

## KLINIKINIAI TYRIMAI

**Association of chronic rhinosinusitis with nasal polyps and asthma: clinical and radiological features, allergy and inflammation markers****Jūratė Staikūnienė, Saulius Vaitkus<sup>1</sup>, Lidija Marija Japertienė<sup>2</sup>, Silvija Ryškienė<sup>3</sup>***Department of Pulmonology and Immunology, <sup>1</sup>Department of Otorhinolaryngology, Kaunas University of Medicine, <sup>2</sup>Department of Pulmonology and Immunology, Kaunas University of Medicine Hospital,**<sup>3</sup>Department of Radiology, Kaunas University of Medicine, Lithuania***Key words:** *chronic rhinosinusitis; nasal polyps; asthma.*

**Summary.** Chronic rhinosinusitis (CRS) with and without nasal polyps represent different stages of one chronic inflammatory disease of the mucosa of the nasal cavity and paranasal sinuses. Coexistence of chronic rhinosinusitis with nasal polyps and asthma and rather similar characteristics of inflammation support assumption that chronic rhinosinusitis and nasal polyps and asthma may be, at least in part, the same disease process. We therefore aimed to evaluate the differences of sinus radiologic findings, systemic inflammation and allergy markers, pulmonary function of chronic rhinosinusitis associated with nasal polyps and asthma.

A total of 121 patients with chronic rhinosinusitis referred to tertiary center were evaluated; 23 healthy persons served as controls. Sinus CT scans and nasal endoscopy were performed. Allergic rhinitis was diagnosed according to history and positive skin prick tests to common inhalant allergens. Asthma was diagnosed according to GINA by history and pulmonary function tests. Aspirin intolerance was assessed by history. Total IgE, *Aspergillus fumigatus*-specific IgE levels, leukocyte and eosinophil count in the peripheral blood were measured.

Nasal polyps were detected in 84 patients (69.4%), asthma diagnosed in 48 patients (39.6%), associated with nasal polyps (91.7%) and allergic rhinitis in 45.5% of patients. Forty-four patients with chronic rhinosinusitis and having nasal polyps and asthma were characterized by older age ( $P<0.01$ ), greater duration of nasal symptoms ( $P<0.001$ ), higher number previous surgeries ( $P<0.01$ ), more severe sinus disease on CT scan ( $P<0.001$ ), greater blood leukocyte and eosinophil count, total IgE level ( $P<0.01$ ), bronchial obstruction ( $P<0.05$ ), incidence of allergic rhinitis ( $P<0.01$ ), and sensitivity to house dust mite *D. pteronyssinus* (47.7%,  $P<0.01$ ) and mold allergens (29.5%,  $P<0.01$ ) comparing to the patients with isolated chronic rhinosinusitis. The extent of sinus CT changes was greater in asthmatics and correlated with greater duration of asthma ( $P<0.0001$ ), higher number of previous surgeries ( $P=0.001$ ), leukocyte count in blood ( $P=0.025$ ), and age ( $P=0.039$ ).

**Conclusion.** Our data indicate that patients with chronic rhinosinusitis compose clinically heterogeneous group and when associated with nasal polyps and asthma constitutes the most severe form of unified respiratory tract disease, which is characterized by older age of the patients, greater duration of nasal symptoms, extent of sinus radiological changes, more prominent systemic inflammation markers, greater bronchial obstruction, incidence of perennial allergic rhinitis.

**Introduction**

Chronic rhinosinusitis (CRS) is an inflammatory disease of the mucosa of the nasal cavity and paranasal sinuses with symptoms lasting longer than 12 weeks. Based on the presence of nasal polyps on endoscopy, CRS is clinically divided in CRS with and without nasal polyps (NPs) (1). The pathogenesis of CRS is poorly understood; however, genetic susceptibility, infection, anatomic abnormalities, and local immunologic imbalance have been postulated to play roles

in its pathogenesis (1–5). Previous data showed that blood eosinophilia and the extent of eosinophilic inflammation is related to the extent of sinonasal mucosal involvement, the severity of nasal disease, and size of nasal polyps suggesting that CRS with and without NPs represent two end of a spectrum of chronic inflammatory disease (6). Recently, differences in the expression of inflammatory mediators and cellular characteristics were demonstrated in CRS and NP mucosal tissue. Most of the studies confirm that

eosinophils and related inflammatory products are the hallmark of NP-associated inflammation. For example, interleukin (IL-5), an eosinophil survival and differentiation factor, and eosinophil cationic protein (ECP), eotaxin, the indicators for eosinophil chemotaxis and activation, Ig E, have been found to be significantly increased in NP vs. CRS and controls (7–12). Expression of cytokines, metalloproteinases and their inhibitors, proinflammatory enzymes (group II subfamily secretory phospholipase A2) may play different roles in the pathogenesis of CRS with and without NPs (7, 9, 13, 14).

