal blockage, cough, and dizziness (Fig. 4).

4. Discussion

To the best of our knowledge, this is the first study to examine the effect of nasal symptoms on the evaluation of asthma control using disease-specific questionnaires. This article described the impact of nasal symptoms on the evaluation of asthma control including QoL, pulmonary function, and emergency clinic visits in a study population with persistent nasal symptoms, even after maximal medical therapy, to emphasize the importance of simultaneous care of nose during management of asthma. In the present study, we used the questionnaires to evaluate nasal symptoms and asthma control among patients with asthma and persistent nasal symptoms, and found that more severe sinonasal symptoms were associated with poorly controlled asthma. ACT scores among patients with asthma and CRS were closely related to the symptoms of cough, post-nasal discharge, dizziness, waking up at night, absence of a good night's sleep, and waking up tired. Furthermore, the predicted FEV_1 among patients with asthma and CR was closely associated with the symptoms of needing to blow nose, runny nose, and cough. In this context, greater amounts of post-nasal discharge, as well as the associated cough and worsened sleep quality, may contribute to reductions in QoL and asthma control among patients with asthma and CRS. However, nose-related allergy symptoms were associated with FEV_1 among patients with asthma and CR. Therefore, our findings appear to indicate that asthma stability is closely related to control of the sinonasal disorder, and vice versa. The nasal symptoms have significant effects on the subjective and objective evaluations of asthma control.

Several tools have been developed to assess the patients' quality of life and symptoms' severity for asthma and for rhinitis, or both.[20–22] However, there is no questionnaire assess CRS and asthma simultaneously.[23] Besides, it is difficult to distinguish between CRS and CR using only symptomatic evaluations of patients with asthma and nasal symptoms, although this evaluation is important for managing the patients' sinonasal conditions.[19] Among the 58 participants in the present study, for example, approximately half of the patients had CRS (52%). Based on the united airways concept, patients with lower airway inflammation typically exhibit parallel inflammation in the upper airway. Most of the inflammation in the upper airway can be managed well with or without medication for nasal symptoms when the asthma were being treated. However, in this study, we prospectively recruited patients with asthma and "persistent" nasal symptoms who were being treated at Thoracic Medicine Department for ≥3 months. The enrolled population was those with more severe symptoms and required surgical intervention. That would be the reason for the high incidence of CRS comorbidity in this study population.

Our results revealed no significant differences in the SNOT-22 total scores and most single-item scores when we compared

