Are objective 'findings' the same as subjective 'severity'? A study of the relationship between computed tomography findings and subjective severity in preoperative CRSwNP patients

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Received October 14, 2018; Accepted January 22, 2020

DOI: 10.3892/etm.2020.9032

Abstract. In pre-surgical patients with chronic rhinosinusitis with nasal polyps (CRSwNPs), positive findings on computed tomography (CT) scans and an exacerbation of symptoms are two possible factors that indicate surgery. However, the relationship between these factors remains unclear. Confirmed CRSwNP patients ready for sinus surgery were consecutively enrolled. The Sino-Nasal Outcome Test 22 (SNOT-22) and visual analog scale (VAS) scoring were completed by these patients, and scores were subjected to factor analysis using a principal component analysis (PCA) to evaluate subjective symptom components related to CRS. Patient CT scores, measured by the Lund-Mackay score (LMS), together with their demographics, medical treatment, and atopy status, were collected and analyzed. A total of 288 patients who met the criteria for CRSwNP and underwent CT scanning prior to surgery in the Eye, Ear, Nose, and Throat Hospital of Fudan University were enrolled. Five components were identified from the PCA of the SNOT-22 results and VAS scores related to subjective symptoms. More severe 'nasal' symptoms (P=0.03; 95% CI, 0.092-1.824), loss of smell and taste (P<0.001; 95% CI, 0.961-1.767) and lower facial pain (P=0.001; 95% CI 1.811 to -0.475), derived from the SNOT-22, were significantly associated with total CT score. For the VAS PCA components, less severe 'ocular' symptoms (P=0.004; 95% CI -1.852 to -0.352), a reduced 'pain' component (P<0.001; 95% CI -2.133 to -0.715), a higher 'nasal' symptom component (P<0.001; 95% CI 0.752-2.257) and, again, loss of smell and taste (P<0.001; 95% CI 0.437-0.811) showed an association with total CT score. 'Allergy-associated symptoms' in both the SNOT-22 and VAS scores and 'loss of smell or taste' and 'hyposmia' were significantly more severe in patients with ethmoid sinus/maxillary sinus (E/M) ratios of >2.59 compared with patients with E/M ratios <2.59. Loss of smell and taste alone was correlated with the LMS in patients with highly positive CT scores. The present study demonstrated associations between several subjective symptoms and objective severity in preoperative CRSwNP patients. Nasal symptoms, including olfaction loss, were correlated positively with CT scores, while ocular- and pain-related symptoms showed an opposite pattern. However, this relationship was not confirmed in patients with highly positive CT scores. A subset analysis confirmed, in terms of symptoms, the value of the E/M ratio for indicating eosinophilic chronic rhinosinusitis.

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Key words: chronic rhinosinusitis, health-related quality of life, factor analysis, Lund-Mackay score

Introduction

The definition of chronic rhinosinusitis (CRS) is proposed in two guidelines as including the presence of nasal obstructions, nasal discharge, loss of smell and facial pain; however, the relationship with subjective symptoms pertinent to CRS is intricate (1,2). The major complaints of patients with CRS, indeed tend to be sinus-specific, including nasal congestion and discharge, facial pain/pressure and/or olfactory disturbances. In addition, some of the less common symptoms, such as fatigue and headache, which are not relevant to sinusitis pathology but rather to a host of other chronic conditions, have also been shown in several studies to have an effect on disease severity (3-5) In previous studies, psychiatric distress, including workplace disturbances, anxiety and depression, have been reported to be associated with increased symptom burden in CRS patients (6,7) Accordingly, several validated patient-reported measures of outcomes have been utilized since the 1990s to evaluate health-related quality of life. Among them, the Sino-Nasal Outcome Tests (SNOTs), including versions such as the SNOT-16, SNOT-2, and Sino-Nasal Assessment Questionnaire 11 (SNAQ-11), which is a modification of the 31-question Rhinosinusitis Outcome Measure (RSOM-31), has mostly been applied in the past decade (8-10).