Further clarifying and understanding the relationship between diseases of the upper and lower respiratory tract is important because of the prevalence of rhinosinusitis and asthma and the resulting burden on patients and the health care system. Rhinosinusitis coexists with asthma in 34–50% of patients (15, 16). Recently, more than 84% of sinus computed tomography (CT) scans were found to be abnormal in severe asthma, with a correlation between the extent of CT changes, sputum eosinophilia and pulmonary function (17–20). Rhinosinusitis and asthma also represent a range of overlapping diseases with a similar pathophysiological mechanism, where chronic airway mucosal inflammation and remodeling are playing a critical and integrating role in these diseases. In CRS and NP, the sinus mucosa contains eosinophils and interleukin-5-producing T lymphocytes as well as asthmatic bronchial mucosa (21–23). The bone marrow may provide the link between the upper and lower airways in creating a common disease. Blood eosinophil count is often increased in asthma and correlates with severity of asthma, and asthmatic patients tend to have more severe nasal polyposis (21, 24). However, other important questions remain, including factors that determine the clinical phenotype in airway disorders and optimal treatment approaches.

The purpose of this study was to compare the possible associations of chronic rhinosinusitis with nasal polyps and asthma and to detect the differences of sinus radiologic changes, systemic inflammation and allergy markers, pulmonary function. To complete this aim, we measured serum IgE level, blood eosinophil and leukocyte count, pulmonary function and detected the sensitivity to inhalant allergens in patients with CRS with and without NPs, with or without concomitant asthma.

## Materials and methods

### Patients

We prospectively collected data of 121 consecutive

patients with chronic sinus disease, referred to tertiary centers of the Kaunas Medical University Hospital – Department of Pulmonology and Immunology and Department of Otorhinolaryngology, over a period from 2002 to 2005. Chronic sinusitis was diagnosed by history, nasal endoscopy, sinus disease extent on computed tomography (CT) scan was categorized according to Lund and Mackay (25). Nasal polyps were detected by nasal endoscopy and graded on a 0–3-point scale. Polyps were scored as grade 1 when restricted to the middle meatus, grade 2 when they reach beyond the middle turbinate, and grade 3 when they reach the inferior turbinate or fill the nasal cavity (26). Asthma was diagnosed according to GINA by history and pulmonary function tests (reversal bronchial obstruction, bronchial hyperreactivity to methacholine) and graded by severity into intermittent, mild, moderate, and severe persistent (27). The patients were divided into four different groups according to endoscopic appearance of nasal polyps and the presence of asthma. The groups were as follows: CRS, no polyps, no asthma (Group 1, CRS); CRS and asthma, no polyps (Group 2, CRS+A); CRS and polyps, no asthma (Group 3, CRS+NPs); CRS, polyps, and asthma (Group 4, CRS+NPs+A). Allergic rhinitis was diagnosed according to symptoms and positive skin prick test to common inhalant allergens. Aspirin intolerance was assessed by history. Patients using systemic steroids during the last 4 weeks before blood sample were excluded. All patients gave their written informed consent, and the Ethics Committee of the Kaunas University of Medicine approved the study.

### Allergy and inflammation markers

The sensitization to the most common allergens found locally was tested by skin prick tests. Sensitization to perennial allergens was tested using allergen extracts of house dust mite *D. pteronyssinus*, cat, dog, cockroach, mold mixture of *Aspergillus*, *Penicillium*, *Cladosporium*, *Alternaria spp.* (Bayer Corporation, USA). Birch, timothy grass, and mugwort weed pollen allergen extracts were used to test skin sensitivity to pollens. Histamine (10 mg/mL) was used as a positive control, diluent of allergen extract – as a negative control. Positive skin prick test was considered when a mean wheal diameter was 3 mm and more than negative control (28). Serum total IgE, *Aspergillus fumigatus*-specific IgE levels were measured by immunoassay ELISA “M.A.S.T. Diagnostica” (Laboratoriums-Präparate GmbH, Germany) according to recommendations of a manufacturer. IgE level greater than 100 kU/L and *Aspergillus fumigatus*-

specific IgE (sIgE) level greater than 0.35 kU/L were considered elevated. Leukocyte and eosinophil count in peripheral blood was detected by automatic cell calculator ADVIA 120.

