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Blood and Sputum Eosinophil Levels in Asthma and Their Relationship to Sinus Computed Tomographic Findings

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Abstract

OBJECTIVE—To investigate the relationship among blood and sputum eosinophil levels, sinus mucosal thickening, and osteitis in patients with asthma.

PATIENTS AND METHODS—We conducted an observational study of 201 patients with asthma who underwent sinus computed tomographic (CT) imaging and induced sputum analysis at Mayo Clinic's site in Rochester, MN, from November 1, 2000, through December 31, 2005. Sinus CT scans were reviewed by an investigator blinded to patients' identity and chart information (J.B.H.) to assess for mucosal thickening. Each scan was assigned a CT score based on the Lund-Mackay staging scale. Approximately 20% of the scans were reviewed at random by a radiologist (N.G.C.) to ensure quality control. Bone changes consistent with osteitis were ascertained from radiology reports. Lung function was measured, and sputum was analyzed by conventional methods.

RESULTS—Sinus CT scans revealed abnormalities in 136 (68%) of the 201 study patients. Severe mucosal thickening (CT score, ≥ 12) was found in 60 patients (30%) and osteitis in 18 patients (9%). There was a positive correlation between CT scores and eosinophil levels in both peripheral blood ($\rho=0.45$; 95% confidence interval, 0.33–0.56; $P<.001$) and induced sputum ($\rho=0.46$; 95% confidence interval, 0.34–0.57; $P<.001$). Further, elevated blood and sputum eosinophil levels were associated with the presence of osteitis on CT scan and previous sinus surgery.

CONCLUSION—Blood and sputum eosinophil levels in patients with asthma are directly correlated with sinus mucosal thickening and are associated with osteitis, lending further support to the hypothesis that asthma and chronic rhinosinusitis are mediated by similar inflammatory processes.

Chronic rhinosinusitis (CRS) affects approximately 30 million Americans and results in an estimated 11.6 million physician visits and \$4.3 billion in health care costs annually.^{1,2} Despite its widespread prevalence, the patho-physiology of CRS is not fully understood, and no optimal treatment has been identified. Chronic rhinosinusitis is a heterogeneous disease with several causes, including infectious and inflammatory processes. Its diagnosis is based on patients' symptoms and evidence of inflammation of the nasal and paranasal sinus mucosa.³ The underlying bone can also undergo changes.⁴ More than half of patients with CRS have asthma; however, the interaction between inflammation of the upper and lower airways is not completely understood.⁵

Sinus computed tomography (CT) can provide accurate imaging of both the anatomy and the extent of mucosal inflammation.⁶ Radiographic evidence of sinus mucosal thickening and opacification is associated with CRS⁷ and shows strong correlation with findings on endoscopy.⁸ In contrast, sinonasal symptoms do not necessarily correlate with CT findings,^{9–12} and mucosal thickening and opacification of the sinuses can be seen in up to 30% to 40% of asymptomatic individuals.¹³ Hence, radiographic findings require clinical correlation before the diagnosis of CRS can be established.

In patients with asthma, peripheral blood eosinophilia has been associated with evidence of extensive sinus disease on CT scan and is a marker of poor prognosis.¹⁴ Recently, ten Brinke et al¹⁵ reported an additional correlation between evidence of sinus mucosal thickness on CT scan and sputum eosinophilia. However, their study was limited to patients with severe asthma and did not address radiographic abnormalities of the bone.

Radiographic and histologic changes of the bone underlying the sinus mucosa have been observed in patients with CRS for many years, but their cause and clinical relevance have not been fully determined. In animal studies, experimentally induced sinusitis has been associated with a periosteal reaction of fibrosis, followed by bone degradation and new bone formation, not only adjacent to the involved sinus but also at a distance from the primary infection.^{16–20} Histomorphometric studies in humans have demonstrated active remodeling in the ethmoid bone of patients with CRS.^{4,21} This finding has led some investigators to hypothesize that chronic inflammation within the bone (ie, osteitis) is responsible for the persistent mucosal inflammation seen in recalcitrant CRS and indicates poor postoperative outcome.^{4,21,22} Studies using single-photon emission CT in patients with CRS have shown increased radionuclide uptake in the sinus areas of these patients compared with controls. In a study of 43 patients undergoing functional endoscopic sinus surgery, Jang et al²³ found an association between increased pre-surgical technetium-99m hydroxymethylene diphosphonate uptake in the ethmoid sinus areas and poor postsurgical outcomes.²³

