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ORIGINAL RESEARCH

Impact of Comorbid Asthma on Life Quality of Patients with Chronic Rhinosinusitis and Nasal Polyps

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Objective: This study aimed to characterize the clinical features of patients with comorbid asthma and chronic rhinosinusitis with nasal polyps and to evaluate the impact of comorbid asthma on the quality of life of these patients.

Methods: Adult patients with bilateral chronic rhinosinusitis with nasal polyps scheduled for sinus surgery were prospectively enrolled. Clinical information of the participants, including laboratory data and computed tomography images. The Sinonasal Outcome Test-22 was used to evaluate nasal symptoms and quality of life impairment of participants.

Results: A total of 170 participants were recruited, of whom 32 (18.8%) had comorbid asthma. Compared to patients with chronic rhinosinusitis with nasal polyps and without comorbid asthma, patients with asthma exhibited significant higher age, computed tomography ethmoid/maxillary ratio, computed tomography olfactory cleft opacification score, serum total IgE, serum eosinophil cationic protein levels, and blood and tissue eosinophil count. Patients with comorbid chronic rhinosinusitis with nasal polyps and asthma exhibited significant higher total, and rhinologic- and sleep-related domains of the Sinonasal Outcome Test-22 than did those without comorbid asthma.

Conclusion: Comorbid asthma is associated with more severe type 2 eosinophilic inflammation and has a significant impact on the nasal symptoms and quality of life of patients with chronic rhinosinusitis with nasal polyps, particularly as shown in the rhinologic- and sleep-related domains of the Sinonasal Outcome Test-22. This information may assist physicians in decision-making when treating these patients.

Plain Language Summary: This study prospectively enrolled 170 adult patients with bilateral chronic rhinosinusitis with nasal polyps including 32 (18.8%) patients had comorbid asthma. Clinical characteristics, computed tomographic features, tissue eosinophil counts, and quality of life of participants were evaluated.

Comorbid asthma is associated with more severe type 2 eosinophilic inflammation including higher computed tomographic ethmoid/maxillary ratio, olfactory cleft opacification score, serum total IgE, serum eosinophil cationic protein levels, blood eosinophil count and tissue eosinophil count, and has a significant impact on the nasal symptoms and quality of life of patients with chronic rhinosinusitis with nasal polyps, particularly as shown in the rhinologic- and sleep-related domains of the Sinonasal Outcome Test-22. This information may assist physicians in decision-making when treating these patients.

Keywords: asthma, chronic rhinosinusitis with nasal polyp, quality of life, sinonasal outcome test-22, sleep dysfunction

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Introduction

Chronic rhinosinusitis (CRS) is defined as a persistent inflammation of the nasal cavity and paranasal sinuses that lasts for more than 12 weeks.[1] It has conventionally been categorized into CRS with (CRSwNP) and CRS without nasal polyps (CRSsNP).[2] CRSwNP comprises about 2% of CRS cases of CRS and usually exhibits a greater burden of disease compared to those without nasal polyps.[3] Besides, CRS is also divided into endotypes based on the activation of different inflammatory T cells and their associated inflammatory mediators.[4,5] According to previous reports, type 2 is the prevalent form of CRSwNP, among for more than 80% of patients in Western countries, and with an incidence of approximately 40–60% in various Asian regions.[6] Pathophysiologically, type 2 CRS is characterized by elevated levels of interleukin (IL)-4, IL-5, and IL-13, and a strong presence of eosinophils, type 2 innate lymphoid cells, macrophages, and mast cells in the nasal tissue.[7,8] This inflammatory cascade contributes not only to the chronic inflammatory state of the sinonasal mucosa, but also to the remodeling and growth of nasal polyps.[9]

Severe type 2 CRSwNP is challenging to treat and is susceptible to recurrence after sinus surgery.[4] Therefore, the latest European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS2020) suggested different therapeutic strategies should be used for patients with type 2 CRS and non-type 2 CRS.[1] This concept is particularly important in managing patients with CRS in an era in which a growing number of biologics targeting type 2 inflammatory mediators are being introduced for CRSwNP.[10]

The prevalence of asthma among patients with CRSwNP is high, based on a concept of united airways and their shared inflammatory pathophysiology.[11] Comorbid asthma is also a significant clinical marker of severe type 2 CRS and is a risk factor for resistance to treatments, such as endoscopic sinus surgery (ESS).[12,13] Compared to CRS patients without asthma, patients with CRS and asthma usually have worse treatment outcomes, a lower quality of life (QoL) improvement, and a higher rate of revision surgery after ESS.[13] Patients with CRSwNP and comorbid asthma may require more intensive clinical care and observation than do those without comorbid asthma.

Therefore, this study characterized the clinical features of patients with comorbid asthma and CRSwNP, and evaluated the impact of comorbid asthma on the QoL of patients with CRSwNP, with a view to helping clinicians better assess patients with CRSwNP and asthma, and providing optimal therapeutic strategies for these patients with severe type 2 airway inflammation.