#### **Pulmonary function test (spirometry)**

All measurements were made in the sitting position. Forced expired volume in one second ( $FEV_1$ ), vital capacity (VC) were obtained from flow/volume curves using spirometer "Custo VitM" (Custo Med, Germany). The largest values obtained for VC,  $FEV_1$  from the first three technically satisfactory forced expirations were selected. All data were expressed in absolute values and in percentage of predicted normal values (% pred),  $FEV_1/VC$  (%) evaluated. The spirometric standards used complied with European Respiratory Society recommendations (29). Lung function was considered as normal if  $FEV_1$  80% predicted,  $FEV_1/VC$  88% predicted for men and 89% predicted for women.

#### **Statistical analysis**

The statistical analysis was performed using SPSS Windows 12.0 version. The frequency analysis of the symptoms and CT scan score distribution was obtained using ANOVA. Differences in proportions were tested by means of chi-square statistics. When comparisons were made between groups, the nonparametric test such as Kruskal-Wallis test was used to establish the significant intergroup variability. The Mann-Whitney test was then used for between-group comparison. Data are presented as individual values or expressed in Box-and-Whisker plots that represent the median, lower and upper quartiles, and the minimum to maximum value. The correlation was detected using Spearman's coefficient. A *P* value of <0.05 was considered statistically significant.

#### **Results**

The study group consisted of 144 persons, 121 with proven chronic rhinosinusitis (41 men and 80 women), and the control group comprised 23 nonatopic persons (6 men and 17 women) without nasal symptoms. The mean±SD age of the patients with chronic rhinosinusitis was 49.1±13.7 years (range, 16–73 years), for the controls 41.9±15.8 years (range, 16–78 years). Two groups did not differ significantly according to age and sex.

The demographic, clinical, and function characteristics of patients with CRS is given in Table. Nasal polyps were detected endoscopically in 84 patients (69.4%); more than half of patients (53.6%) had pol-

yps of third degree. Sinus CT scores ranged between 1 and 24 ( $13.8\pm6.9$ ) of a maximum achievable score of 24. No significant gender difference according to duration of disease, CT score was shown. The patients with a history of aspirin hypersensitivity had greater sinus radiological changes (mean sinus CT score,  $18.3\pm6.3$ ) compared to aspirin-tolerant patients (mean sinus CT score,  $13.1\pm6.8$ ) ( $P=0.005$ ). More than half of patients (64.5%) complained of olfactory impairment; olfactory loss was present in 30.6% of patients only with NPs. The radiologic sinus changes did not differ between the patients with hyposmia and anosmia, but the patients with higher degree of NP had greater CT score ( $P<0.01$ ). More than half of patients (58.7%) have been treated surgically for their chronic sinus disease from 1 to 10 times (mean number,  $2.37\pm2.2$ ), more often men than women ( $P=0.02$ ). Less than half of surgically treated patients (46.5%) undergone surgery once; 2 patients with CRS and NPs and asthma (2.8%) have been operated for 10 times. Asthma was diagnosed in 48 patients (39.6%); 32 (66.6%) of them had asthma of moderate severity. Majority of patients (91.7%) with asthma had NPs. Mean duration of asthma in patients without NPs was  $11.7\pm11.3$  years and  $9.9\pm9.7$  years in patients with NPs. Allergic rhinitis and sensitivity to common inhalant allergens was proved in 45.5% of patients, and its incidence differed significantly among the groups of patients, more often associated with asthma. Most often the patients had positive skin tests only to perennial indoors allergens (21.5%) or both to perennial and pollen allergens (14%). Less than one-third (28.9%) of patients had positive skin tests to house dust mite *D. pteronyssinus*, 14% to cockroach, 13.2% to molds, 11.6% to grass and weed pollen allergens. Sensitization pattern to perennial inhalant allergens differed significantly among four groups (Table). Seropositivity of IgE specific to *Aspergillus fumigatus* was detected in 19 of the 63 tested patients (30.2%) with no differences among groups of patients.

The patients with CRS had higher blood eosinophil count and serum IgE level than the controls ( $P<0.05$ ) (Fig. 1). Pulmonary function test showed the reduced  $FEV_1/VC$  ratio, a marker of bronchial obstruction, in patients with CRS compared to controls ( $P<0.05$ ). Comparing the patients with CRS, NPs, and asthma (Group 4) with control group, they had significantly higher IgE level, blood eosinophilia, and reduced  $FEV_1/VC$  ratio ( $P<0.01$ ).