Lower airway inflammation is a key characteristic of asthma and the primary target of asthma treatment. Measurement of markers of inflammation in induced sputum, which has gained acceptance as a safe and reliable method to assess lower airway inflammation, is sometimes used as an outcome indicator in asthma clinical trials.²⁴ Recently, a treatment strategy based on assessment of sputum eosinophils has been shown to reduce asthma exacerbations without the need for additional anti-inflammatory treatment.²⁵ At our institution, induced sputum analysis has been available since 2000 as a clinical tool to monitor asthma control and evaluate lower respiratory symptoms.

In the current study, we sought to further delineate the relationship among sinus mucosal thickening, osteitis, and markers of eosinophilic inflammation in a heterogeneous group of patients with asthma. We speculated that sinus mucosal thickening and osteitis are both related to chronic local eosinophilic inflammation.

PATIENTS AND METHODS

From our database, we identified 519 patients with asthma who underwent sputum analysis at Mayo Clinic's site in Rochester, MN, from November 1, 2000, through December 31, 2005. In most instances, the test was obtained either to monitor asthma control or to evaluate lower respiratory symptoms, such as shortness of breath, wheeze, chest tightness, or cough. Approximately half (n=245) of these patients also underwent sinus CT imaging within 3 months of sputum collection to evaluate for chronic sinusitis due to sinonasal symptoms, namely rhinorrhea, nasal congestion, headache, facial pain, or diminished sense of smell. Most

of these patients had undergone skin testing (n=175) and full pulmonary function tests, including diffusion capacity (n=163).

Asthma was defined solely by physician diagnosis in the electronic medical record. Reversibility in FEV₁ of 12% or more of predicted was documented in most cases but was not a requirement. Atopy was determined by positive results on a skin prick test (≥ 3 mm wheal) to at least 1 in a standard panel of allergens that included trees, grasses, weeds, molds, dust mites, cats, dogs, and cockroaches. Because cigarette smoking can influence sputum inflammatory markers, active smokers were excluded. Patients with a physician diagnosis of chronic obstructive pulmonary disease were also excluded. The study was approved by the Mayo Clinic Institutional Review Board. All patients provided informed consent to have their medical records reviewed.

Pulmonary Function Tests

Spirometry was performed according to current American Thoracic Society guidelines.²⁶ Lung volumes were obtained by whole-body plethysmography. Diffusing capacity of lung for carbon monoxide (D_{LCO}) was measured using the single-breath method.

Sputum Induction and Analysis

As a general rule, patients were not asked to discontinue their medications. Those with a current respiratory infection or who had had a respiratory infection in the past 4 weeks were excluded and did not proceed to sputum collection. Whole expectorated sputum was induced and processed based on a previously validated protocol by Fahy et al²⁴ used at our institution. Briefly, baseline FEV₁ was obtained by handheld spirometer. Each patient received 180 μ g of albuterol, and FEV₁ was remeasured after 15 minutes. Sputum induction was carried out by inhalation of 3% hypertonic saline by ultrasonic aerosol generator (UltraNeb 99/100; DeVilbiss, Somerset, PA) for 12 minutes. To avoid salivary contamination, patients were instructed to rinse their mouth with saline before each attempt to cough.

The volume of the induced sputum sample was determined, and an equal amount of 0.1% dithiothreitol was added. The sample was homogenized by gentle mixing with a vortex at room temperature for 15 minutes. The sample was filtered with a 40 μ m-pore nylon mesh and centrifuged at 4°C for 10 minutes at 400g. The pellet was resuspended in 1 mL of phosphate-buffered saline by means of gentle vortexing. Cytospin slides were prepared and stained using Diff-Quik stain (Baxter Scientific Products, Miami, FL). Differential cell counts were determined by manually counting nonsquamous cells and converting to a percentage. A sputum sample was considered inadequate if its volume was less than 1 mL.