Methods

Patients

After approval of the study by the Institutional Review Board of Chang Gung Medical Foundation (IRB numbers: 202002219A3, 202102257A3, and 202202075A3), consecutive adult patients with bilateral CRSwNP were prospectively recruited between 2020 and 2023. Patients who were enrolled signed informed consent. All study procedures were performed in accordance with the relevant guidelines and regulations, and the Declaration of Helsinki.

The diagnosis of CRSwNP followed the EPOS2020 definition.[1] In these patients, conservative medical treatments, including intranasal corticosteroids and nasal douches, had failed and they were scheduled for ESS. Comorbid asthma was diagnosed based on fulfillment of the diagnostic criteria of the Global Initiative for Asthma guidelines.[14] Patients with comorbid asthma maintained moderate to good control of asthma under inhaled corticosteroid prior to ESS. The presence of nasal polyps was confirmed on the basis of endoscopic evaluations.

Individuals with sinonasal neoplasms, simultaneous immunological complications, or mucociliary disorder, such as cystic fibrosis and primary ciliary dyskinesia; or a history of taking systemic corticosteroids or immunosuppressive therapy within 3 months before enrolment, were excluded.

Clinical information of the participants, including a medical history of allergy, relevant clinical symptoms, laboratory data, and imaging studies were collected. Laboratory examinations included peripheral blood inflammatory cell counts, total IgE, immunoCAP tests, and eosinophil cationic protein (ECP) levels. A nasal polyp scoring system was used on nasal endoscopy findings, as described previously.[15]

Computed Tomographic (CT) Image Evaluation

The Lund–Mackay (L-M) score was used for radiologic quantification of CRS severity.[16] Two rhinologists (C.-C. H. and P.-W.W.) independently reviewed the CT images based on consensus. In brief, the frontal, anterior and posterior ethmoidal, maxillary, and sphenoid sinuses, and ostiomeatal complex were assigned scores of 0 (no abnormalities), 1 (partial opacification), or 2 (complete opacification), respectively. The CT score for each patient ranged from 0 to 24. Then, the ethmoid sinus/maxillary sinus (E/M) ratio was calculated by dividing the average CT scores of the anterior and posterior ethmoid sinuses by that of the maxillary sinuses.[17,18] On the other hand, the degree of opacification in the olfactory cleft (OC) was assessed on CT images and was rated from 0 to 3, as clear (score 0), less than half (score 1), more than half (score 2), or total opacification (score 3), on each side of the OC, respectively.[19]

QoL Evaluation

The Sinonasal Outcome Test-22 (SNOT-22) was used to assess the preoperative nasal symptoms and QoL of participants.[20] The SNOT-22 is a 22-item therapeutic outcome measure designed for patients with chronic sinonasal conditions. Patients completed the survey 1 day before surgical treatment. The participant evaluated the questions based on a scale, where 0 indicates no problem, 1 indicates a very mild problem, 2 indicates a mild or slight problem, 3 indicates a moderate problem, 4 indicates a severe problem, and 5 indicates a problem as severe as it could be. Higher scores on the SNOT-22 survey indicate more severe symptoms or worse patient function (total score range from 0 to 110). For analysis, the SNOT-22 questionnaire was categorized into five domains according to previous studies: rhinologic domain, ear/facial domain, sleep domain, functional domain, and emotional domain.[21]

Quantification of Tissue Eosinophil Count

Hematoxylin and eosin staining was performed on a standard 5-μm section of a nasal polyp specimen. The tissue eosinophil count (TEC) was determined in three microscopic fields (× 400 magnification' high-power field, HPF) with the most severe inflammatory cell infiltration and intact epithelium per tissue section.

Statistical Analyses

Data are reported as mean ± standard deviation or number (%). Statistical analyses were performed using SPSS Statistics v27.0. (IBM Corp, Armonk, NY, USA) and GraphPad Prism 5 (GraphPad Prism Software, Inc, San Diego, CA, USA). Categorical variables were analyzed using the x^2 test or Fisher's exact test, as appropriate. Continuous variables were compared between the two groups using the Mann–Whitney *U*-test. Regression analyses were performed to assess the association between comorbid asthma and clinical variables. Receiver operating characteristic (ROC) curves were generated and the area under the ROC curve (AUC) was calculated to identify the cutoff values of clinical variables for predicting comorbid asthma in patients with CRSwNP. A nomogram model was constructed to predict the probability of comorbid asthma being present in patients with CRSwNP, based on the results of the regression analysis. $P < 0.05$ was defined as statistical significance. The power was calculated as 83.7% of the difference between the primary outcomes in the study groups.