The age, duration of nasal symptoms, sinus radiological changes, immunological parameters (IgE level, leukocyte and eosinophil counts in a peripheral blood),

**Table. Demographic, clinical, and function characteristics of patients with chronic rhinosinusitis (CRS), with CRS and asthma (CRS+A), with CRS and nasal polyps (CRS+NPs), and with CRS, nasal polyps, and asthma (CRS+NPs+A)**

Variable	All	Group 1 CRS	Group 2 CRS +A	Group 3 CRS+NPs	Group 4 CRS+NPs+A	P value
N	121	33	4	40	44	
Mean age, years (SD)	49.1 (13.7)	42.9 (13.9)	53 (15.6)	50.5 (14.6) <sup>□</sup>	52.2 (11.1)**	<b>0.036</b>
Sex (F/M)	80/41	7/26	1/3	21/19	12/32	<b>0.036</b>
Mean duration of nasal symptoms, years (SD)	11.5 (9.5)	7.5 (7.5)	13.7 (7.5)	11.2 (9.8)	14.6 (9.8)***	<b>0.007</b>
Normal smell, n (%)	43 (35.5)	30 (90.9)	2	8	3	<b>&lt;0.0001</b>
Reduced smell, n (%)	41 (33.9)	3	2	18	18	
Anosmia, n (%)	37 (30.6)	0	0	14	23	
Sinus CT scan score, mean, (SD)	13.8 (6.9)	7.8 (4.8)	11.7 (8.9)	14.8 (5.2) <sup>□□□</sup>	17.6 (6.5)***	<b>&lt;0.0001</b>
Grade of nasal polyps:						
Grade 1, n (%)	5(6)	–	–	1 (2.5)	4 (9.1)	0.485
Grade 2, n (%)	34 (40.5)	–	–	17 (42.5)	17 (38.6)	
Grade 3, n (%)	45 (53.5)	–	–	22 (44)	23 (52.3)	
Mean number of previous surgery (SD)	2.4 (2.2)	1.23 (0.4)	1 (0)	2.4 (2.5) <sup>□</sup>	2.9 (2.4)**	<b>0.005</b>
History of aspirin intolerance, n (%)	16 (13.4)	0 (0)	0 (0)	2 (1.7)	14 (11.8)	<b>&lt;0.0001</b>
Severity of persistent asthma:						
Mild, n (%)	8 (16.7)	–	1 (25)	–	7 (15.9)	0.371
Moderate, n (%)	32 (66.6)	–	3 (75)	–	29 (65.9)	
Severe, n (%)	8 (16.7)	–	0 (0)	–	8 (18.2)	
FEV <sub>1</sub> , L/s, mean (SD)	2.7 (0.9)	2.9 (0.7)	2.1 (0.8) <sup>‡</sup>	3.3 (0.9)**	2.4 (0.9)	<b>0.017</b>
Percentage FEV <sub>1</sub> /VC predicted, mean (SD)	89.9 (17.6)	99.9 (9.4)	87 (25.4)	102.7 (8.5)**	83.7 (17.7)*	<b>0.004</b>
Allergic rhinitis, n (%)	55 (45.5)	10 (30.3)	2 (50)	15 (37.5)*	28 (63.6)**	<b>0.007</b>
Sensitization to perennial inhalant allergens, n (%)	26 (21.5)	4 (12.1)	1 (25)	8 (20)	13 (29.5)	<b>0.013</b>
Sensitization to pollen allergens, n (%)	12 (9.9)	3 (9.1)	1 (25)	5 (12.5)	3 (6.8)	
Mixed sensitization, n (%)	17 (14)	3 (9.1)	0 (0)	2 (5)	12 (27.3)	

