

Computed tomography evaluation of paranasal sinuses in asthma: Is there a tendency of particular site involvement?

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ABSTRACT

Although the precise mechanism is unclear, asthma and chronic sinusitis are associated frequently. Computed tomography (CT) is a sensitive modality for documenting sinonasal mucosal abnormalities. The aim of this study was to evaluate paranasal mucosal abnormalities in asthma and whether there was a relationship with asthma severity. One hundred fifty-five patients with asthma and 36 normal control subjects were assessed with coronal sinus CT. Asthma was classified as mild, moderate, or severe. Scoring of paranasal sinus abnormalities were assessed for total sinus, total mucosal, and individual sites. The mean scores of total mucosal changes (8.45 points versus 4.67 points, $p < 0.001$) and total sinus scores (5.50 versus 2.69, $p < 0.005$) were significantly higher in the asthmatic patients compared with controls. Nasal passage and frontal sinus involvements were not statistically different between groups, but all other individual scores were significantly higher in asthmatic patients. There was an involvement site tendency with respect to increasing severity of asthma. Mean total mucosal CT scores (12.57 points versus 7.33 points, $p < 0.05$) and individual site scores were statistically higher in asthmatic patients with high blood eosinophil levels compared with those patients with normal blood eosinophil counts except for nasal passage disease. There was no significant relationship between total IgE level and CT scores. Total mucosal and sinus scores were significantly related with asthma severity. There was an involvement tendency of sinuses and sites. Nasal passage involvement was unrelated with asthma. Ethmoidal sinuses and ostiomeatal complexes were involved significantly in patients with mild asthma, whereas maxillary, frontal, and sphenoidal sinuses were involved significantly in patients with severe asthma.

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Sinusitis is an inflammatory condition that affects one or more paranasal sinuses. Particularly in severe asthma, chronic sinusitis and bronchial inflammation are associated frequently.¹ In asthmatic patients there is a chronic inflammation of the paranasal mucosa rather than an acute bacterial sinusitis and related mucosal swelling.² Recent evidence proposes that involvement of paranasal mucosa and asthma are both manifestations of a common inflammatory process.^{1–3} Although the exact mechanism of this coexistence is not explained exactly, several mechanisms have been proposed as the basis such as bacterial seeding of the lungs, reflex bronchospasm, and enhanced β -adrenergic blockade.⁴ In asthma the severity of sinonasal disease is thought to correlate with the severity of bronchial inflammation.^{1,3,5–8} Despite the proper treatment of sinonasal disease, which has been shown to alleviate both sinonasal and asthmatic symptoms, its recurrent resistant nature seems to result in failure in many cases in the long term.^{1,9} Data in the literature

seem to support the hypothesis that sinonasal disease is another dimension of an active immune system reaction, such as sinusitis seen in other types of allergy.⁵ Computed tomography (CT) offers superior sensitivity in detecting sinus abnormalities and the extent of disease. Data regarding the mechanism relationship between sinus abnormalities and asthma were previously accessed mostly by conventional radiographies, but there are relatively few reports using sinus CT.^{1,3,6,7} In this prospective study, we aimed to evaluate the extent and characteristics of paranasal sinus abnormalities on CT scans and whether there was a relationship between these findings and disease severity in asthmatic patients.

MATERIALS AND METHODS

Patients

Our case series included two groups. One hundred fifty-five patients, 40 men and 115 women, (age range, 16–68 years) with bronchial asthma constituted the patient group. Thirty-six patients, 16 men and 20 women, (age range, 14–78 years) were considered as the control group. Bronchial asthma was diagnosed clinically by the presence of recurrent symptoms of wheezing, shortness of breath, cough, and demonstration of objective signs of reversible airway obstruction as stated by American Thoracic

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Table 1 Scoring points for mucosal thickening in paranasal CT*

Site of Mucosal Thickening (mm)	Score Points			
	0	1	2	3
Frontal sinus (n = 2)	0–1	2–5	6–9	≥10
Maxillary sinus (n = 2)	0–1	2–5	6–9	≥10
Sphenoidal sinus (n = 1)	0–1	2–5	6–9	≥10
Ethmoidal sinus (n = 2)	0	1	2–3	≥4
Nasal passage (n = 1)	None	Mild	Moderate	Severe
OMC (n = 2)	None	Mild	Moderate	Severe

Source: Modified from Ref. 1.