Sinus CT Imaging

Coronal sinus CT was performed according to institutional protocol and CT scans were retrospectively reviewed by an investigator blinded to patients' identity and chart information (J.B.H.) to assess for mucosal thickening. Each scan was assigned a CT score based on the Lund-Mackay staging scale and categorized as normal (CT score, ≤ 3), mild-moderate (CT score, 4–11), or severe (CT score, ≥ 12). Approximately 20% of the scans were scored at random by a staff radiologist (N.G.C.) to ensure quality control. The presence of osteitis was ascertained by reviewing each radiology report. Osteitis was considered to be present if any of the following terms were used to describe bony changes: osteitis, neo-osteogenesis, remodeling, sclerosis, erosion, increased density, or thickening. The severity of osteitis was not characterized, given the lack of a standardized grading system.

Statistical Analyses

Results were expressed as mean $\pm$ SD, except for data that did not have normal distribution (inflammatory parameters), which were expressed as median and interquartile range. Values for FEV₁ were based on prebronchodilator handheld spirometer values obtained at the time of sputum induction. Patients were categorized according to mucosal thickening on the basis of CT scores and also according to the presence of osteitis and prior sinus surgery. Differences between groups were analyzed using unpaired *t* tests, χ^2 tests, analysis of variance, or nonparametric tests, when appropriate. Differences in inflammatory parameters were assessed with Mann-Whitney tests when comparing 2 groups and Kruskal-Wallis followed by Dunn multiple comparison tests when comparing 3 groups. Correlations between sinus CT scores and blood and sputum eosinophil levels, serum IgE, and lung function were calculated by linear regression analysis, Pearson product moment correlation, or Spearman rank correlation test, as appropriate. Intervariable dependence was assessed by bivariate analyses. All statistical tests were 2-sided and performed using JMP 6.0 software (SAS Institute, Cary, NC) or Prism 5.0 (GraphPad Software, San Diego, CA). The α value was set at 0.05. Statistical significance was set at $P < .05$.

RESULTS

Of the 519 patients with asthma who underwent sputum analysis, 245 had undergone sinus CT within 3 months of sputum collection. Of these, 27 patients were excluded because of an inadequate sputum sample, and 8 were excluded because they were active smokers. An additional 9 patients were excluded because of a physician diagnosis of chronic obstructive pulmonary disease. The remaining 201 patients (66 men, 135 women) were included in our study. Mean predicted FEV₁ was 83% (range, 41%–132%). Daily inhaled corticosteroid (ICS) use was reported in 131 patients (65%); 95 (47%) were taking long-acting β_2 -agonists; 77 (38%) used daily intranasal corticosteroids; and 41 (20%) had taken systemic corticosteroids in the past 6 months. Of the 175 patients who underwent skin testing, 63 (36%) did not have atopy; 18 (10%) tested positive exclusively to seasonal allergens; 37 (21%), exclusively to perennial allergens; and 58 (33%), to both seasonal and perennial allergens.

Sinus CT Findings

Sinus CT revealed mucosal abnormalities in 136 cases (68%). Mild-moderate and severe mucosal thickening was noted on 76 (38%) and 60 (30%) scans, respectively. Inter-rater agreement was excellent ($r=0.91$; $P<.001$). Median CT-scan score was 7 (range, 0–23). Of the 72 patients (36%) who had undergone at least 1 prior sinus surgery, 63 (88%) had mild-moderate to severe mucosal thickening on their CT scan. Bone changes consistent with osteitis were present in 18 (9%) of patients; most of these patients had severe mucosal thickening and a history of sinus surgery. Radiographic examples of mucosal thickening and osteitis are illustrated in Figure 1.

When groups were compared on the basis of sinus CT scores, no significant differences in age, smoking history, or body mass index were found (Table 1). The proportion of male patients was higher in the severe group, although women outnumbered men overall. Medication profiles were similar except for ICS use, which was higher in the severe than in the mild-moderate group. Mean FEV₁ was lower in patients with severe mucosal thickening, but the difference was not statistically significant. Serum IgE was higher in the severe group; no differences in atopic status were observed. Nasal polyps and hyposmia were both more prevalent in the severe than in the normal group. Previous sinus surgery was associated with more extensive mucosal thickening.