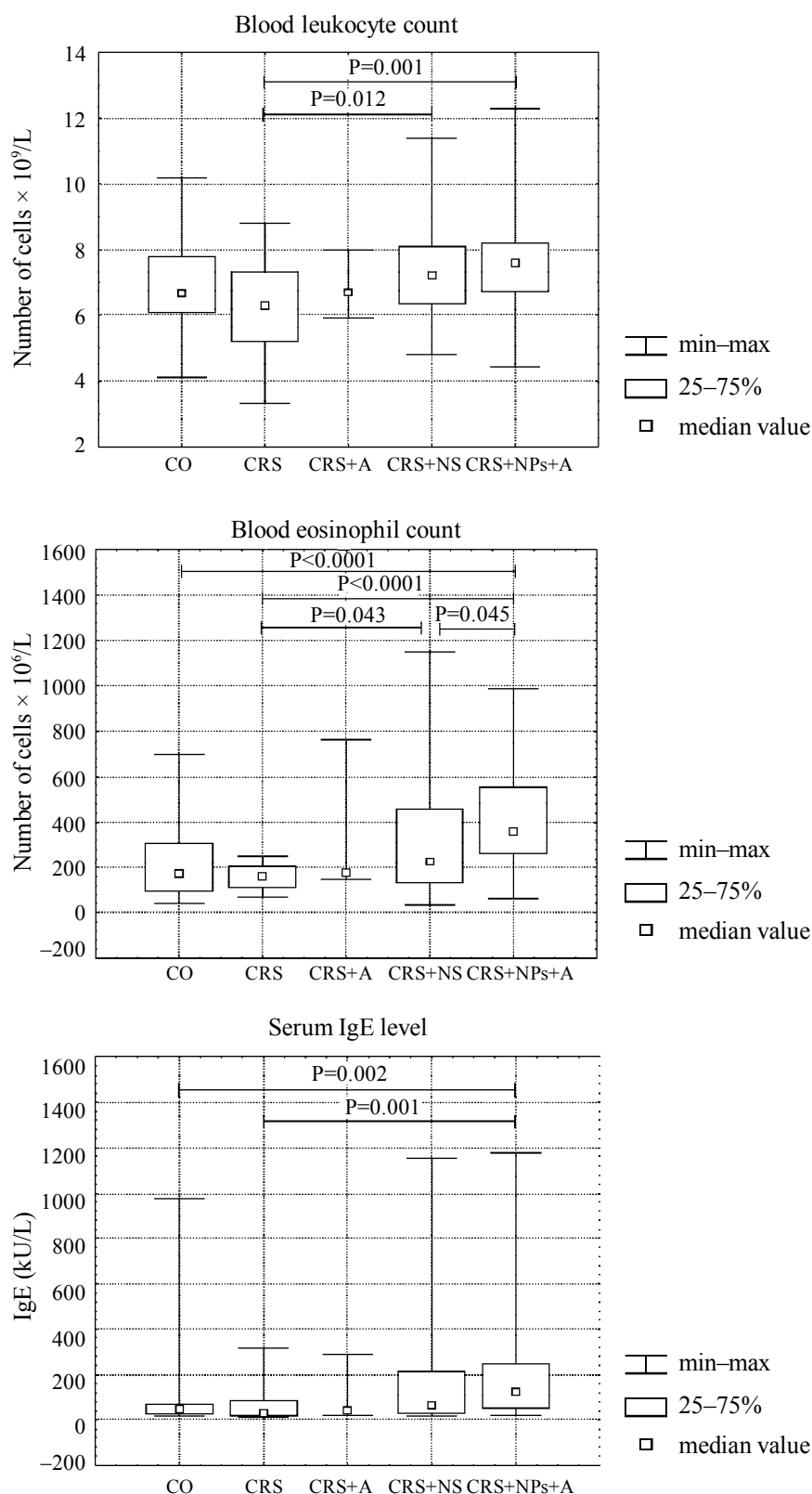
FEV<sub>1</sub> – forced expired volume in one second; VC – vital capacity; CT – computed tomography;  
CD – standard deviation.

□P<0.05; □□P<0.01; □□□P<0.001 1 vs. 3;

\*P<0.05; \*\*P<0.01; \*\*\*P<0.001 1 vs. 4;

‡P<0.05; ‡‡P<0.01; ‡‡‡P<0.001 2 vs. 3;

•P<0.05; ••P<0.01; •••P<0.001 3 vs. 4.



**Fig. 1. Measurement of blood leukocyte count, eosinophil count, and IgE level in 23 controls (CO), 33 patients with chronic rhinosinusitis (CRS), 4 patients with CRS and asthma (CRS+A), 40 patients with CRS and nasal polyps (CRS+NPs), and 44 patients with CRS, nasal polyps, and asthma (CRS+NPs+A)**

Data are expressed in Box-and-Whisker plots that represent the median, the lower and upper quartiles, and the minimum to the maximum value.

skin sensitivity pattern to tested aeroallergens, and the results of pulmonary function tests of the patients with CRS without NPs did not differ irrespective of concomitant asthma (Group 1 and 2) (Table, Fig. 1). Patients with CRS without asthma and without NPs (Group 1) were significantly younger, had lower sinus CT scan score ( $P<0.001$ ), blood leukocyte count, eosinophil count in comparison to patients with NPs (Group 3) ( $P<0.05$ ). Comparing the patients with isolated rhinosinusitis (Group 1) with the CRS patients with NPs and asthma (Group 4), the latter were characterized by older age ( $P<0.01$ ), greater duration of nasal symptoms ( $P<0.001$ ), higher number previous surgery ( $P<0.01$ ), more severe sinus disease on CT scan ( $P<0.001$ ), more prominent systemic inflammatory markers, including serum total IgE level ( $P<0.01$ ), more severe bronchial obstruction ( $P<0.05$ ), higher incidence of allergic rhinitis ( $P<0.01$ ) and sensitivity to house dust mite *D. pteronyssinus* (47.7% compared to 15.2%,  $P<0.01$ ) and mold allergens (29.5% compared to 6.1%,  $P<0.01$ ). Comparing the patients with NPs with and without asthma (Group 3 and 4), the patients with symptoms of upper and lower respiratory tract disorder had higher blood eosinophil count ( $P<0.05$ ), more severe sinus disease ( $P<0.05$ ), more prominent bronchial obstruction ( $P<0.01$ ), and more frequently concomitant allergic rhinitis ( $P<0.05$ ), sensitization to house dust mite *D. pteronyssinus* (47.7% compared to 20%,  $P<0.01$ ), molds (29.5% compared to 2.5%,  $P<0.01$ ), and dog allergens (11.4% compared to 2.5%,  $P<0.05$ ).