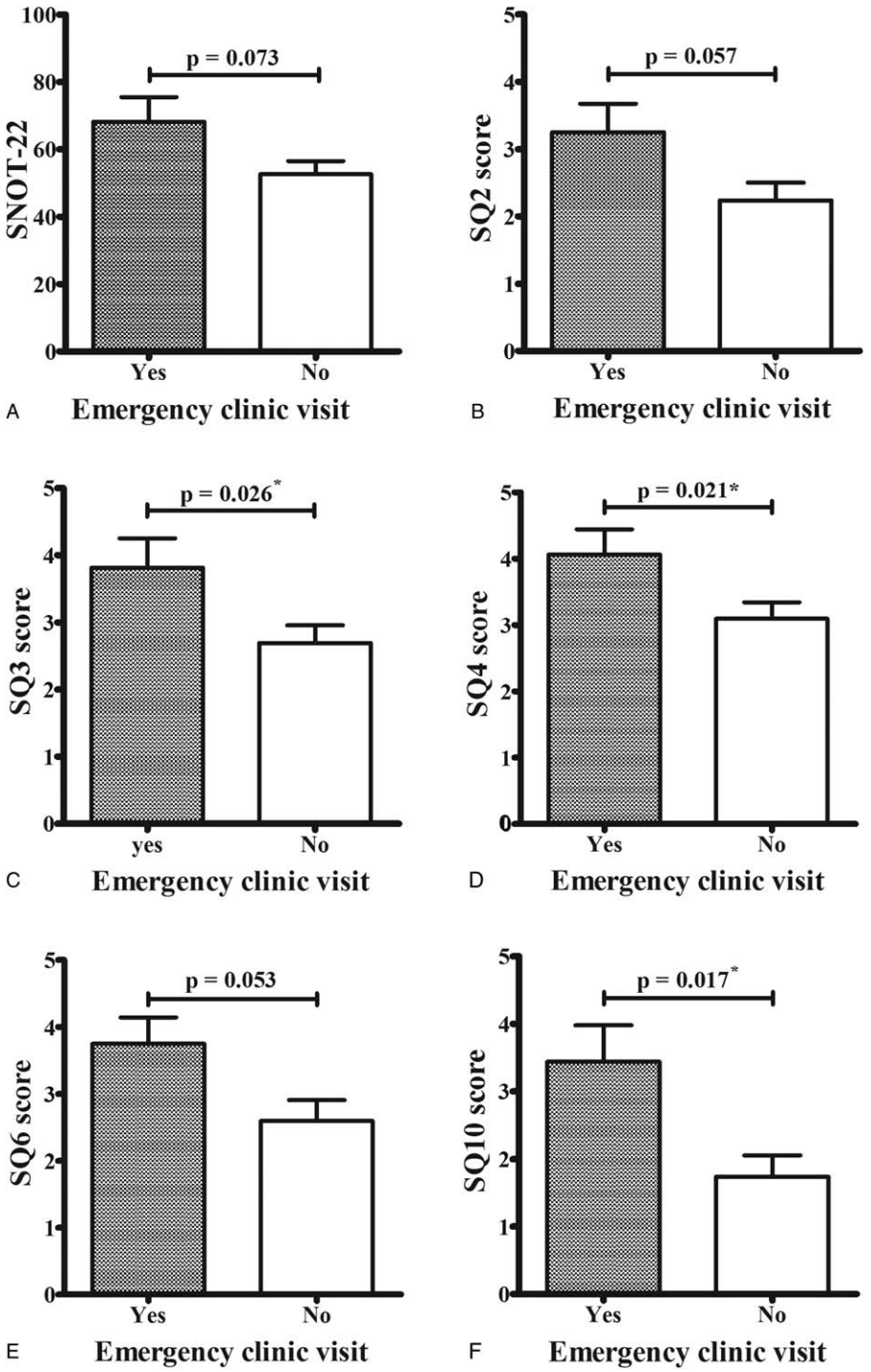

Figure 4. Nasal symptoms and emergency clinic visits for acute asthma exacerbation. Patients with emergency clinic visits during the previous 3 months had higher SNOT-22 scores (A), especially for the symptoms of sneezing (SQ2, B), runny nose (SQ3, C), nasal blockage (SQ4, D), cough (SQ6, E), and dizziness (SQ10, F). *Statistical significance was set at $P < 0.05$.

the subgroups with the 3 different sinonasal conditions. The notable exceptions were patients with CRS exhibiting higher scores for fullness, and the patients with CRSwNP exhibiting higher scores for decreased sense of smell/taste and facial pain/pressure, compared to their counterparts who did not have these conditions. Therefore, endoscopy and CT appear to be the most reliable methods for diagnosing these sinonasal conditions.

Emergency clinic visits because of acute asthma exacerbation is another important indicator of asthma control, risk of adverse outcomes, and increased healthcare utilization.[24] In the present study, patients with an emergency clinic visit because of acute asthma exacerbation during the previous 3 months exhibited relatively high SNOT-22 scores, especially for the symptoms of sneezing, runny nose, nasal blockage, cough, and dizziness. Therefore, it appears that it is important to simultaneously

evaluate and treat nose-related conditions in patients with asthma.

Given that the airway is a continuous structure that extends from the nose to the alveolar units of the lung, which is constantly exposed to the outside world, inflammation throughout the airway may be induced by exposure to various irritants, allergens, micro-organisms, and other environmental factors.[25–27] Furthermore, upper and lower airway inflammation may be triggered by a systemic response to mediators of inflammation. Moreover, changes in the inspired air (e.g., dry air, cold air, or nitric oxide-depleted air) can be caused by nasal obstruction or aspiration of sinus secretions into the lower airways, which would interfere with the function of the lower airway.[11,28,29] Therefore, although asthma and sinonasal disorders (e.g., CRS and CR) appear to be distinct diseases, we believe that they should be viewed and treated as common airway diseases.

The present study has several limitations that warrant consideration. The first limitation is the absence of strict inclusion criteria, which created a heterogeneous group of patients with various sinonasal diseases, asthma severities, and treatment modalities. Nevertheless, our patient population's heterogeneity reflects the reality of daily clinical practice at an outpatient clinic, and it is important to note that we found that sinonasal symptoms had significant effects on the subjective and objective aspects of asthma control. The second limitation is that we performed a cross-sectional analysis and are unable to comment on the dynamic changes in the evaluation and control of the upper and lower airways (e.g., before and after nasal surgery or medical treatment). The cross-sectional design also precludes any conclusions regarding the causality of the relationships that we observed. Therefore, longitudinal cohort studies are needed to validate our findings regarding the connections between nasal symptoms and asthma control evaluation.

5. Conclusion

We found that sinonasal symptom severity was closely associated with asthma control status (i.e., ACT score, FEV_1, and acute exacerbation) among patients with asthma and persistent nasal symptoms. This result highlights the importance of simultaneously managing sinonasal disorders during the evaluation and treatment of patients with asthma. Furthermore, based on our findings, we believe that upper and lower airway inflammation should be considered and treated concurrently.

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