Society guidelines.¹⁰ Patients, who were diagnosed with bronchial asthma with these criteria, taken into survey by our Pulmonology Department, were enrolled into the study. All of the patients recruited were informed about the (CT) procedures and consented to participate in the study. This study was performed during a period of 3 years, between 2000 and 2003.

Control subjects were chosen consecutively within the patients who were ordered paranasal sinus CT for other than sinonasal complaints (plastic surgery, ophthalmic problems, etc.). None of the control subjects had a history of experiencing any wheezing, dyspnea, chronic cough or sputum production, or atopy.

All patients and control subjects were evaluated with coronal sinus CT. None of the subjects reported an episode of acute sinusitis or respiratory tract infection during the previous 4 weeks or within the study period and no subjects were smokers. In addition, none of our patients were using nasal or systemic steroids or decongestants within the same period. Peripheral blood eosinophil count was obtained from a complete blood count test and was performed by automated analysis. Blood eosinophil counts $>350/\mu\text{L}$ were considered as higher than normal. Total serum IgE levels also were determined in asthmatic patients and values of >180 IU/mL were considered as higher than normal limits.

Clinically, asthma severity was graded as mild, moderate, or severe according to recent guidelines.¹¹ Atopy diagnosis was made based on patients' historical data and a positive skin-prick test response to the following common aeroallergens (a wheal size ≥ 3 mm): *Dermatophagoides pteronyssinus*, *D. farinae*, a mixture of grasses pollens, a mixture of weeds pollens, a mixture of trees

pollens, a mixture of cereal pollens, a mixture of molds, and animal epithelia.

CT Evaluation and Scoring

All patients and control subjects were scanned with a high-resolution scanner (Toshiba Xvision XT, Toshiba Medical Systems Corp., Tochigi-ken, Japan) in coronal plane, with 30-mm thick slices at 3-mm intervals. All subjects were scanned in prone position. All images were hard copied in wide window settings. CT scans were evaluated using a formerly published scoring system by an experienced radiologist, who was blinded to subjects' clinical condition (Table 1).¹ Maximal mucosal thickening of a single wall in millimeters was measured in all paranasal sinuses and rated from 0 to 3 points for each sinus. Nasal passages and ostiomeatal complexes (OMC) were assessed separately as 0 points for no disease, 1 point for mild disease, 2 points for moderate disease, and 3 points for severe mucosal disease. Total sinus scores were calculated as the sum of sinus scores and a range of possible scores from 0 to 21 were achieved for each patient. To evaluate total sinonasal mucosal changes, another score is contemplated by adding nasal passage and OMC scores to total sinus score, which then is called total mucosal score. Total mucosal score rendered a range of possible points from 0 to 30. In addition to total sinus and total mucosal scores, individual scores for evaluation sites also were determined to evaluate any specific association between mucosal disease localization and asthma. Anatomic variations such as concha bullosa, agger nasi cells, Haller cells, deviated septum, which may alter the mucociliary transport and predispose to sinusitis, also were taken into consideration and each

Table 2 Score points for each site and total sinus mucosal scores in patient group ($n = 155$) and control subjects ($n = 36$)

Site of Mucosal Abnormality	Score Points							Mean	SD	Significance
	0	1	2	3	4	5	6			
Nasal Passage										
Patient	40	85	20	10				1.00	0.81	$p > 0.05$
Control	8	21	7					0.97	0.65	
OMC										
Patient	45	24	37	23	7	7	12	1.95	1.82	$p = 0.005$
Control	19	4	7	6				1.00	1.20	
Frontal sinus										
Patient	103	16	20	1	7		8	0.87	1.59	$p > 0.05$
Control	7	5	4					0.36	0.68	
Maxillary sinus										
Patient	62	12	20	22	19	3	17	2.01	2.07	$p < 0.05$
Control	21	3	2	5	3		6	1.28	1.83	
Sphenoidal sinus										
Patient	116	29	2	8				0.37	0.76	$p < 0.05$
Control	33	1	1	1				0.17	0.61	
Ethmoidal sinus										
Patient	38	18	38	21	21	5	14	2.26	1.86	$p < 0.001$
Control	23	8	4	1				0.89	1.26	
Score points	0–4	5–9	10–14	15–19	20–24	25–29	30			
Total sinus score*										
Patient	87	40	12	4	5			5.50	5.47	$p < 0.005$
Control	26	9	1					2.69	2.78	
Total mucosal score*										
Patient	58	48	23	8	9	4	5	8.45	7.65	$p < 0.001$
Control	22	10	4					4.67	3.48	