Comparing the patients without NPs with concomitant asthma (Group 2) with the patients with NPs without asthma (Group 3) only the difference in forced

expiratory flow was detected ( $P<0.05$ ). There was no significant difference between the patients with concomitant asthma irrespective of the presence of NPs (Group 2 and 4) according to age, duration of nasal symptoms, radiological sinus changes, systemic inflammatory markers, pulmonary function, and allergy to inhalant allergens.

The patients with CRS and asthma had more prominent sinus radiological changes which were greatest in severe asthma (Fig. 2). The extent of sinus CT changes correlated positively and significantly with a number of previous surgeries ( $r=0.31$ ,  $P=0.001$ ), leukocyte count in blood ( $r=0.24$ ,  $P=0.025$ ), duration of asthma ( $r=0.36$ ,  $P<0.0001$ ), and age ( $r=0.19$ ,  $P=0.039$ ), and there was a trend towards greater blood eosinophil count ( $r=0.2$ ,  $P=0.072$ ) and serum IgE level ( $r=0.22$ ,  $P=0.078$ ). No significant correlation of sinus radiological changes with spirometry results was detected.

### Discussion

According to most recent position statements in chronic sinus disease, CRS is considered a disease continuum with “extremes,” such as CRS with and without NPs (1). Recent progress in understanding the biology of airway disease has identified inflammation as playing a critical and integrating role in rhinosinusitis and asthma; however, other important questions remain, including factors that determine the clinical phenotype in airway disorders and optimal treatment approaches. In this study, we aimed to characterize the chronic rhinosinusitis and its associations with nasal polyps and asthma. Moreover, our results indicate that looking from a clinical point of view, there is an apparent profile of symptoms, sinus

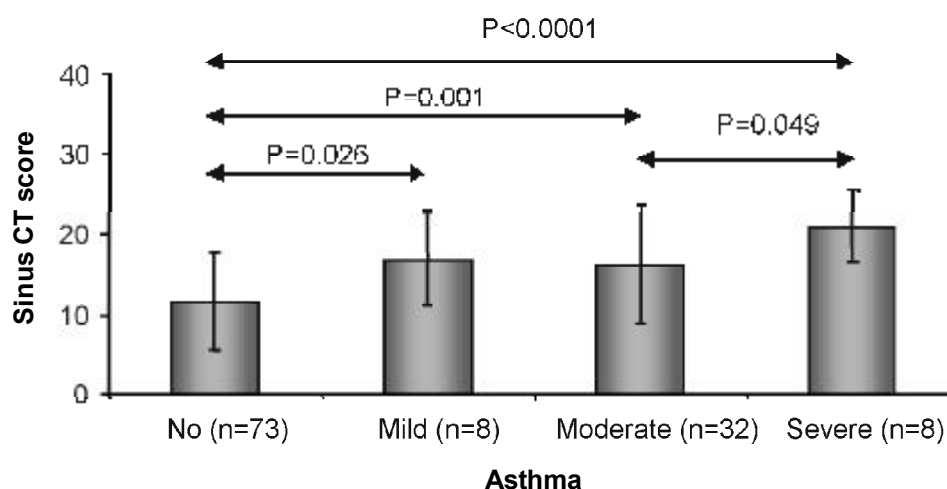


Fig. 2. The sinus CT score in patients with chronic rhinosinusitis without asthma and with persistent mild, moderate, and severe asthma

radiologic changes, allergy, pulmonary function, and systemic inflammatory markers in different subgroups of CRS.