Osteitis was almost exclusively limited to patients with severe mucosal thickening (median CT score, 13) and was associated with nonatopic status and a trend toward a lower FEV₁ value. More than half of these patients had undergone sinus surgery. Distribution of all other characteristics, including sex, was similar (Table 2).

Inflammatory Parameters

Severe mucosal thickening was associated with higher eosinophil levels in blood and sputum, both in differential and absolute values (Table 3). As shown in Figure 2, a positive correlation was observed between sinus CT scores and eosinophil levels in peripheral blood ($\rho=0.45$; 95% confidence interval [CI], 0.33–0.56, $P<.001$) and induced sputum ($\rho=0.46$, 95% CI, 0.34–0.57, $P<.001$). Elevated blood and sputum eosinophil levels were also associated with osteitis and prior sinus surgery (Table 4). Although blood and sputum eosinophil levels were highly correlated ($\rho=0.56$; 95% CI, 0.45–0.65; $P<.001$), they were both independently associated with mucosal thickening and osteitis.

Blood and sputum neutrophil levels were similar across all groups and were not associated with sinus mucosal thickening or osteitis. Further, we found no significant association with age, smoking history, corticosteroid use (oral or inhaled), or lung function (data not shown).

Pulmonary Function

As a group, patients with severe mucosal thickening had a statistical trend toward a lower mean FEV₁ than those in the normal and mild-moderate categories. When patients were analyzed individually, however, only a weak correlation was found between FEV₁ and CT scores ($r=-0.20$; 95% CI, -0.34 to -0.06 ; $P=.007$). There was no significant correlation between CT scores and maximal forced expiratory flow, midexpiratory phase forced expiratory flow, forced vital capacity, postbronchodilator FEV₁, or D_{LCO}. Blood and sputum eosinophil levels were poorly correlated with pulmonary function parameters (data not shown).

DISCUSSION

The current study found radiographic abnormalities of the sinus mucosa in most patients with asthma who underwent sputum analysis and presented with sinonasal symptoms. The extent of mucosal thickening on sinus CT directly correlated with blood and sputum eosinophil levels, which are markers of lower airway eosinophilic inflammation. These findings are in agreement with those of ten Brinke et al,¹⁵ who found a direct association between evidence of sinus mucosal thickness on CT and sputum eosinophilia in patients with severe asthma.¹⁵ Our findings extend these observations by showing a similar association in a heterogeneous group of patients with asthma with varying degrees of lung function impairment. Our study confirmed previous findings that patients with more advanced mucosal thickening had a higher serum IgE²⁷ but no differences in atopic status.²⁸ Nasal polyps, which were also more prevalent among patients with severe mucosal thickening, were associated with hyposmia, likely from nasal obstruction, and were unrelated to atopic status.

Eosinophilic inflammation is the histologic hallmark of both asthma and chronic hyperplastic eosinophilic sinusitis, the predominant subtype of CRS.²⁹ Eosinophils are also the predominant inflammatory cells found in nasal polyps. Major basic protein, released from activated eosinophils, appears to have a pivotal role in damaging the respiratory mucosa.³⁰ According to proponents of the unified airway hypothesis, eosinophilic inflammation in the upper and lower airways can be considered as a continuum, with inflammation in one part of the airway influencing its counterpart.³¹ Indeed, there is mounting evidence from animal and human studies that allergic inflammation is not confined locally but generates a secondary systemic response. This response can feed back to the original site of inflammation and lead to distant

manifestations; however, the exact mechanisms have not been fully elucidated.³² We hypothesized that activated eosinophils within the sinus mucosa may be releasing T_H2 cytokines into the circulation, inducing the systemic recruitment of eosinophils from the bone marrow to sites of preexisting inflammation, such as the lungs and sinuses.

Of note, the most extensive mucosal thickening and the highest blood and sputum eosinophil levels were found in patients who had undergone sinus surgery. Although this could represent a selection bias, it could alternatively reflect ongoing upper airway eosinophilic inflammation. If corroborated in prospective studies, this finding would suggest the continued need for aggressive postoperative anti-inflammatory therapies, at least in patients with asthma, who are likely to have the chronic hyperplastic eosinophilic form of CRS.³³ In our study, only 44% of patients who had undergone sinus surgery reported regular intranasal corticosteroid use.