*Total mucosal and total sinus scores are presented in score groups.

anatomic variation was scored as positive or negative for each subject.

Statistical Analysis

SPSS for Windows was used for statistical analysis (version 11.5, SPSS, Inc., Chicago, IL). Anatomic variations between patients and control subjects were analyzed with chi-square test. Mann-Whitney U test was used to analyze nonparametric data. Because our CT scoring data is nonparametric, parametric data such as blood eosinophil count and IgE levels were transformed into nonparametric scores as high and normal. A value of $p < 0.05$ was considered statistically significant. Results are expressed as mean $\pm$ SD. Mean values are arithmetic unless otherwise stated.

RESULTS

Our study included 155 patients (115 women and 40 men) and 36 control subjects (20 women and 16 men). The age of asthmatic patients ranged from 16 to 68 years (40.6 ± 11.5 years). Control subjects' ages were

between 14 and 78 years (39.2 ± 18.3 years). The mean duration of asthma was 7.1 ± 5.9 years and mean FEV₁ was $78.8 \pm 18.9\%$ in patient group. Clinically asthma severity was graded as mild in 108 (69.6%) patients, moderate in 33 (21.3%) patients, and severe in 14 (9.0%) patients. Thirty-five patients were had allergic asthma (22.7%).

Scores for total mucosal changes of asthma patients ranged from 0 to 30 points (8.5 ± 7.7 points) and for control subjects total mucosal changes ranged from 0 to 12 points (4.7 ± 3.5 points), and total sinus scores were 0–21 points (5.5 ± 5.5 points) and 0 to 10 points (2.7 ± 2.7 points), respectively. Individual site CT scores for asthmatic patients and control subjects and statistical evaluation of comparisons are listed in Table 2.

Analysis of individual site CT scores in patient group revealed that mucosal thickening of nasal passages and frontal sinuses were not statistically different from the control group ($p > 0.05$). However, all other CT scores significantly indicated that mucosal changes were associated with asthma ($p < 0.05$).

Table 3 Statistical levels of importance of CT score comparisons within asthma severity groups (mild, $n = 108$; moderate, $n = 33$; severe, $n = 14$) and between each asthma severity group and controls ($n = 36$)

	Mild vs Moderate	Mild vs Severe	Moderate vs Severe	Mild vs Control	Moderate vs Control	Severe vs Control
Nasal passage	NS	NS	NS	NS	NS	NS
OMC	NS	$p < 0.01$	NS	$p < 0.05$	$p < 0.05$	$p < 0.001$
Frontal sinus	NS	$p < 0.05$	NS	NS	NS	$p < 0.01$
Maxillary sinus	NS	$p < 0.05$	NS	NS	NS	$p < 0.005$
Sphenoidal sinus	NS	$p < 0.05$	$p < 0.05$	NS	NS	$p < 0.005$
Ethmoidal sinus	NS	NS	NS	$p < 0.001$	$p < 0.005$	$p < 0.001$
Total sinus score	NS	$p < 0.05$	NS	$p < 0.05$	$p < 0.05$	$p < 0.001$
Total mucosal score	NS	$p < 0.05$	NS	$p < 0.05$	$p < 0.05$	$p < 0.001$

NS = not significant.