As we studied the patients referred to tertiary university center, they consisted a group of patients with nasal symptoms lasting more than a decade, who had high sinus CT score, were treated surgically repeatedly for their sinus disease, and can be characterized as having symptoms of severe CRS. Our results agree with the previous data that olfactory impairment is common in patients with CRS, although a complete olfactory loss was a characteristic feature of NPs (7, 30). History of aspirin intolerance is one of disease-aggravating factor leading to nasal polyps and more associated with asthma (8, 31). Various authors have highlighted the variable incidence of sinusitis in asthmatic patients as detected by conventional radiography, such variability reflecting the difficulty of accurately diagnosing sinus disease using conventional sinus radiography. In our study, we used sinus CT scan as the most suitable technique for studying paranasal sinuses. As described before by other authors, scoring of sinus CT scan with the Lund-Mackay score clearly revealed that NP patients have more extensive opacification compared with CRS patients (7, 26, 30). Nasal endoscopy made it possible to directly investigate the upper airway and the extent and severity of sinonasal polyposis. It should be mentioned that in half of cases, NPs were diagnosed late when filling the nasal cavity, and this suggests inadequate, ineffective, or delayed treatment of patients with CRS, referred to a tertiary center.

CRS can be regarded as a progressive chronic disorder of upper airways, and the longer duration of nasal symptoms resulted in greater radiological sinus changes and higher incidence of nasal polyps and asthma. In our study, we described the combination of upper and lower airways disease symptoms in 39.6% of patients; moreover, 91.7% of patients with asthma had NPs. This incidence of concomitant asthma is similar to previously reported incidence of 34–50% in patients with CRS (15, 16). It should be noted that in more than half of cases persistent asthma was of moderate severity, and these data could clarify why the asthmatic patients had greater bronchial obstruction and reduced FEV<sub>1</sub> comparing to patients with CRS without asthma and controls. In our study we described the associated severity of upper and lower airway disease as severe asthma was diagnosed only together with NP and the greater sinus radiologic changes were characteristic to the greater severity of asthma. Probably because of asthma control with maintenance treatment of inhaled corticosteroids with

or without long-acting bronchodilators, we could not prove the described before positive correlation between the extent of sinus CT changes and pulmonary function test results in patients with asthma but we detected that the more severe asthma is, the greater sinus CT scan score is (17, 19).

A number of authors have investigated the cytokine and mediator pattern in different subgroup of chronic rhinosinusitis. Nasal polyps have repeatedly been characterized as eosinophilic inflammation, with highly increased concentrations of eosinophil cationic protein (ECP), as a marker of eosinophil activation, and of eotaxin, a CC chemokine, which cooperates with IL-5 to recruit and activate eosinophils (7–12). Although the blood inflammatory markers of the patients with isolated CRS symptoms did not differ from those of the controls, we proved that patients with nasal polyps and asthma had the highest blood leukocyte and eosinophil count and IgE level. Recently the positive correlation between sinus CT scans and blood eosinophilia was proved, but not total IgE, and our results showed a trend towards positive correlation between sinus CT stage and both inflammatory markers, leukocyte count and asthma duration as well (32). Our data support that CRS and asthma are not simply localized disease processes but part of a systemic inflammatory disease affecting the respiratory tract, and it seems that the greater level of inflammatory mediators and cells in the peripheral blood contributes to the extension of nasal and paranasal inflammation to lower airway.

The association of allergy and sinusitis reported in several studies has varied from 25% to 70% and the role of allergy is still unclear (8, 33). Our data proved that CRS in almost half of cases was combined with allergic rhinitis and hypersensitivity to inhaled allergens and allergic patients were prone to develop asthma. We carried out skin prick test with aeroallergens, which is considered a sensitive, inexpensive test that simply and safely diagnoses IgE sensitization to tested allergens (28). It is documented from epidemiologic studies that the sensitization to indoor allergens, particularly house dust mite, and higher serum IgE level are associated with asthma (22, 34). One-third of the patients were allergic to perennial indoor allergens and the house dust mite *Dermatophagoides pteronyssinus* was the most relevant local sensitizing agent. Allergy to this perennial allergen may be one of the underlying inflammatory factors in these patients with chronic sinusitis. While allergic fungal rhinosinusitis is a well-defined clinical entity with recognized diagnostic criteria, we aimed to detect IgE me-

diated type I allergy to molds, including the most common *Aspergillus fumigatus* (35). Skin sensitivity to mold *Aspergillus*, determined by positive skin prick test, was determined in 13.2% of patients, in one-third of cases, IgE specific to *Aspergillus fumigatus* in serum was detected. The link between fungi and severe asthma is recognized, and even the term “severe asthma with fungal sensitization” is proposed by several authors (36). In our study, the patients with CRS and asthma more frequently had mold allergy, which could be recognized as a disease-aggravating factor.

