

The Effect of Eosinophilia Levels on the Radiological Severity of the Disease in Patients with a Nasal Polyp

Fatma Nur Yıldırım , Yaşar Can Akar , Ceren Günel , Hatice Sema Başak 

Department of Otorhinolaryngology/Head and Neck Surgery, Adnan Menderes University School of Medicine, Aydın, Turkey

Abstract

Objective: In recent years, a different subtype, characterized by eosinophilia infiltration that is associated with T-helper cell type 2 (Th2) inflammation is known to worsen disease prognosis in patients with a nasal polyp. We aimed to assess the correlation of serum and tissue eosinophil levels and the radiological severity of the disease in our own patient group.

Material and Methods: Total 201 patients, including 131 men and 70 women who had undergone endoscopic sinus surgery for nasal polyp from 2013 to 2017 at the Aydın Adnan Menderes University Hospital were enrolled in our study. The eosinophil rates in the preoperative whole blood hemogram examinations and the rates of eosinophils in surgical pathologies were compared; the paranasal sinus computed tomography (CT) sections were evaluated as per the Lund-Mackey score and Kennedy osteitis score (KOS). Osteitis was scored radiologically as per the KOS systems. As per the tissue eosinophil count, more patients had an eosinophil count >10 eosinophil count/HPF (large magnification; 400×) and fewer had eosinophil count ≤10 eosinophil/HPF count.

Results: The Lund-Mackey scores were significantly higher in those with high eosinophil levels in the pathological specimens. The KOS were also found to be high in patients with high Lund-Mackey scores. In patients with higher eosinophil levels in the blood sample, the tissue eosinophil value in pathology samples was also high.

Conclusion: In patients with eosinophilia in the tissue or blood, the radiological prevalence and the osteitis scores of chronic sinusitis are expected to be high.

Keywords: Nasal polyp, eosinophilia, tomography, recurrence

INTRODUCTION

In recent years, several trials have been performed on a different group of patients characterized by eosinophilic infiltration associated with chronic rhinosinusitis (CRS) T-helper cell type 2 (Th2) inflammation with or without nasal polyps. These patients have demonstrated worse prognosis following medical and surgical treatment than those with low eosinophil levels (1). Th-2 cells increase the number and activity of eosinophil cells in the inflammation pathway, while eosinophil cells increase the secretion of various cytokines and the chemotaxis of inflammatory cells and molecules to the target tissue and permeability to the extracellular space (2, 3).

The bony tissue under the mucosa of the paranasal sinuses is also affected by soft tissue inflammation. Histopathological examinations of chronic rhinosinusitis (CRS) patients have shown signs of new bone formation, bone resorption, and inflammation findings of the bone tissue, such as fibrosis and osteitis (4). Recent studies have shown that osteitis is strongly associated with disease severity and recurrence (5). Snidvongs et al. (5) have suggested that disease severity and eosinophilia level could be predicted using both, the KOS and Global Osteitis Score (GOS).

We aimed to determine whether there is a relationship between tissue and peripheral eosinophilia and understand the radiological severity of the disease in CRS with nasal polyps.

MATERIAL AND METHODS

This retrospective study included 201 patients, including 131 men and 70 women with nasal polyps who had undergone endoscopic sinus surgery for CRS from 2013 to 2017 at the Aydın Adnan Menderes University Hospital.

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Address for Correspondence: Fatma Nur Yıldırım

E-mail: f1t9m9@hotmail.com

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The eosinophil rates in the preoperative whole blood hemogram analyses of the patients were compared with the tissue eosinophil rates in the surgical pathologies. Moreover, paranasal sinus computed tomography (CT) sections were evaluated as per Lund-Mackay scoring and KOS.

We excluded those patients who were operated with a pre-diagnosis of CRS with nasal polyps but had a different pathological diagnosis postoperatively. Further, those with CT sections of poor quality were excluded.