Endoscopic signs of nasal polyps or edema in the middle meatus have invariably been considered objective evidence of

rhinosinusitis. A well-performed evaluation by an experienced rhinologist using endoscopy can be pivotal in measuring mucosal inflammation during the primary diagnosis of the condition (11). Computed tomography (CT) scanning, however, due to its better ability to display the paranasal sinus and the soft tissue, is used frequently following medical treatment failure. Kennedy (12) suggested in 1992 that the extent of a disease evaluated by CT was the only potential factor affecting surgical outcomes. In addition, CT scans can provide endoscopic visualization of sinus tissue abnormalities and allow more rigorous assessment when referenced to a grading system (13). This is in addition to the practical difficulties of obtaining a clear endoscopic picture for primary unit physicians.

Nasal polyps appear in almost 20% of CRS patients and may increase the severity of mucosal inflammation (1). It has been reported that positive radiological findings are more common in patients with CRS with nasal polyps compared with those without (14). In addition, complaint profiles between patients with the two phenotypes of CRS are quite different. In CRSwNP patients who fail to see improvements following adequate medical treatment, surgical interventions may generally be the next option. When evaluating medical treatments and making the decision for surgery, radiological findings and self-reported symptoms are the most frequently used assessments (15). Any positive radiological findings or deterioration in self-reported symptoms may contribute to a choice for surgery. Therefore, it is of great significance to determine the severity of symptoms and the objective nasal condition prior to surgery. However, the correlation between these two signs remains controversial. Several previous studies using cumulative scores from a symptom questionnaire failed to confirm the relationship of self-reported symptoms with CT scores (10,11,15). This may be due to the diversity in the spectrum of symptoms, as some of the symptoms cannot be explained by the severity of sinus inflammation and thus do not correlate with radiological findings. Therefore, to determine which symptoms actually relate to CT scores, these questionnaires must be subcategorized. Kenny *et al* (16) selected 7 commonplace symptoms and demonstrated that 5 of them were correlated with CT scores in patients with CRS or acute rhinosinusitis. Bhattacharyya (17) examined 115 adult patients with CRSwNP using the Rhinosinusitis Symptom Inventory (RIS), which has 4 domains for symptom evaluation, and found that none of the domains correlated with Lund scores. Notable among these studies was the use of factor analysis to make the research clinically meaningful. Browne *et al* (8) first proposed the use of subscales derived by factor analysis. Recent studies then compared the constructs of the SNOTs with Lund scores in patients both with and without nasal polyps and detected a relation only for the nasal symptom subset (18,19). Sedaghat *et al* (19) also found that many confounding factors such as sex and disease history may influence subjective symptoms.

The present study evaluated the associations between disease severity, measured by CT scores, and symptoms, while controlling for several confounding demographic factors, among preoperative CRSwNP patients. In addition, in order to avoid the flaws in the Lund-Mackay score (LMS) caused by the large range of the scoring interval (0-24) and in consideration of the possibility of a relationship between the symptoms of patients with subtle or less positive CT scores and the LMS, a subgroup analysis of patients with 'very positive' CT scores was performed. It was hypothesized that the constructs of the SNOT-22 that were associated with symptoms may be associated with radiological findings when adjusted for demographic covariances and that these differences may exist in patients with a more severe condition as shown by CT scores.

Materials and methods

Participants and setting. The present study was conducted at the Department of Otolaryngology, Head and Neck Surgery at the Affiliated Eye, Ear, Nose and Throat Hospital of Fudan University. A total of 288 adult CRSwNP patients (>18 years) referred for endoscopic sinus surgery were consecutively recruited between September 2015 and February 2017. Diagnoses of CRSwNP were in accordance with the criteria defined by the EPOS 2012 position paper as the presence of two or more specific symptoms together with endoscopic signs of nasal polyps (20). All the patients were admitted for sinus surgery following unsuccessful previous medical treatment for 3 continuous months. All the participants were followed up for at least 3 months post-surgery. Exclusion criteria included acute exacerbation of a severe disease or the existence of conditions that may affect the mucosa of the sinus or nasal cavities, such as trauma, tumors or choanal polyp before surgery. Participants were also excluded if they had not undergone a CT scan within 1 month prior to surgery. Patient details are given in Table I.