### Conclusions

Our data indicate that patients with CRS compose

clinically heterogeneous group. CRS associated with nasal polyps and asthma is the most severe form of unified respiratory tract disease characterized by older age of the patients, greater duration of nasal symptoms, extent of sinus radiological changes, greater bronchial obstruction and incidence of allergic rhinitis and sensitization to perennial indoor allergens. At the same time more prominent systemic inflammation markers, blood leukocyte and eosinophil count, higher IgE level extend chronic sinus disease to nasal polyps and asthma. From the clinical standpoint, these observations support that in patients with chronic sinus disease, both upper and lower airways need to be evaluated and treated.

## Lėtinio rinosinusito derinys su nosies polipais ir astma: klinikiniai ir radiologiniai požymiai, alergijos ir uždegimo žymenys

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**Raktažodžiai:** lėtinis rinosinusitas, nosies polipai, astma.

**Santrauka.** Lėtinis rinosinusitas su nosies polipais ir be jų yra skirtingos lėtinės nosies gleivinės ir prienosinių ančių uždegiminės ligos stadijos. Kadangi lėtinis rinosinusitas, nosies polipai ir astmos derinys bei panašios uždegimo savybės gali pasireikšti kartu, tai galima daryti prielaidą, kad šios ligos yra vienos ligos išraiškos. Mūsų tyrimo tikslas – nustatyti sergančiųjų lėtiniu rinosinusitu ir jo deriniu su nosies polipais bei astma prienosinių ančių radiologinių požymių, sisteminio uždegimo ir alergijos žymenų, kvėpavimo funkcijos rodmenų skirtumus.

Ištyrėme 121 sergantįjį lėtiniu rinosinusitu, kuris atvyko specialisto konsultacijos į tretinio lygio centrą, ir 23 sveikus kontrolinės grupės asmenis. Atliktos prienosinių ančių kompiuterinės tomogramos, nosies endoskopinis tyrimas. Alerginis rinitas nustatytas remiantis simptomais ir teigiamais odos dūrio mėginiais su dažniausiais oro alergenais, astma diagnozuota pagal tarptautinės astmos diagnostikos ir gydymo rekomendacijas (GINA), remiantis simptomais ir kvėpavimo funkcijos tyrimo duomenimis. Pagal anamnezę nustatytas aspirino netoleravimas. Periferiniame kraujyje nustatytas bendrojo E imunoglobulino (IgE), *Aspergillus fumigatus* alergenui specifinio IgE kiekis, leukocitų ir eozinofilų skaičius.

84 tiriamiesiems (69,4 proc.) nustatytas lėtinis rinosinusitas su nosies polipais; astma diagnozuota 48 tiriamiesiems (39,6 proc.), 91,7 proc. atvejų kartu su nosies polipais ir 45,5 proc. atvejų kartu su alerginiu rinitu. 44 tiriamieji, kuriems nustatytas lėtinio rinosinusito derinys su nosies polipais ir astma, buvo vyresnio amžiaus ( $p<0,01$ ), jų ligos simptomai truko ilgiau ( $p<0,001$ ), dėl to buvo dažniau operuoti ( $p<0,01$ ), nustatytas didesnis radiologinių prienosinių ančių pokyčių indeksas ( $p<0,001$ ), kraujyje rastas didesnis leukocitų, eozinofilų, bendrojo IgE kiekis ( $p<0,01$ ), didesnė bronchų obstrukcija ( $p<0,05$ ), dažniau nustatytas alerginis rinitas ( $p<0,01$ ) ir įsijautrinimas namų dulkių erkių *D. pteronyssinus* (47,7 proc.,  $p<0,01$ ) ir pelėsių alergenais (29,5 proc.,  $p<0,01$ ) nei sergantiesiems tik lėtiniu rinosinusitu. Sergantiesiems ir astma nustatyta didesnių prienosinių ančių radiologinių pokyčių, kurie siejosi su ilgesne astmos trukme ( $p<0,0001$ ), buvusių operacijų skaičiumi ( $p=0,001$ ), didesniu kraujo leukocitų ir eozinofilų skaičiumi ( $p=0,025$ ), tiriamųjų amžiumi ( $p=0,039$ ).

**Išvada.** Pagal klinikinius požymius sergantieji lėtiniu rinosinusitu sudaro nevienalytę grupę. Lėtinio rinosinusito derinys su nosies polipais ir astma yra sunkiausia vieningos kvėpavimo takų ligos išraiška, kuria susergera vyresnio amžiaus pacientai, jiems yra ilgesnė rinosinusito simptomų trukmė, didesni prienosinių ančių radiologiniai pokyčiai, sisteminio uždegimo žymenys, bronchų obstrukcija, nuolatinis alerginis rinitas.



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