Results

Clinical Characteristics of Participants

A total of 170 adult patients with bilateral CRSwNP were enrolled, including 121 males and 49 females. Demographic data are shown in Table 1. Comorbid asthma was present in 32 (18.8%) patients, including 14 (43.8%) patients who had a history of previous sinus surgery. The average Endoscopic Nasal Polyp scores were 5.4 ± 1.6, 5.4 ± 1.8 and 5.5 ± 1.6 in total, patients with and without asthma respectively. The average CT L-M scores were 17.0 ± 3.8, 17.9 ± 3.8 and 16.8 ± 3.8 in total, patients with and without asthma, respectively. These values indicated a high disease burden in this study cohort. Compared to patients without comorbid asthma, patients with asthma exhibited significantly higher age, CT E/M ratio, CT OC score,

Table 1 Clinical Characteristics of Participants

	Total	With asthma	Without asthma	P value†
Number	170	32	138	
Age (years)	46.6 ± 13.6	51.0 ± 11.4	45.6 ± 13.9	0.026*
Female: male	49:121	13: 19	36:102	0.102
Smoking, n (%)	47 (27.6%)	6 (18.8%)	41 (29.7%)	0.212
Allergy	84 (49.4)	23 (71.9%)	61 (44.2%)	0.005**
Previous sinus surgery, n (%)	55 (32.4%)	14 (43.8%)	41 (29.7%)	0.126
Nasal polyp score	5.4 ± 1.6	5.4 ± 1.8	5.5 ± 1.6	0.896
CT L-M score	17.0 ± 3.8	17.9 ± 3.8	16.8 ± 3.8	0.129
CT E/M ratio	1.2 ± 0.4	1.3 ± 0.4	1.1 ± 0.3	0.011*
CT OC score	4.2 ± 1.9	4.9 ± 1.5	4.1 ± 1.9	0.011*
Serum IgE (KU/L)	210.9 ± 451.1	441.4 ± 880.0	158.9 ± 254.6	<0.001***
ECP (μg/L)	42.3 ± 47.8	68.8 ± 71.1	36.3 ± 38.7	0.015*
WBC (1000/uL)	7.4 ± 1.8	7.4 ± 2.0	7.4 ± 1.8	0.930
Neutrophil (%)	60.2 ± 8.8	58.8 ± 10.0	60.5 ± 8.5	0.421
Lymphocyte (%)	29.1 ± 7.0	27.4 ± 7.1	29.5 ± 7.0	0.113
Eosinophil (%)	4.3 ± 4.1	6.8 ± 6.1	3.7 ± 3.2	0.003**
BEC (/uL)	304.9 ± 283.4	463.3 ± 377.7	268.1 ± 244.1	0.002**
TEC, (/HPF)	43.5 ± 56.7	73.2 ± 69.5	36.6 ± 51.2	0.002**

Notes: Data are represented as mean ± stand deviation. SNOT-22, sinonasal outcome test-22; †Comparison between the participants with and without asthma was performed using the Mann–Whitney *U*-test for continuous variables and Chi-square test or Fisher exact test for categorical variables. *P < 0.05, **P < 0.01, ***P < 0.001.

Abbreviations: CT, computed tomography; L-M score, Lund-Mackay score; E/M ratio, ethmoid/maxillary ratio; OC score, olfactory cleft opacification score; IgE, immunoglobulin E; ECP, eosinophil cationic protein; WBC, white blood cell; BEC, blood eosinophil count; TEC, tissue eosinophil count; HPF, high power field.

serum IgE, serum ECP, blood eosinophil percentile and count (BEC), and TEC values. These findings indicated that more severe type 2 eosinophilic inflammation was observed in patients with CRSwNP and comorbid asthma.

QoL Evaluation

The result of preoperative SNOT-22 was demonstrated in Table 2. The average scores of SNOT-22 were 48.3 ± 19.8, 55.5 ± 18.2 and 46.7 ± 19.9 in total, patients with and without asthma respectively. The average Asthma Control Test score was 19.4 ± 4.2 in participants with asthma. Compared to patients without comorbid asthma, patients with asthma exhibited significant higher total,

Table 2 SNOT-22 Questionnaire Evaluation of Participants

	Total	With Asthma	Without Asthma	P value†
Number	170	32	138	
SNOT-22 total	48.3 ± 19.8	55.5 ± 18.2	46.7 ± 19.9	0.020*
Rhinologic domain	24.4 ± 7.8	28.1 ± 5.7	23.5 ± 7.9	0.005**
1. Need to blow nose	3.3 ± 1.4	3.7 ± 1.2	3.2 ± 1.4	0.039*
2. Sneezing	2.1 ± 1.3	2.5 ± 1.2	2.0 ± 1.3	0.067
3. Runny nose	3.0 ± 1.4	3.4 ± 1.3	3.0 ± 1.5	0.161
4. Nasal blockage	3.9 ± 1.3	4.4 ± 0.9	3.8 ± 1.3	0.017*
5. Decreased sense of smell/taste	3.7 ± 1.7	4.3 ± 1.2	3.6 ± 1.7	0.048*
6. Cough	1.9 ± 1.5	2.6 ± 1.4	1.7 ± 1.4	0.001**
7. Post-nasal discharge	3.2 ± 1.5	3.8 ± 1.4	3.1 ± 1.5	0.006**
8. Thick nasal discharge	3.3 ± 1.5	3.4 ± 1.5	3.2 ± 1.4	0.464

(*Continued*)

Table 2 (Continued).