Ethical considerations. The present study was approved by the Ethics Committee of the Affiliated Eye, Ear, Nose and Throat Hospital of Fudan University (Shanghai, China) and was conducted in accordance with the Declaration of Helsinki. Written consent was obtained from patients following they had been given written and oral information about the study and the potential side effects.

Indicators and measurement tools

Demographic information. Demographic information, including sex, age, medication history, duration of symptoms, history of previous surgeries, concurrent asthma, cigarette smoking and allergies to relevant airborne allergens were collected (Table I). The atopic status of the patients was evaluated by a skin prick test or an ImmunoCAP test (Phadia, Thermo Fisher Scientific, Inc.) to detect IgE antibodies against various common inhalant allergens.

CT scanning. CT scanning was performed using 1-mm axial images, which were reconstructed offline and reformatted to 3-mm coronal images for analysis (Toshiba Aquilion, Toshiba Medical Systems). All CT scans were scored following the Lund-Mackay system by an independent radiologist (21). The total score was the total LMS, with a maximum of 16 points. A total LMS of 0 was classified as negative; a unilateral LMS of 10 to 12 or a bilateral LMS of 12 to 24 was classified as 'very positive'. The ethmoid sinus/maxillary sinus (E/M) ratio was defined as the ratio of the CT-derive ethmoid sinus and maxillary sinus scores (22).

Table I. Demographics of subjects.

Items	CRSwNP patients (n=288)
Age (years)	46.5±14.5 (18-79)
Sex	
Male (%)	64.2
Female (%)	35.8
Smoking (%)	28.8
Atopy (%)	25.3
Asthma history (%)	9.0
Previous surgery (%)	23.6

CRSwNP, chronic rhinosinusitis with nasal polyps.

Subjective symptoms. Patients' subjective symptoms were evaluated using two questionnaires around the time of the CT scan. A visual analog scale (VAS) was used to assess major and minor symptoms according to several guidelines. The symptoms assessed by this questionnaire included the following: Nasal obstructions, purulent nasal discharge, watery rhinorrhea, nasal itching, sneezing, facial pain, headache, itchy eyes, watery eyes, red eyes, eye pain, suffocation feeling, gasping for breath and oppressive feelings. Patients indicated their subjective symptoms on a straight line from 0 to 10 cm to describe the intensity of the symptoms. The SNOT is a patient-reported measure of outcomes in nasal and sino-nasal disorders, which has been validated and is commonly used in health-related quality of life assessments to describe patients' burdens and clinical effectiveness (23). This questionnaire consists of 22 items covering physical and functional problems together with emotional disorders.

Data analysis. A regression model was selected to fit previously considered confounders of the symptoms related to CRS with a lower likelihood of an association with CT scores. Redundant non-significant independent variables (multivariate P-value >0.100) were removed from the multivariate model using backward elimination. All remaining variables were adjusted when evaluating the relationship between subjective symptoms and the LMS.

As the two questionnaires contained a total of 16 or 22 items, both were subjected to factor analysis using PCA with Kaiser normalizations and varimax rotations to identify the subset of principle symptom components for regression analysis. Components that met the criteria (initial eigenvalues >1.0) were identified and explained according to the related primary symptoms. Symptoms from the SNOT-22 and VAS with low communalities (<0.5) were excluded from the factor analysis and analyzed separately. Statistical analyses were performed with SPSS version 19 (IBM Corp.).

Results

Characteristics of study subjects. In total, 369 patients who met the criteria for CRSwNP and were ready for sinus surgery were consecutively assessed for eligibility. A total of 81 participants were excluded based on the exclusion criteria, which left a total sample of 288 patients (185 male and 103 female) enrolled in this cross-sectional study. Clinical and demographic characteristics are listed in Table I. The mean age of the patients was 46.5±14.5 years, 28.8% had a history of smoking, 25.3% had a concurrent atopy status, and 9% had a history of asthma. The average total LMS was 9.55 (standard deviation, 6.70), and the average SNOT-22 score was 23.18 (standard deviation, 21.02).