The KOS system was used radiologically for osteitis scoring. The details of the method have been described by Snidvongs et al (5). As per this method, when the sinus bone thickness is >3 mm at any point, it is defined as osteitis, and each sinus is scored as 0 (<3 mm), 1 (3-5 mm) or 2 (>5 mm) (Figure 1).

The Lund-Mackay CT scores that indicated the disease severity were obtained from the medical records of the patients. In the Lund-Mackay scoring system, each sinus is evaluated by scoring separately as 0 (no pathology), 1 (partial opacity), or 2 (opacity filling the sinus completely), with the total score ranging from 0 to 24 (5, 6) (Figure 2).

The study period was 5 y; therefore, the samples were evaluated by different pathologists. As per the tissue eosinophil count examined by pathologists after staining, (eosinophil count >10 eosinophil count/HPF highest possible frequency), the patients with the greatest magnification were identified as having high tissue eosinophilia, and patients with eosinophil count ≤ 10 eosinophils/HPF were identified as having low tissue eosinophilia (7, 8). Data on peripheral eosinophils were obtained from the patient's medical files. All the serum samples collected from the patients

were evaluated in the biochemistry laboratory of our hospital. We determined whether there was a relationship between the Lund-Mackay CT score and KOS and high or low tissue and peripheral eosinophilia. Moreover, the presence of a relationship between tissue eosinophilia and peripheral eosinophilia was analyzed.

Statistical Analysis

Whether quantitative variables were normally distributed in the groups was checked using the Kolmogorov-Smirnov test. The Mann-Whitney U test was used for independent group comparisons, and the Kruskal-Wallis H test was used when the number of groups was more than two. The direction and strength of the linear relationship among quantitative variables were investigated using the Spearman correlation analysis. The Pearson's chi-square analysis was used to test whether there was any dependency among the qualitative variables. Descriptive statistics for variables are shown as median (25th to 75th percentile) for quantitative variables and frequency (%) for qualitative variables. Values of $p < 0.05$ were considered statistically significant. For all of the statistical analysis IBM Statistical Package for the Social Sciences software version 22.0 (IBM SPSS Corp.; Armonk, NY, USA) was used.

Ethical Considerations

Before conducting the research, approval was obtained from the Non-Invasive Clinical Research Ethics Committee of Adnan Menderes University (Approval Date: January 18, 2018; Approval Number: 2018/1293), and written permission was taken from the institutions where the research would be conducted. The study was conducted as per the principles of the Helsinki Declaration.

RESULTS

The mean age of the 201 study subjects was 43.16 ± 16.752 y; 70 (34.8%) patients were women and 131 (65.2%) were men.

High Lund-Mackay scores of the patients were significantly correlated with both high eosinophil levels in the tissue samples ($p < 0.001$, $r = 0.390$) and high peripheral eosinophilia levels ($p < 0.001$, $r = 0.449$) (Figure 3, Figure 4). It was observed that patients with high Lund-Mackay scores had high KOS ($p < 0.001$, $r = 0.264$) (Figure 5).

Tissue eosinophil levels were higher in patients with higher peripheral eosinophil levels ($p < 0.001$, $r = 0.383$) (Figure 6).

The KOS values of the patients and the peripheral eosinophil values were compared; no significant relationship was found ($p = 0.182$) (Figure 7). In

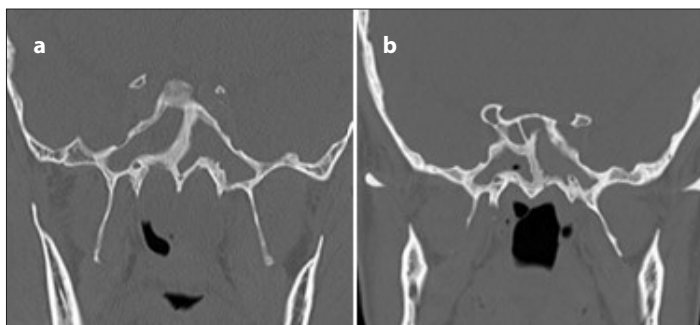


Figure 1. a, b. Axial (a) and coronal (b) CT images show that in both patients with CRS with nasal polyp, osteitic change is observed in the sphenoid sinus walls.