	Total	With Asthma	Without Asthma	P value†
Ear/facial domain	4.4 ± 4.1	4.5 ± 3.6	4.4± 3.2	0.568
9. Ear fullness	1.7 ± 1.6	1.8 ± 1.7	1.7 ± 1.6	0.626
10. Dizziness	1.3 ± 1.4	1.3 ± 1.2	1.3 ± 1.4	0.793
11. Ear pain	0.7 ± 1.0	0.7 ± 1.0	0.7 ± 1.0	0.875
12. Facial pain/pressure	0.7 ± 1.2	0.6 ± 1.0	0.7 ± 1.3	0.981
Sleep related domain	9.1 ± 6.1	11.3 ± 6.3	8.6 ± 6.0	0.029*
13. Difficulty falling asleep	2.0 ± 1.7	2.8 ± 1.7	1.9 ± 1.7	0.009**
14. Wake up at night	2.1 ± 1.7	2.8 ± 1.8	1.9 ± 1.7	0.013*
15. Lack of a good night's sleep	2.5 ± 1.8	3.0 ± 1.8	2.4 ± 1.7	0.049*
16. Wake up tired	2.5 ± 1.6	2.7 ± 1.8	2.5 ± 1.6	0.372
Functional domain	6.4 ± 4.1	6.6 ± 4.4	6.3 ± 4.1	0.703
17. Fatigue	2.4 ± 1.6	2.6 ± 1.8	2.4 ± 1.5	0.451
18. Reduced productivity	2.0 ± 1.5	1.9 ± 1.6	2.0 ± 1.5	1.000
19. Reduced concentration	2.0 ± 1.4	2.0 ± 1.4	2.0 ± 1.4	0.761
Emotional domain	4.1 ± 3.9	5.1 ± 4.3	3.8 ± 3.8	0.142
20. Frustrated/restless/irritable	1.7 ± 1.6	2.1 ± 1.6	1.6± 1.5	0.160
21. Sad	1.3 ± 1.4	1.6 ± 1.6	1.2 ± 1.4	0.165
22. Embarrassed	1.1 ± 1.3	1.4 ± 1.6	1.0 ± 1.2	0.371

Notes: Data are represented as mean ± stand deviation. SNOT-22, sinonasal outcome test-22. †Comparison between the participants with and without asthma was performed using the Mann–Whitney *U*-test. *P < 0.05, **P < 0.01.

rhinologic domain, and sleep-related domains of the SNOT-22 questionnaire. Specifically, patients with comorbid CRSwNP and asthma experienced more severe symptoms in terms of needing to blow their nose, sneezing, nasal blockage, decreased sense of smell/taste, coughing, post-nasal discharge, difficulty falling asleep, waking up at night, and lacking a good night's sleep than did those without asthma.

Logistic Regression Analysis

Associations between clinical variables and comorbid asthma in patients with CRSwNP were determined using logistic regression analysis (Table 3). In univariate analysis, age, SNOT-22 score, E/M ratio, OC score, serum total IgE level, serum ECP, BEC, and TEC were all significant predictors of comorbid asthma. Age, SNOT-22 score, E/M ratio, serum ECP, BEC, and TEC remained statistically significant in multivariate analysis.

Table 3 Logistic Regression Analyses of Clinical Variables for Comorbid Asthma in Patients with CRSwNP

Variables	Univariate Analysis		Multivariate Analysis	
	Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
Age	1.03 (1.00–1.06)	0.044*	1.01 (1.00–1.02)	0.014*
Gender	0.52 (0.23–1.15)	0.105		
Smoking	0.54 (0.21–1.41)	0.209		
Previous sinus surgery	1.84 (0.84–4.05)	0.129		
SNOT-22	1.02 (1.00–1.04)	0.024*	1.04 (1.01–1.07)	0.016*
Nasal polyp score	0.98 (0.78–1.24)	0.870		
L-M score	1.08 (0.97–1.20)	0.147		
E/M ratio	4.46 (1.54–12.92)	0.006**	6.77 (1.16–39.66)	0.034*

(*Continued*)

Table 3 (Continued).