Factor analysis. Exploratory factor analysis using PCA was performed to identify the subscale factors that explained the variance in the CT scores. In the SNOT-22, 3 items (loss of smell and taste, postnasal discharge and facial pain) and 2 items in the VAS (cough and hyposmia) were excluded from factor analysis in the first run as a result of the low communalities (<0.5) that they conveyed. Following application of Kaiser normalization and varimax rotations, 5 unique constructs each were found within the SNOT-22 and VAS results. These constructs were then labeled in accordance with the topics they addressed, which were 'working disturbances', 'sleeping disorders', 'nasal symptoms', 'otology symptoms', and 'allergy-associated symptoms' within the SNOT-22 (Table II) and 'ocular symptoms', 'pectoral symptoms', 'allergy-associated symptoms', 'pain', and 'nasal symptoms' within the VAS (Table III). All factor scores were preserved for regression analysis.

Confounding factors. The patient characteristics measured included previous surgeries, history of asthma and other demographic characteristics, which are presented in Table III. The associations of age, sex, history of asthma and allergies, smoking status and previous endonasal surgery with CT scores were tested separately using backward elimination from the multivariate model. Smoking status, age and previous endonasal surgery were consecutively removed from the regression model on the basis of a multivariate P-value >0.100 in three runs. History of asthma, sex, and other characteristics were not included in the regression because they were not significant (P>0.1).

Associations between symptoms and CT score. The constructs of the SNOT-22/VAS and the items excluded from the factor analysis were assessed for associations with LMS, adjusted for 'sex' and 'history of asthma'. No significant association was identified between the total SNOT-22 score and the LMS, while a slightly positive association existed between the total VAS score and the LMS (P=0.008). Several positive and negative correlations were found between constructs extracted from the SNOT-22 and VAS (Tables IV and V). The 'nasal symptoms' construct (P<0.001) and 'loss of smell and taste' construct (P<0.001) of the SNOT-22 as well as chest symptoms (PCA of the VAS; P=0.022), nasal symptoms (PCA of the VAS; P<0.001) and 'hyposmia' (P<0.001) were positively correlated with the LMS. Meanwhile, otologic symptoms (PCA of the SNOT-22; P=0.008), 'facial pain' (P=0.018), ocular symptoms (PCA of the VAS; P=0.035) and pain-related symptoms (PCA of the VAS; P=0.031) were negatively associated with LMS. The analysis of a subset of patients with a 'very positive' LMS is also shown in Table IV. Items associated with olfaction were the only factors that had a strong relationship with the LMS in both subsets (P<0.001). A total of 3 factors, the 'sleeping disorder' construct in the SNOT-22, the 'otology symptoms' construct in the SNOT-22 and the 'ocular symptoms' construct

Table II. Summary of factor analysis using PCA for the SNOT-22 questionnaire.

Symptoms	Working disturbance	Sleeping disorder	Nasal symptoms	Otology symptoms	Allergy associated symptoms
Need to blow nose	-0.021	-0.119	0.424	-0.003	-0.074
Nasal obstruction	-0.052	0.006	0.297	-0.085	0.046
Sneezing	-0.016	-0.049	-0.051	-0.112	0.611
Running nose	-0.080	-0.059	0.319	-0.030	0.158
Cough	-0.059	-0.073	-0.081	0.076	0.558
Thick nasal discharge	-0.042	-0.035	0.389	0.086	-0.275
Ear fullness	-0.098	-0.004	0.038	0.434	-0.097
Dizziness	0.031	-0.132	-0.032	0.354	0.033
Ear pain	-0.151	0.018	-0.052	0.507	-0.007
Difficulty falling asleep	-0.215	0.423	-0.003	0.086	-0.069
Wake up at night	-0.109	0.406	-0.084	-0.016	-0.040
Lack of good night's sleep	-0.063	0.347	-0.024	-0.084	-0.019
Wake up tired	0.074	0.187	-0.070	-0.052	-0.008
Fatigue	0.121	0.131	-0.033	-0.120	0.005
Reduced productivity	0.164	0.045	0.001	-0.065	-0.063
Reduced concentration	0.242	-0.061	-0.033	-0.097	0.016
Sad	0.281	-0.124	-0.051	-0.040	-0.005
Frustrated/restless/irritated	0.295	-0.157	-0.034	-0.010	-0.044
Embarrassed	0.288	-0.192	0.008	-0.016	-0.010
Variance explained	21.617%	14.565%	13.724%	11.517%	7.558%

'Loss of smell and taste' (communality=0.453), 'post nasal discharge' (communality=0.465) and 'facial pain' (communality=0.454) were excluded from factor analysis and analyzed separately. Kaiser-Meyer-Olkin=0.906; Bartlett's sphericity, P<0.001 [χ^2=3212.3, degrees of freedom (df)=171]. The bold underlined figures for each construct represent the correlation of these variables that can be transferred to one independent component. PCA, principal component analysis; SNOT, Sino-Nasal Outcome Test.