Figure 2. a, b. Axial (a) and coronal (b) CT images show that the Lund-Mackay scoring for CRS with nasal polyps (23 points middle meatus unilateral partial, maxillary sinus bilateral partially obstructed, other sinuses full obstructed).

contrast, the KOS values were higher among those with increased tissue eosinophils ($p=181$, $r=0.201$) (Figure 8).

In patients with a high tissue eosinophil count, peripheral eosinophil ratios and Lund-Mackay CT scores were significantly higher (Figure 6, Figure 3).

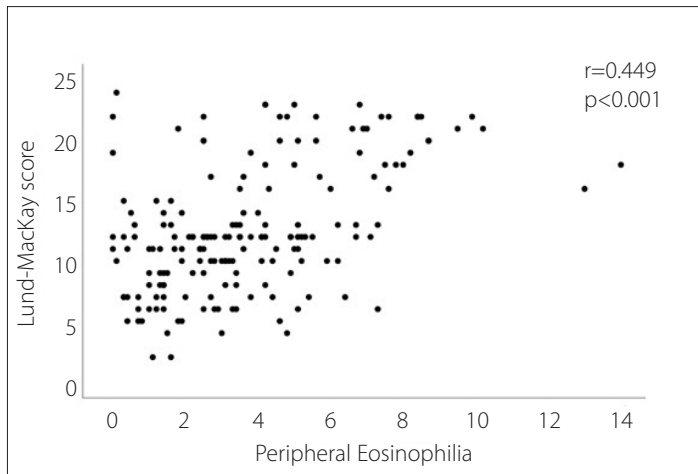


Figure 3. Relationship between the Lund-Mackay score and peripheral eosinophilia.

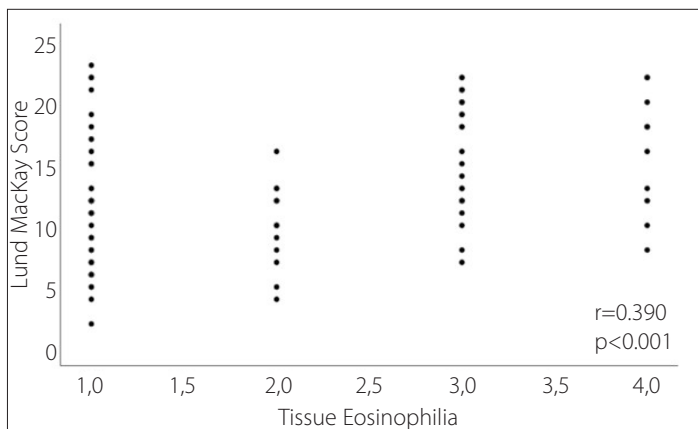


Figure 4. Relationship between the Lund-Mackay score and tissue eosinophilia.

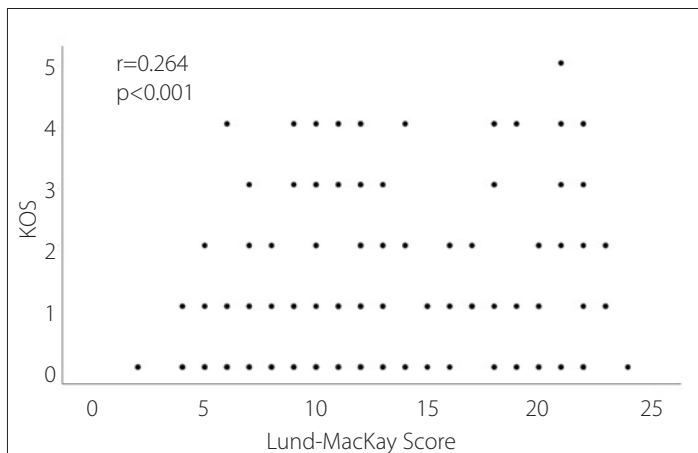


Figure 5. Relationship between the Lund-Mackay score and KOS.