Variables	Univariate Analysis		Multivariate Analysis	
	Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
OC score	1.36 (1.05–1.75)	0.020*	1.06 (0.77–1.46)	0.744
Serum IgE (KU/L)[a]	1.00 (1.00–1.00)	0.026*	1.00 (0.99–1.00)	0.276
Serum ECP (μg/L)	1.01 (1.00–1.02)	0.008**	1.01 (1.00–1.02)	0.037*
BEC (/uL)	1.00 (1.00–1.00)	0.002**	1.00 (1.00–1.01)	0.018*
TEC (/HPF)	1.01 (1.00–1.02)	0.002**	1.01 (1.00–1.02)	0.049*

Note: *P < 0.05, **P < 0.01.

Abbreviations: CI, confidence interval. SNOT-22, sinonasal outcome test-22; L-M score, Lund-Mackay score; E/M ratio, ethmoid/maxillary ratio; OC score, olfactory cleft opacification score; IgE, immunoglobulin E; ECP, eosinophil cationic protein; BEC, blood eosinophil count; TEC, tissue eosinophil count; HPF, high power field.

Associations between SNOT-22 subdomains and comorbid asthma in patients with CRSwNP were also evaluates by using logistic regression analysis. In univariate analysis, rhinologic domain (odds ratio [OR] 1.10, P = 0.003) and sleep-related domain scores (OR 1.08, P = 0.027) were significant predictors of comorbid asthma. The rhinologic domain score (OR 1.09, P = 0.013) remained statistically significant in multivariate analysis.

Using Clinical Variables to Predict Comorbid Asthma

ROC curves were generated, and AUC values were calculated to evaluate the sensitivity and specificity of clinical variables for predicting comorbid asthma in the current study cohort (Figure 1). The ROC curves of BEC (1a, AUC = 0.680, P = 0.002), serum total IgE (1b, AUC = 0.717, P < 0.001), serum ECP (1c, AUC = 0.648, P = 0.014), E/M ratio (1d, AUC = 0.643, P = 0.012), OC score (1e, AUC = 0.640, P = 0.014), SNOT-22 (1f, AUC = 0.632, P = 0.020), age (1g, AUC = 0.626, P = 0.026), and TEC (1h, AUC = 0.678, P = 0.002) had AUCs significantly greater than 0.5. The optimal cutoff values for these clinical variables were indicated (maximizing the sum of sensitivity and specificity). In the subdomain analysis of the SNOT-22 data, the ROC curves of rhinologic (AUC = 0.662, P = 0.004) and sleep-related (AUC = 0.624, P = 0.048) domains exhibited AUCs significantly greater than 0.5.

Nomogram for Predicting Comorbid Asthma in Patients with CRSwNP

Given the absence of a single ideal predictor in the ROC analysis, a nomogram was constructed to predict the probability of comorbid asthma in patients with CRSwNP, based on the results of the logistic regression analysis (Figure 2). In the nomogram, each variable value indicated a corresponding score. The total points were obtained by summing the corresponding scores from the four variables and indicated the predicted probability of comorbid asthma being present in an individual (2a). The ROC curve illustrated the nomogram's discrimination ability, with an AUC of 0.844 (95% confidence interval, 0.813–0.876) (2b).

Discussion

This study sought to identify the clinical features of patients with comorbid asthma and CRSwNP and to evaluate the impact of comorbid asthma on the QoL of these patients. We found that patients with comorbid asthma were older, and had significantly higher CT E/M ratios, CT OC scores, serum total IgE, serum EC, BEC, and TEC values. Moreover, their total, and rhinologic- and sleep-related domain scores on the SNOT-22 scores were higher than those of patients without comorbid asthma.

Epidemiological, clinical, and pathophysiological studies have suggested that CRSwNP and asthma are closely linked and frequently coexist.[22,23] Mucosal inflammation in the sinonasal area and lower airways is directly associated, and the type 2 inflammatory profiles of nasal and bronchial biopsies in patients with CRSwNP are significantly correlated, further supporting the united airways concept.[24,25] CRSwNP with comorbid asthma is characterized by tissue eosinophilia and high local IgE