Table 4 Relationship of site and total CT scores with eosinophilia

	Eosinophilia	Mean	SD	Significance
Nasal passage	+	1.33	1.08	$p > 0.05$
	−	0.91	0.69	
OMC	+	2.73	2.31	$p < 0.05$
	−	1.74	1.61	
Frontal sinus	+	1.61	2.19	$p < 0.05$
	−	0.67	1.32	
Maxillary sinus	+	3.09	2.43	$p < 0.005$
	−	1.71	1.86	
Sphenoidal sinus	+	0.73	1.07	$p < 0.01$
	−	0.27	0.62	
Ethmoidal sinus	+	3.09	2.24	$p < 0.05$
	−	2.03	1.69	
Total sinus score	+	8.51	7.17	$p < 0.05$
	−	4.68	4.61	
Total mucosal score	+	12.57	10.30	$p < 0.05$
	−	7.33	6.36	

Individual site CT scores were not statistically different between mild and moderate asthmatic patients ($p > 0.05$). Analyses of scores between moderate and severe asthmatic patients for individual sites were not significantly different ($p > 0.05$), except for sphenoidal sinus, which was more prevalently involved in patients with severe asthma ($p < 0.05$). Differences in other scores were not statistically significant between groups. Comparisons of individual site scores between patients with mild, moderate, and severe asthma and controls are shown in Table 3.

Anatomic variations such as Haller cells, agger nasi cells, and concha bullosa were detected in both groups and were not statistically different between asthmatic patients and controls ($p > 0.05$). However, deviated septum was detected in 58 patients and 24 controls, which was relatively more prevalent in the control group ($p < 0.005$).

Blood eosinophil counts ranged from 1 to $2800/\mu\text{L}$ (296 ± 354). Blood eosinophil counts were higher than normal in 42 (27.1%) asthmatic patients. Mean total CT score was 12.6 ± 10.3 in patients with high blood eosinophil counts, whereas it was 7.3 ± 6.3 in asthmatic patients with normal blood eosinophil counts ($p < 0.05$). All individual site scores were significantly different in asthmatic patients with high blood eosinophil counts compared with those patients with normal blood eosinophil counts ($p < 0.05$), except for nasal passage disease ($p > 0.05$; Table 4).

Total IgE levels ranged from 4 to 2160 IU/mL (84 ± 310 [Geometric mean]). There was no difference in normal levels of total IgE regarding individual site and total mucosal and total sinus scores ($p > 0.05$). In addition, statistical analysis from the aspect of chronic sinusitis showed no difference between atopic and nonatopic asthmatic patients ($p > 0.05$).

DISCUSSION

The relationship between asthma and chronic sinonasal mucosal disease has long been known. There are numerous studies implying this relationship.^{1,2,6-9,12} Compared with conventional radiographs CT is much more sensitive to detecting sinus abnormalities.¹³ For these reasons, some older studies should be regarded as incapable of accurately documenting sinonasal abnormalities, in all aspects. CT scans in patients with chronic sinusitis reflect sinonasal mucosal thickening. People with no complaints of sinus disease also may present mucosal abnormalities.^{9,14,15} Some older studies suggested that mucosal thickening in maxillary sinus was common in the asymptomatic population and, alone, it might be unrelated to any pathological process and be clinically insignificant; but other sinuses and nasal passages were considered frequently effected through the pathological process.³ Despite data regarding the involvement of sinonasal mucosa in asthma, to the best of our knowledge, there is no study performed to evaluate the tendency of the involvement site. Most previous studies dealt with total sinonasal CT scores and classified their CT scores for limited (CT scores ≤ 11) and extensive (CT scores ≥ 12) sinonasal involvement.^{1,6} We accepted our CT score data as a continuum and did not arbitrarily classify it as limited and extensive involvement. In this respect we analyzed our data on the basis of individual site scores as well as total mucosal and total sinus scores. In contrast to former findings, our study showed that maxillary sinus involvement is related closely to asthma. Ethmoidal sinus and OMC diseases showed the most significant relationship, whereas frontal sinus and nasal passage involvements were found unrelated with asthma. Sphenoid sinus involvement also is related closely with asthma. Total sinus and total mucosal CT scores were significantly different from the controls, which is completely compatible with former findings.