Table III. Summary of factor analysis using PCA for VAS scores.

Symptoms	Ocular symptoms	Asthma associated symptoms	Allergy associated symptoms	Pain	Nasal symptoms
Nasal obstruction	-0.047	-0.027	0.083	-0.075	0.549
Thick nasal discharge	0.029	-0.103	-0.117	0.020	0.638
Running nose	-0.147	0.026	0.361	-0.045	0.087
Itchy nose	-0.006	-0.097	0.391	0.053	-0.067
Sneezing	-0.003	-0.079	0.430	-0.042	-0.085
Facial pain/pressure	-0.050	-0.135	0.030	0.575	0.033
Headache	-0.128	0.020	-0.060	0.602	-0.067
Itchy eyes	0.329	-0.112	0.084	-0.045	-0.064
Watery eyes	0.325	-0.072	0.009	-0.091	0.007
Swelling around eyes	0.393	-0.056	-0.129	-0.152	0.064
Eye sore	0.340	-0.087	-0.102	0.072	-0.026
Shortness of breath	-0.065	0.438	-0.069	-0.104	-0.016
Wheezing	-0.091	0.453	-0.055	-0.060	-0.036
Chest tightness	-0.110	0.418	-0.016	0.049	-0.100
Variance explained	20.114%	17.242%	16.311%	11.770%	10.565%

'Hyposmia' (communality=0.472) and 'cough' (communality=0.489) were excluded from factor analysis and analyzed separately. Kaiser-Meyer-Olkin=0.796; Bartlett's sphericity, P<0.001 [χ^2=1741.0, degrees of freedom (df)=91]. The bold underlined figures for each construct represent the correlation of these variables that can be transferred to one independent component. PCA, principal component analysis; VAS, visual analog scale.

Table IV. Relationship between the constructs of the SNOT-22 and LMS.

Construct	P (α=0.05)	Estimate (95%CI)
SNOT-22 total score		
Overall	0.122	0.031 (-0.008,0.070)
In patients with very positive CT scores	0.346	0.023 (-0.026,0.072)
'Working disturbance'		
Overall	0.990	0.005 (-0.837,0.848)
In patients with very positive CT scores	0.494	-0.298 (-1.160,0.564)
'Sleeping disorder'		
Overall	0.267	-0.465 (-1.288,0.358)
In patients with very positive CT scores	0.428	0.360 (-0.540,1.259)
'Nasal symptoms'		
Overall	<0.001	1.594 (0.805,2.384)
In patients with very positive CT scores	0.103	0.757 (-0.155,1.669)
'Otology symptoms'		
Overall	0.008	-1.143 (-1.980, 0.306)
In patients with very positive CT scores	0.460	0.412 (-0.693,1.516)
'Allergy associated symptoms'		
Overall	0.905	0.050 (-0.779,0.879)
In patients with very positive CT scores	0.331	-0.441 (-1.338,0.456)
Loss of smell and taste		
Overall	<0.001	1.276 (0.904,1.648)
In patients with very positive CT scores	<0.001	1.021 (0.612,1.429)
Postnasal discharge		
Overall	0.303	-0.278 (-0.252,0.808)
In patients with very positive CT scores	0.983	0.006 (-0.578,0.591)
Facial pain		
Overall	0.018	-0.763 (-1.395, 0.131)
In patients with very positive CT scores	0.147	-0.606 (-1.431,0.218)

SNOT, Sino-Nasal Outcome Test; LMS, Lund-Mackay score; CT, computed tomography.

in the VAS, showed a difference between the two subsets and the LMS. Though no significant difference was observed between the interaction of the 2 subsets with symptoms, this could indicate that in patients with different imaging findings, the causes of symptoms might also differ.