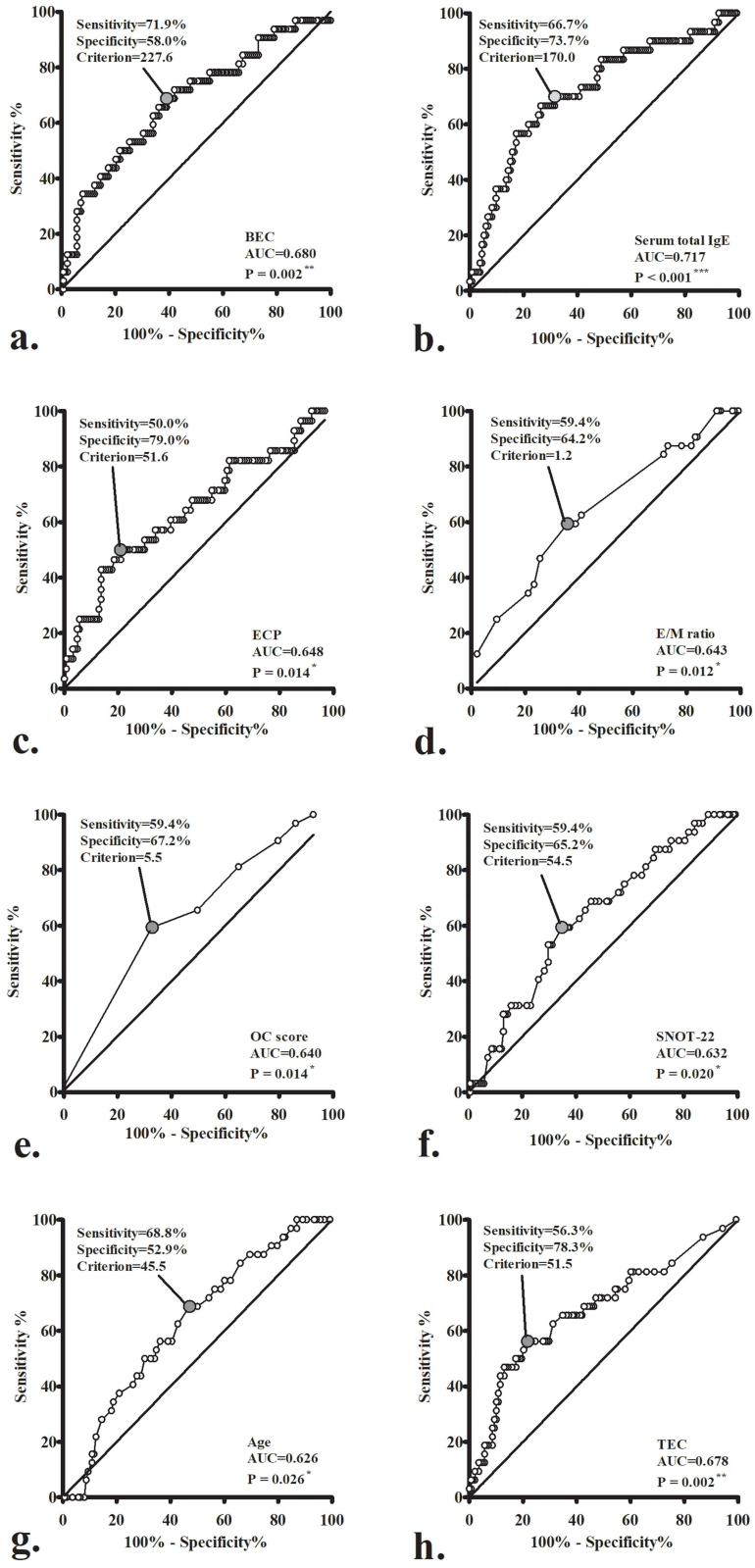

Figure 1 Receiver operating characteristic curves to detect comorbid asthma in patients with chronic rhinosinusitis and nasal polyp using the clinical variables including blood eosinophil count (BEC) (**a**), serum total IgE (**b**), serum eosinophil cationic protein (**c**), ethmoid/maxillary (E/M) ratio (**d**), olfactory cleft opacification (OC) score (**e**), sinonasal outcome test-22 (SNOT-22) (**f**), age (**g**), and tissue eosinophil count (TEC) (**h**). AUC, area under curve. *P< 0.05; **P < 0.01; ***P < 0.001.

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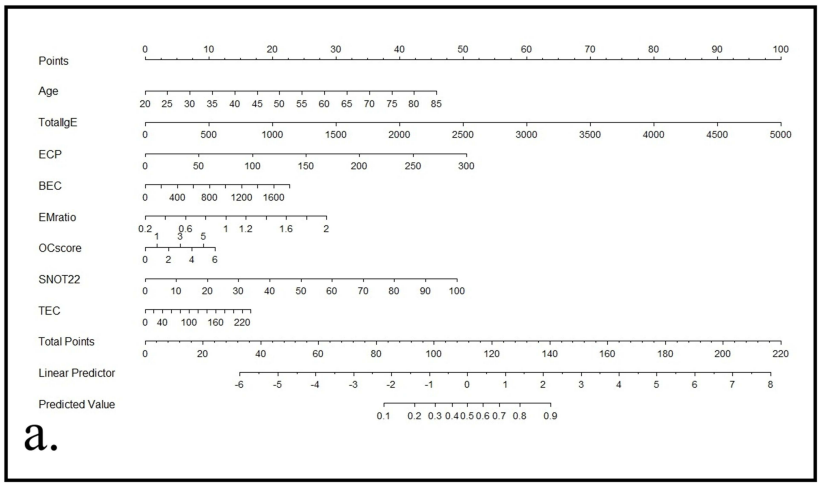