DISCUSSION

Tissue eosinophilia and peripheral eosinophilia have been accepted as predictors of disease severity and treatment response in CRS (9). Accordingly, the number of tissue and peripheral eosinophils was expected to be higher radiologically in relation to the severity and prevalence of osteitis.

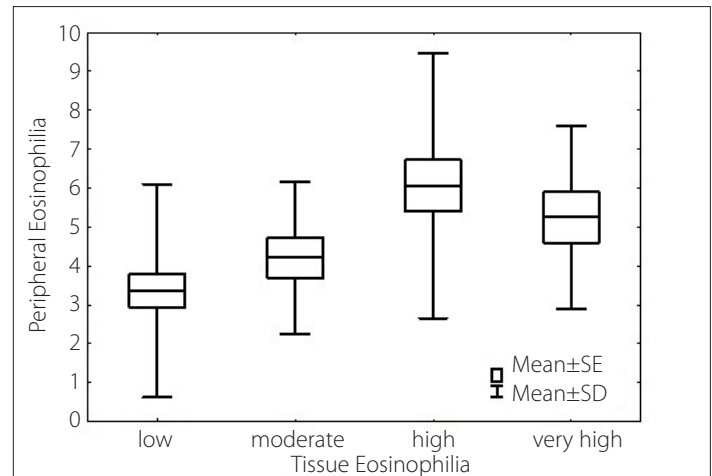


Figure 6. Relationship between the peripheral eosinophilia and tissue eosinophilia.

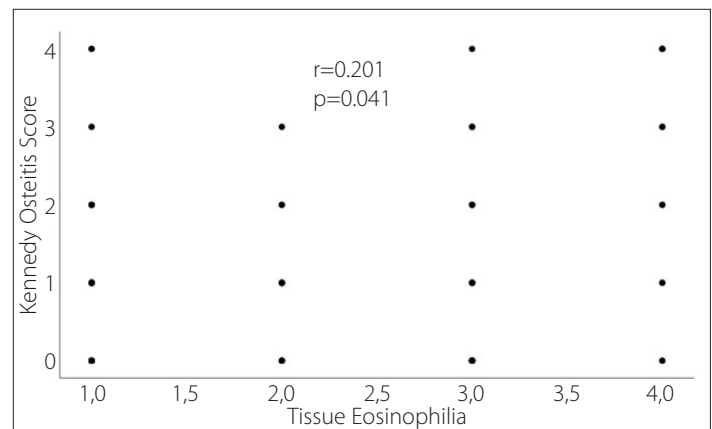


Figure 7. Relationship between the Kennedy osteitis score and tissue eosinophilia.

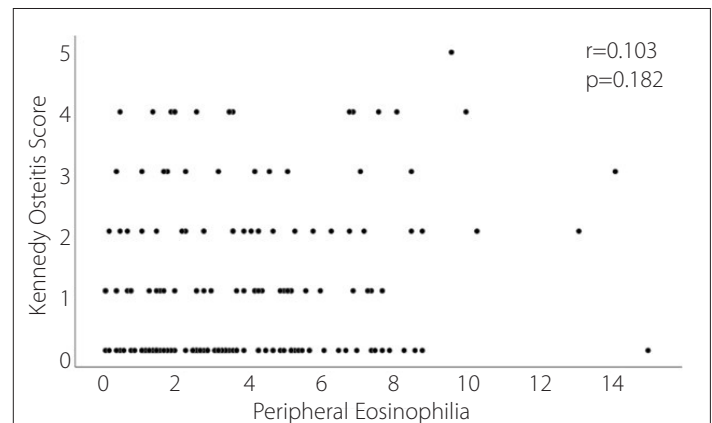


Figure 8. Relationship between the Kennedy osteitis score and peripheral eosinophilia.