Recently, there has been some speculation in the literature about the potential role of neutrophils in asthma. A growing body of evidence suggests considerable neutrophilic inflammation in patients with severe, persistent asthma.^{34–36} Some authors have even suggested the existence of a subtype of patients with noneosinophilic asthma.³⁷ In light of these developments, we also examined blood and sputum neutrophil levels but were unable to find any association with sinus mucosal thickening or osteitis.

We noted radiographic abnormalities of the bone in a number of CT scans, consistent with previous observations. Findings of osteitis, which were almost exclusively limited to patients with severe mucosal thickening, were associated with substantial blood and sputum eosinophilia but not with an elevated serum IgE or positive atopic status. We speculate that these bone changes are mediated largely by localized mucosal eosinophilic inflammation and may be a hallmark of the chronicity of sinus disease. Our hypothesis is supported by the high prevalence of bony erosions and remodeling noted in patients with allergic fungal sinusitis, a disease characterized by eosinophilic mucin. For example, in a recent retrospective review of 65 patients with documented eosinophilic fungal sinusitis, Vlamincx et al³⁸ reported osteitis in 25 cases (38%).

Bone remodeling is a dynamic process that depends on a balance between the bone-forming activities of osteoblasts and the bone-resorbing activities of osteoclasts. Regulation of this activity is controlled in part by a class of signaling molecules known as *bone morphogenetic proteins*, members of the transforming growth factor β (TGF- β) superfamily.³⁹ The potential role of eosinophils in bone remodeling is of particular interest. Eosinophils secrete mediators, namely TGF- β , which directly affect osteoblasts.⁴⁰ A recent report showed that TGF- β ₂ expression is markedly increased in the eosinophils of patients with severe asthma.⁴¹ Conversely, eosinophil chemotactic factor L has been shown to be a potent osteoclast-stimulating factor.⁴² Eosinophils are also a major source of a number of other inflammatory cytokines and tissue remodeling factors that could be directly or indirectly implicated in osteitis.

Among the potential shortcomings of our study, we must first acknowledge its observational, retrospective nature and the possibility of patient selection bias. Indeed, most patients presented with some degree of lower airway and sinonasal symptoms, prompting the physician to obtain a sputum analysis and sinus CT. However, given the heterogeneity of FEV₁ and sinus CT scores, we do not think our patients had more severe asthma or sinus disease than other tertiary care patients. The fact that women outnumbered men in our study is not surprising, given epidemiological data that more adult women than men have asthma and that their asthma is more severe.⁴³ Second, asthma was defined solely by physician diagnosis and therefore could be subject to bias or error. However, most patients were assessed by specialists, who are well trained in recognizing asthma, and therefore the likelihood of an incorrect diagnosis is low.

Third, measurement of eosinophilic airway inflammation was based solely on induced sputum eosinophil levels. Markers of eosinophilic activation, such as major basic protein and eosinophil cationic protein levels, were not measured. Further, more novel noninvasive surrogate markers of airway inflammation, such as exhaled nitric oxide, exhaled breath condensate pH, and exhaled breath condensate nitrogen oxides, were not examined because they were unavailable to us at the time of the study. Fourth, in our analysis of inflammatory parameters, we were unable to adjust for the exact dose and interval of medication use before sputum induction because these details were not reproducibly available in the medical records. However, despite higher ICS use among patients with more severe sinus disease and lower FEV₁ values, blood and sputum eosinophil levels were nonetheless elevated, suggesting persistent eosinophilic inflammation. Finally, in spite of our best efforts to take into consideration most of the relevant clinical variables, the possibility of confounding factors makes it difficult to reach definitive conclusions. Moreover, we recognize that several factors not considered, such as local anatomy, bacterial or fungal colonization, host immunity, and lifestyle issues, can be equally important in influencing sinus mucosal thickening and bone remodeling. Future prospective studies are needed to address some of these methodological limitations.