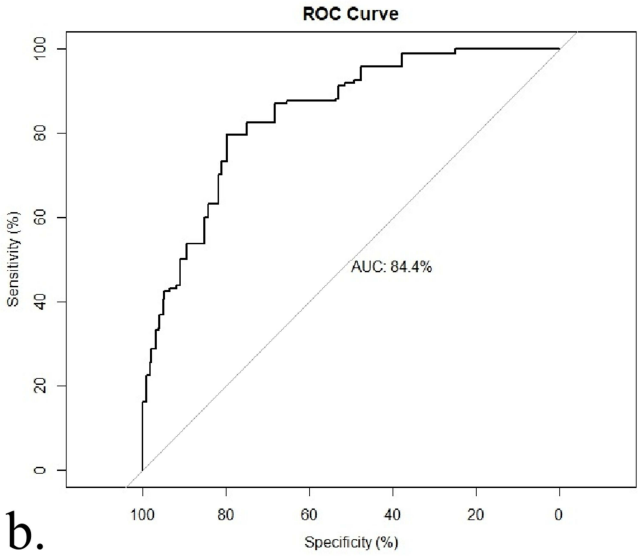

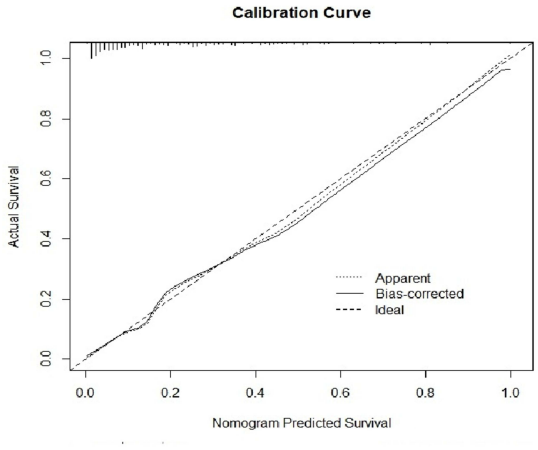

Figure 2 The nomogram developed to predict the probability of comorbid asthma in patients with chronic rhinosinusitis and nasal polyp (**a**). Receiver operating characteristic curve of the nomogram model was plotted (**b**). Calibration curve of nomogram model was presented (**c**). The ideal line represents the ideal model which predicts probabilities that perfectly match the actual probabilities. The Apparent line and bias-corrected line represent the nomogram model before and after bootstrap resampling method, respectively.

levels.[11,26,27] Patients with CRSwNP and asthma had higher counts of type 2 biomarkers compared with patients with CRSwNP but without asthma. Significant correlations were observed between SNOT-22 vs BEC and total IgE.[28] Thus, comorbid asthma is a significant clinical marker of severe type 2 CRSwNP and is an important risk factor for resistance to therapeutic interventions, such as recurrence of polyps after ESS.[12,13] On the other hand, patients with moderate to severe asthma and nasal polyps have higher levels of BEC and FeNO than those without nasal polyp.[29] Furthermore, asthma is usually difficult to control in the presence of nasal polyposis, is more prone to exacerbation, and presents with increased airway obstruction and more extensive eosinophilic inflammation.[23,30] Therefore, identifying comorbid asthma is important in managing patients with CRSwNP, and vice versa.[31]

In the current study, 32 of 170 patients with CRSwNP had confirmed comorbid asthma and exhibited more severe type 2 inflammatory characteristics, including higher E/M ratios, OC scores, serum total IgE levels, serum ECP levels, BECs, and TECs, than those without asthma. Patients with CRSwNP and comorbid asthma also experienced more severe symptoms and poorer QoL than those without asthma, as evaluated by using the SNOT-22, particularly in the rhinologic- and sleep-related subdomains. The results indicated a significant higher disease burden of airway inflammation in patients with CRSwNP and comorbid asthma, which implies that they require more intensive clinical care and observation, not only in terms of nasal symptoms, but also in terms of sleep dysfunction.

According to previous reports, type 2 eosinophilic CRS is prevalent among more than 80% of CRSwNP patients, while the prevalence of comorbid asthma in CRS patients is around 60% in Western countries.[6] However, in various Asian regions, the incidence of type 2 CRS in patients with CRSwNP is approximately 40–60%, while the prevalence of comorbid asthma in CRS patients is about 10–20%.[6,32,33] Mixed-type CRSwNP is also more prevalent in Asian patients.[34] In the current study cohort, the prevalence of comorbid asthma in patients with CRSwNP was 18.8%, although the disease extent as evaluated by the nasal polyp score and CT L-M score were high. The inflammatory patterns in CRSwNP in patients from different regions differ significantly.[6] This further emphasizes the importance of identifying comorbid asthma in CRSwNP patients in these areas, because it may be easily undiagnosed due to its relatively low prevalence. Previous studies have also revealed that, in many patients with CRSwNP, asthma remained undiagnosed.[11] For example, Ragab et al[35] reported that 60% of patients with CRSwNP have some form of lower airway involvement, including asthma in 24% of patients and small airway disease in 36% of patients. On evaluation of bronchial hyperresponsiveness in adults with CRSwNP, 28–40% of adults were found to have previously undiagnosed asthma.[36–38] Thus, clinicians should familiarize themselves with the characteristics of patients with CRSwNP and comorbid asthma when managing patients with CRS.