Subsets based on E/M Lund ratios. As shown in Figs. 1-4, when sorted by the E/M ratio, with a cutoff value of 2.59, which was proposed in a previous study as an indication of CRS (eCRS) (22), 'allergy-associated symptoms' in both the SNOT-22 and the VAS, 'loss of smell or taste' and 'hyposmia' were significantly more severe in patients with an E/M ratio of >2.59 compared with those with a ratio <2.59. In addition, 'otologic symptoms' within the SNOT-22 showed less severity in patients with an E/M ratio >2.59.

Discussion

Judging the severity of CRS and assessing treatment options are predicated mainly upon clinical symptoms and radiographic findings. Previous studies of these two types of assessment have failed to confirm an established association (10,11,15,17). It should be noted that several patients in previous studies met the criteria for CRS with no evidence of abnormalities on CT scans (24). By contrast, under the symptomatic definition of CRS, up to 20% of the 'normal' population also presented with incidental abnormalities in a previous study (21). Using different questionnaires, including the RSI, Chronic Sinusitis Survey, SNAQ and SNOTs, for symptom assessment, many earlier studies have indicated a lack of an association between symptoms and CT scores (10,11,15-17,19,21,24). Among these questionnaires, the total score of the SNOT-20 or SNOT-22 (which is more commonly used) showed, with no exceptions, that there was no association with the LMS. Interestingly, Kenny *et al* (16) identified 5 out of 7 symptoms that were associated with the severity of CT scores, with the only exceptions being facial pain and headache. Although these questionnaires consist of many items, few studies have compared the relationship between specific symptoms and CT scores using these instruments. To address these problems, factor analyses have been applied to the results of these questionnaires. Several studies using factor analysis categorized 4 or 5 domains of the

Table V. Relationship between constructs of VAS score and LMS.

Construct	P (α=0.05)	Estimate (95%CI)
'Ocular symptoms'		
Overall	0.035	-0.912 (-1.760, 0.065)
In patients with very positive CT scores	0.311	0.532 (-0.507,1.571)
'Pectoral symptoms'		
Overall	0.022	0.955 (0.141,1.769)
In patients with very positive CT scores	0.446	0.309 (-0.494,1.112)
'Allergy associated symptoms'		
Overall	0.982	0.009 (-0.815,0.833)
In patients with very positive CT scores	0.944	-0.031 (-0.924,0.862)
'Pain'		
Overall	0.031	-0.933 (-1.779, 0.086)
In patients with very positive CT scores	0.691	-0.230 (-1.374,0.914)
'Nasal symptoms'		
Overall	<0.001	2.294 (1.513,3.075)
In patients with very positive CT scores	0.068	0.796 (-0.059,1.650)
Cough		
Overall	0.127	0.335 (-0.095,0.765)
In patients with very positive CT scores	0.534	0.135 (-0.295,0.565)
Hyposmia		
Overall	<0.001	0.690 (0.512,0.867)
In patients with very positive CT scores	<0.001	0.531 (0.314,0.748)

VAS, visual analog scale; LMS, Lund-Mackay score; CT, computed tomography.

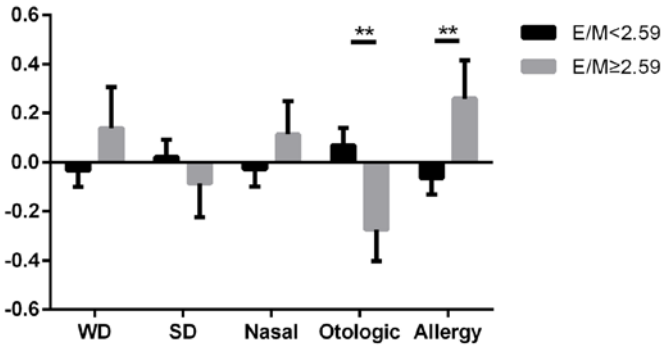

Figure 1. Components derived from SNOT-22 in patients subgroup with a CT scan score of E/M ≥2.59 or <2.59. 'allergy-associated symptoms' were significantly more severe in patients with an E/M ratio of >2.59 compared with those with a ratio <2.59 (P=0.043). 'otologic symptoms' within the SNOT-22 showed less severity in patients with E/M >2.59 (P=0.032). **P<0.05. SNOT, Sino-Nasal Outcome Test; CT, computed tomography; E/M, ethmoid sinus/maxillary sinus ratio; WD, working disturbance; SD, Sleeping disorder,