Findings from our study could have clinical implications for the treatment of patients with asthma. Given the frequent coexistence of CRS, clinicians might consider periodic evaluation of the sinuses, especially in patients with asthma that is difficult to control. In some cases, it may be less expensive and more convenient to perform a rhinoscopy than obtain a sinus CT. Findings of sinus mucosal thickening or osteitis may prompt the physician to pursue more aggressive anti-inflammatory therapies, even in the absence of sinonasal symptoms. In the future, markers of airway eosinophilic inflammation could be used to monitor sinus disease and have a particularly useful role after sinus surgery, when continuing medical assessments and management are required.

CONCLUSION

Our study provides evidence of a direct relationship in patients with asthma among sinus mucosal thickening, osteitis, and markers of eosinophilic inflammation, both in the lower airways and the periphery. Together, these findings lend further support to the unified airway hypothesis. A better understanding of this paradigm could ultimately lead to improved diagnostic and therapeutic tools in the treatment of both CRS and asthma.

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Glossary

CI	confidence interval
CRS	chronic rhinosinusitis
CT	computed tomography
D _{LCO}	diffusing capacity of lung for carbon monoxide
FEV ₁	forced expiratory volume in the first second of expiration
ICS	inhaled corticosteroid
TGF- β	transforming growth factor β

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FIGURE 1.

Computed tomograms (CTs) showing mucosal thickening and osteitis and their correlation with scores derived from Lund-MacKay staging. A, CT score, 0; no mucosal thickening; sharply demarcated and well corticated paranasal sinus walls. B, CT score, 5; mild mucosal thickening in the right anterior ethmoid cells. C, CT score, 11; mucosal thickening in the right maxillary sinus and right anterior ethmoid cells; obstruction of the right ostiomeatal complex. D, CT score, 18; extensive mucosal thickening in the maxillary and ethmoid sinuses bilaterally; obstruction of the left ostiomeatal complex despite previous surgery. E, Chronic osteitis. Note the areas of bone thickening (arrows).

FIGURE 2.

Correlation between computed tomographic (CT) score derived from Lund-MacKay staging and sputum (top) or blood (bottom) eosinophil (Eo) counts.

TABLE 1

Patient Characteristics According to the Lund-MacKay Staging Score^{a,b}

	Normal 0–3 CT score (n=65)	Mild-moderate 4–11 CT score (n=76)	Severe ≥12 CT score (n=60)	P value
Age (y), mean ± SD	51.0±15.4	51.2±15.3	53.5±15.0	.59
Male	13 (20)	27 (36)	26 (43) ^c	.01
Positive atopic status	38 (58)	43 (57)	31 (52)	.73
Total serum IgE, median (IQR)	35 (67)	40 (92)	73 (146) ^c	.02
FEV ₁ (% predicted), mean ± SD	84.9±20.6	84.4±17.9	76.8±18.1	.05
Body mass index (kg/m ²), mean ± SD	31.4±7.6	29.5±8.1	30.2±7.4	.18
Asthma medications				
Nasal corticosteroid	22 (34)	26 (34)	29 (48)	.14
Inhaled corticosteroid	42 (65)	43 (57)	46 (77) ^d	.04
Oral corticosteroid in past 6 mo	12 (18)	16 (21)	13 (22)	.93
Long-acting β ₂ -agonist	31 (48)	32 (42)	32 (53)	.36
Leukotriene modifier	21 (32)	24 (32)	15 (25)	.60
Prior smoker	16 (25)	24 (32)	20 (33)	.42
Nasal polyp	0 (0)	3 (4)	6 (10) ^e	.03
Hyposmia	3 (5)	9 (12)	15 (25) ^e	.04
Previous sinus surgery	9 (14)	32 (42) ^c	31 (52) ^e	<.001

^a CT = computed tomographic; FEV₁ = forced expiratory volume in the first second of expiration; IQR = interquartile range.^b Data are presented as number of patients (percentage) unless otherwise indicated.^c $P < .05$, compared with normal.^d $P < .05$, compared with mild-moderate.^e $P < .01$, compared with normal.