According to previous epidemiological studies, CRSwNP tends to be associated with late-onset adult asthma (onset after 40 years of age) and is not usually linked to childhood asthma.[39] In contrast, CRSsNP has been linked to childhood-onset asthma (onset before 16 years of age) and to adult early-onset asthma (onset before 40 years of age).[38] Another study reported an age-related increase in the prevalence of asthma and nasal polyps in CRS patients.[40] In the current study cohort, patients with CRSwNP and comorbid asthma were older than those without comorbid asthma. The prevalence of CRSwNP and concomitant asthma increases with age, implying that the disease burden is likely to increase and accumulate with age in these patients.[39,40]

Penezić et al compared 60 patients with CRS with and without asthma and found no difference in the total SNOT-22 score between the two groups.[41] However, CRS patients with asthma had significantly greater impairment of smell and taste than did those without asthma. Ho et al reported that atopy was associated with increased severity in the nasal symptom score, as well as worse scores in the loss of smell/taste and the need for nose-blowing in the CRS population.[42] Nevertheless, these studies evaluated the impact of asthma and atopy on QoL in patients with CRS, most of whom had CRSsNP. The current study focused on patients with nasal polyposis, due to the close association between asthma and CRSwNP, and revealed a significantly higher symptom burden and QoL impairment, particularly in the rhinologic- and sleep-related domains of the SNOT-22, in patients with CRSwNP with comorbid asthma than in those without asthma.

A nomogram was constructed to predict the probability of comorbid asthma in patients with CRSwNP, as no single ideal predictor of comorbid asthma was found by ROC analysis. The predicted probability of comorbid asthma was calculated by adding the corresponding scores of the clinical variables in the nomogram. Identifying patients with

CRSwNP and comorbid asthma preoperatively is important for clinicians to provide treatment strategies before surgery and to recommend the intensity of postoperative care based on the severity of type 2 inflammation.

This study had some limitations. First, patients with milder disease or unwillingness to undergo surgery were not included, potentially introducing selection bias. Second, the disease severity of CRSwNP may have been higher than that of the general population, because all participants were recruited from a tertiary referral medical center. However, this study included patients with a high nasal polyp score, CT L-M score, and symptom score to focus on patients who may be refractory to treatment and may require multiple treatment modalities, such as surgery as well as biologics, which warrants further investigation. Third, the detail in lung function was not available because we did not routinely perform pulmonary function test at enrollment before surgery. However, comorbid asthma was confirmed by previous pulmonary function test and inhaled corticosteroid usage, and fulfillment of the diagnostic criteria of the Global Initiative for Asthma guidelines.[14] Fourth, external validation of the nomogram with an independent dataset is necessary to assess generalizability in the future. Consecutive cases with CRSwNP during study period were enrolled for analysis, so that the results of current study were representative. Last, the treatment response was not assessed in this cross-sectional study, highlighting the need for future investigations with short- and long-term postoperative follow-up in CRSwNP patients with and without asthma. However, our findings emphasized the impact of comorbid asthma on nasal symptoms and QoL impairment in patients with CRSwNP.

Conclusion

Comorbid asthma was associated with more severe type 2 eosinophilic inflammation and a significant impact on nasal symptoms and QoL impairment in patients with CRSwNP, particularly in the rhinologic- and sleep-related domains of the SNOT-22. Our findings may facilitate clinicians' evaluation of the clinical characteristics of patients with CRSwNP and asthma to assist them in providing optimal therapeutic strategies and to develop a clinical decision support tool and practical guidelines to implement the united airway disease concept in practice in the future.

Abbreviations

CRS, Chronic rhinosinusitis; CRSwNP, CRS with nasal polyps; CRSsNP, CRS without nasal polyps; IL, interleukin; EPOS 2020, European Position Paper on Rhinosinusitis and Nasal Polyps 2020; ESS, endoscopic sinus surgery; QoL, quality of life; ECP, eosinophil cationic protein; CT, computed tomography; L-M score, Lund–Mackay score; EM ratio, ethmoid/maxillary ratio; OC, olfactory cleft; TEC, tissue eosinophil count; HPF, high-power field; ROC, Receiver operating characteristic; AUC, area under the curve; BEC, blood eosinophil count; OR, odds ratio.

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Disclosure

The authors declare no conflicts of interest in this work.

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