Our study showed that paranasal mucosal thickening is prominent in asthma, which is in accordance with former studies. However, asthma is a heterogeneous disease presenting a clinical spectrum from mild to severe. To assess the relationship between asthma severity and sinonasal involvement, we also evaluated the effect of asthma severity on sinonasal involvement. The only study performed, by Bresciani *et al.*, evaluated the relationship between asthma severity and paranasal CT score.⁷ Bresciani *et al.* concentrated on the comparison of mucosal changes in mild-to-moderate and severe asthma; however, their study also was performed using total sinonasal mucosal CT scores.⁷ Bresciani *et al.* reported that the frequency of sinonasal involvement is similar in mild-to-moderate and severe asthma groups; however, severe steroid-dependant

asthma was associated with significantly greater CT scores.⁷ There was no other study that was interested in individual site involvement tendency in asthma and its relationship with asthma severity. On the basis of individual site CT scores, involvement of ethmoidal sinuses was not different between asthma severity groups. This finding suggests that ethmoidal sinuses probably represent the most initial inclined site of involvement. OMCs seem to represent the second-most prone site. Sphenoidal, maxillary, and frontal sinuses are the other sites, showing involvement tendency, with respect to increasing severity of asthma (Table 3). Two different comparisons of CT scores of asthmatic patients with controls are completely compatible except for the frontal sinus involvement. Because frontal sinus involvement significantly differs from control groups in severe asthmatic patients, insignificance, first, might be caused by the relatively few numbers of severe asthma cases among total asthma patients. It is interesting to note that nasal passage mucosal disease is completely unrelated with asthma as well as its severity. No other study documented this finding. Total mucosal and total sinus CT scores also are significantly different from the control group in all asthma severity groups. Currently, it is not possible to explain why nasal passage disease is unrelated to asthma. Because nasal passage abnormalities are widely seen in the population, we might speculate that the abnormalities seen in asthmatic patients could be a continuation of this attribute. In addition, the results support previous data that there is a relationship between the involvement of the sinuses in asthma.

Although chronic sinusitis in asthma is a remote disease and the relationship with asthma is not clearly defined, there are some suggestions that the mucosal disease is commonly related with eosinophilia. Previous studies investigating asthma and related sinusitis have stressed this finding.^{1,3,12} Moreover, Newman *et al.* stated that inflammation in the sinuses is a stimulus for eosinophilia rather than coexistent asthma and allergy. In this study, nasal passage disease seems to be unrelated, but all sinus and OMC involvements are significantly related with eosinophilia. Patients with high eosinophil levels in their blood have a mean score of 12.6 points for total mucosal disease, compatible with extensive sinusitis, which is described in previous studies as those having a score of >11 points. Therefore, for practical purposes, this breakpoint for total mucosal disease score seems useful for evaluation of extensive sinusitis. Our results are in concordance with previous findings that eosinophilia is strongly related with sinusitis in asthma patients.

Total IgE level association with chronic sinusitis is controversial.^{1,16} Although some studies proposed that total IgE levels correlated with sinusitis, there is no clear evidence of association of IgE levels with chronic

sinusitis in asthma.¹ Our results also found no significant relation between total IgE levels and chronic sinusitis in patients who have asthma.

Ideally, a scoring system that could be used to assess chronic sinusitis is expected to quantify total extent of mucosal disease in chronic sinusitis. This could be achieved by assessing the total volume of mucosal thickening. Because it takes too long to perform volume quantification on a large number of CT scans, practically assessing the total volume of abnormal mucosa is nearly unattainable.³ For these reasons, there is a need for an approximation. The scoring system we used was accepted as practical and easy to apply and we believe it fulfills the need for an approximation. On the basis of this approximation, the result of this study is in concordance with all previous studies, reporting the association of chronic sinusitis with asthma. In addition, we found that nasal passage disease is statistically unrelated to chronic sinusitis in asthma, but OMC and sinus mucosal diseases are significantly related. Moreover, there is an involvement tendency of individual sites. Ethmoidal sinuses and OMC seem to be involved significantly in patients with mild asthma, whereas maxillary, frontal, and sphenoidal sinuses were involved significantly in patient with severe asthma compared with the control group.

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