TABLE 2

Patient Characteristics According to the Presence of Osteitis^{a,b}

	Osteitis		P value
	No (n=183)	Yes (n=18)	
Age (y), mean $\pm$ SD	51.3 $\pm$ 15.3	51.8 $\pm$ 15.6	.96
Male	57 (31)	5 (28)	.77
Positive atopic status	106 (58)	6 (33)	.04
Total serum IgE, median (IQR)	40 (90)	61 (188)	.53
FEV ₁ (% predicted), mean $\pm$ SD	83.9 $\pm$ 18.8	73.0 $\pm$ 17.5	.05
Body mass index (kg/m ²), mean $\pm$ SD	30.4 $\pm$ 7.4	29.1 $\pm$ 11.0	.86
Asthma medications			
Nasal corticosteroid	62 (34)	8 (44)	.19
Inhaled corticosteroid	117 (64)	13 (72)	.44
Oral corticosteroid in past 6 mo	62 (34)	7 (39)	.50
Long-acting β_2 -agonist	84 (46)	11 (61)	.26
Leukotriene modifier	55 (30)	6 (33)	.52
Prior smoker	55 (30)	5 (28)	.81
Nasal polyp	7 (4)	1 (5)	.83
Previous sinus surgery	62 (34)	10 (56)	.02
CT score, median (IQR)	5 (10)	13 (4)	<.001

^aCT = computed tomographic; FEV₁ = forced expiratory volume in the first second of expiration; IQR = interquartile range.

^bData are presented as number of patients (percentage) unless otherwise indicated.

TABLE 3

Inflammatory Markers According to the Lund-MacKay Staging Score^a

	Normal 0–3 CT score (n=65)	Mild-moderate 4–11 CT score (n=76)	Severe ≥12 CT score (n=60)	P value
Sputum				
Eosinophil levels (/ μ L)	4 (22)	8 (68)	57 (259) ^b	<.001
Eosinophil (%)	1 (3)	3 (18) ^b	12 (37) ^c	<.001
Neutrophil levels (/ μ L)	170 (261)	148 (281)	131 (408)	.76
Neutrophil (%)	61 (32)	54 (36)	57 (36)	.22
Blood				
Eosinophil levels ($\times 10^9$ /L)	0.2 (0.2)	0.2 (0.3)	0.4 (0.3) ^d	<.001
Eosinophil (%)	2.0 (2.3)	2.6 (4.0)	5.1 (5.2) ^e	<.001
Neutrophil levels ($\times 10^9$ /L)	4.2 (1.8)	4.3 (2.1)	4.9 (2.0)	.07
Neutrophil (%)	61 (14)	62 (12)	62 (11)	.80

^a All data are reported as median (interquartile range). CT = computed tomographic.^b $P < .01$, compared with normal.^c $P < .001$ compared with normal and $P < .05$ compared with mild-moderate.^d $P < .001$ compared with normal and mild-moderate.^e $P < .001$ compared with normal and $P < .01$ compared with mild-moderate.

TABLE 4
Inflammatory Markers According to the Presence of Osteitis and Prior Sinus Surgery^a

	Osteitis		Prior sinus surgery		P value
	No (n=183)	Yes (n=18)	No (n=129)	Yes (n=72)	
Sputum					
Eosinophil levels (/μL)	7 (60)	62 (158)	7 (36)	37 (199)	.001
Eosinophil (%)	2 (14)	14 (22)	2 (7)	9 (34)	<.001
Neutrophil levels (/μL)	140 (284)	210 (591)	147 (312)	163 (348)	.80
Neutrophil (%)	58 (35)	60 (35)	61 (38)	54 (29)	.10
Blood					
Eosinophil levels ($\times 10^9/L$)	0.2 (0.3)	0.4 (0.4)	0.2 (0.2)	0.3 (0.4)	<.001
Eosinophil (%)	2.8 (4.1)	4.6 (3.8)	2.4 (3.1)	4.1 (5.2)	<.001
Neutrophil levels ($\times 10^9/L$)	4.4 (2.2)	5.2 (1.8)	4.4 (2.0)	4.7 (2.2)	.31
Neutrophil (%)	61 (12)	63 (11)	62 (13)	63 (11)	.83

^a All data are reported as median (interquartile range).