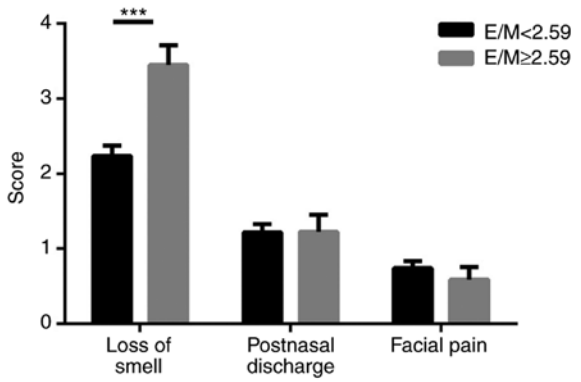

Figure 2. Excluded symptoms from SNOT-22 in patients subgroup with a CT scan score of E/M ≥2.59 or <2.59. 'Loss of smell and taste' were significantly more severe in patients with an E/M ratio of >2.59 compared with those with a ratio <2.59 (P<0.001). ***P<0.01. SNOT, Sino-Nasal Outcome Test; CT, computed tomography; E/M, ethmoid sinus/maxillary sinus ratio.

SNOT-20/22 and suggested that the questionnaire was actually evaluating more than one specific construct (8,18,19,23,25). The present study also identified 5 constructs using PCA for factor analysis. These constructs broke down into 5 symptom-related domains: 'working disturbances', 'sleeping disorders', 'nasal symptoms', 'otology symptoms' and 'allergy-associated symptoms'. The symptoms in one specific domain may relate to a certain disease subtype or to health-related quality of life.

In two previous studies that used PCA to analyze the constructs of SNOTs that related to CT scores, only nasal symptoms were positively associated (10,26). In the present study, following adjustment for the influential demographic factors of sex and history of asthma, several symptoms and symptom constructs that had a positive relationship with the LMS were found in this cohort. Olfaction and nasal symptoms, including running nose, nasal obstructions and thick nasal discharge specifically, showed quite strong correlations with CT scores

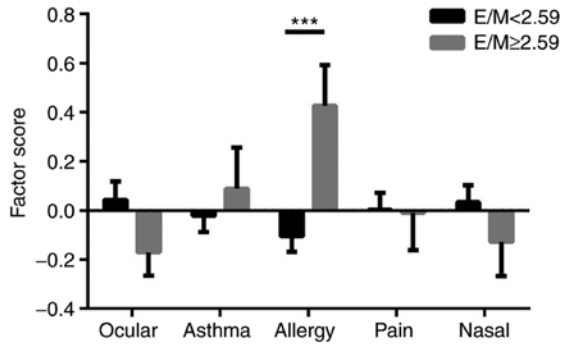

Figure 3. Components derived from VAS in patients subgroup with a CT scan score of E/M ≥2.59 or <2.59. 'allergy-associated symptoms' were significantly more severe in patients with an E/M ratio of >2.59 compared with those with a ratio <2.59 (P=0.001). ***P<0.01. VAS, visual analog scale; CT, computed tomography; E/M, ethmoid sinus/maxillary sinus ratio.

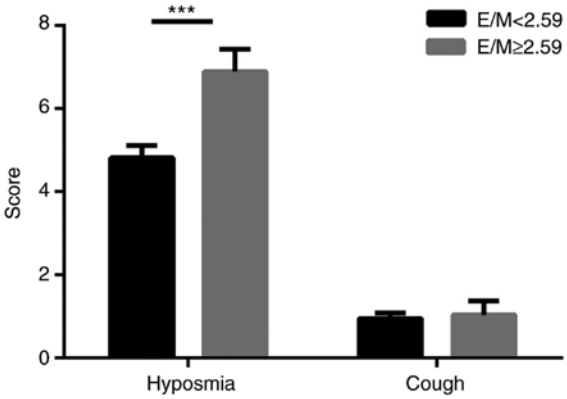

Figure 4. Excluded symptoms from VAS in patients subgroup with a CT scan score of E/M ≥2.59 or <2.59. 'Hyposmia' were significantly more severe in patients with an E/M ratio of >2.59 compared with those with a ratio <2.59 (P=0.001). ***P<0.01. VAS, visual analog scale; CT, computed tomography; E/M, ethmoid sinus/maxillary sinus ratio.

in both the SNOT-22 and VAS questionnaires. Therefore, in patients with refractory nasal symptoms, radiological findings are more likely to be positive, which may make these patients more likely to consider a surgical option.

Meng *et al* (22) reported in a recent study that the E/M ratio based on CT scores may predict the phenotype of eCRS. The cut-off value presented in that study was used to test for symptom differentiation between the two subsets. The results showed that olfaction- and allergy-associated symptoms were significantly more severe in patients with E/M ratios >2.59, which coincided with the characteristics of eCRS reported in a previous study (27). This result confirmed the value of the E/M ratio as a predictor for eCRS in terms of symptoms.

The negative correlation between 'pain' and CT scores in Gregurić *et al* (18) is also of interest. The present study also reported that pain-related symptoms were negatively associated with radiological findings. Similar results were reported previously in a long-term follow-up study that compared the relationship between facial pain and CT scores, where CRS patients with a primary symptom of facial pain tended to have negative CT scores (4). As the negative relationship did not exist in the subset of patients with CT scores of >12, the CT scores among 3 group of patients with L-M scores of 4-12, 13-24 and <4 were compared. Patients with relatively few findings on the CT scans and L-M scores of <4 tended to display higher facial pain symptom scores than the other 2 groups. The negative correlation was due to patients presenting with facial pain being more likely to have a negative CT scan appearance. As facial pain is among the major symptoms of CRS and motivates patients to seek medical attention, decisions should be made more carefully when clinicians encounter this kind of situation. In the cohort of the present study, some patients with a severe condition, as measured by CT scores, might still have had slight symptoms of CRS, and patients with extremely diseased unilateral lesions or extensive bilateral pathological changes were included in the analyzed groups. Patients with 'very positive' CT scores alone, however, can be considered to have undergone failed medical treatments. The present study investigated in particular the correlation between symptoms and radiological findings in these patients and found some subtle differences compared with the results of the overall cohort. In this subgroup of patients, only the loss of smell and taste remained associated with the LMS, which indicates a more complicated pattern of symptom severity in these patients. In patients with severe mucosal or sinus inflammation, the symptom of inflammation may be influenced by a threshold of sensation that different individuals feel quite differently.

The present study demonstrated the presence of a positive relationship between symptom subsets such as nasal symptoms and loss of smell, as well as a negative relationship between symptoms such as pain and ocular symptoms, with objective radiological findings in patients with pre-surgical CRSwNP. In addition, when sorted by the E/M ratio, with a cutoff of 2.59, allergy-associated symptoms and olfactory symptoms showed significant differences between the 2 subgroups. In patients with very severe imaging findings, only a loss of smell remained correlated with the LMS.

Acknowledgements

The authors would like to thank Dr Wanpeng Li, Department of Otorhinolaryngology, Eye, Ear, Nose and Throat Hospital of Fudan University (Shanghai, China) for providing statistical advice in the present study.

Funding

This work was supported by the Natural Science Foundation of China (grant no. 81500781).

Availability of data and materials

All data generated or analyzed during this study are included in this published article or are available from the corresponding author on reasonable request.

Authors' contributions

Ha. L and ZL designed the study and wrote the manuscript. LH and XF were responsible for collecting and analyzing data. YG, Hou. L, Hua. L and DW were responsible for recruitment, carrying out the endoscopic examination.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of the Affiliated Eye, Ear, Nose and Throat Hospital of Fudan University (approval no. 2016009; Shanghai, China) and was conducted in accordance with the Declaration of Helsinki. Written consent was obtained from patients following they had been given written and oral information about the study and the potential side effects.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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