Eosinophilic CRS is considered a subtype of CRS that is characterized by Th2. Inflammation associated with T-helper 2 plays a role in the pathogenesis of bone remodeling as well as eosinophilia (1). Cho et al. (2) also emphasized that CRS with nasal polyps occurred in a Th2 cell-mediated inflammation process characterized by high tissue eosinophil infiltration.

CRS patients with eosinophilic nasal polyps (ENPCR) had a longer symptom duration, higher tissue eosinophil count, higher blood immunoglobulin E level, and higher KOS and Lund-Mackay scores than other CRS subtypes. The surgical incidence and symptom scores were higher. It was suggested that eosinophilic CRS could be well controlled with corticosteroid therapy (7, 8).

Hoover et al. (10) conducted the first large series on the relationship between disease severity and eosinophilia in CRS. Nakayama et al. (11) reported that eosinophilia was an important prognostic factor for postoperative recurrence.

In CRS, a periosteal reaction and subsequently osteitis formation occur in the infected mucosa (12, 13). Various mediators released from the diseased mucosa increase the osteoblastic/osteoclastic activity. Osteitis is a common feature in CRS and is important in terms of disease severity and recurrence tendency. Osteolytic bone often causes permanent mucosal inflammation. Studies have shown that radiographic osteitis scores are associated with eosinophilic inflammation (14, 15). Snidvongs et al. (5) reported that eosinophilic mucosal inflammation could initiate periosteal reaction, osteoclast proliferation, bone resection, and new bone formation.

When Snidvongs et al. (5, 8) compared patients with and without ECRS, they found that endoscopic scores and CT scores were more severe in ECRS patients. As per their study results, they concluded that tissue eosinophilia might be a good marker of CRS (5, 8).

Aslan et al. (16) examined 53 patients who underwent FESS. As in our study, in patients with high mucosal eosinophil count, the Lund-Mackay CT score and Lund-Kennedy endoscopic score were high.

Brinke et al. (17) found that the pathology was more limited in patients with low peripheral eosinophil levels. Moreover, as in our study, eosinophils in the peripheral blood were significantly and positively correlated with the CT scores.

Kountakis et al. (18) reported a relationship between peripheral eosinophil count and preoperative CT scores ($r=0.78$, $p<0.05$) as well as between peripheral eosinophilia and endoscopic scores ($p<0.05$). Further, they reported a relationship between tissue eosinophil count and peripheral eosinophil count ($r=0.50$, $p<0.05$).

Significant results were obtained in our study conducted to determine the relationship between peripheral eosinophil level and tissue eosinophilia and disease severity. The peripheral eosinophil level increased, the tissue eosinophil level increased, and the radiological severity of the disease increased with the increase of these two values.

Many studies have shown that nasal polyps with high levels of eosinophilia exhibit more aggressive clinical features and tend to recur following medical or surgical treatment (9). Our current study supports this information.

When our study is compared with similar previous reports, it shows a satisfactory number of cases in terms of the number of patients examined ($n=201$). The peripheral eosinophil values were not associated with the osteitis scores, while tissue eosinophilia was significantly associated with

the radiological severity and peripheral eosinophilia of the disease. From this point of view, we believe that disease severity can be predicted as per the rate of postoperative tissue eosinophilia and will contribute to the management of the next process.

CONCLUSION

We found that the tissue and peripheral eosinophilia levels were closely related to the prevalence and severity of CRS with nasal polyps. The fact that the study duration was long (5 y) and that 201 patients were included in the study eliminates our doubts about this issue. Moreover, we suggest that using tissue eosinophilia as a predictor factor in disease severity is more significant than peripheral eosinophilia.

Ethics Committee Approval: Ethics committee approval was received for this study from the Non-Invasive Clinical Research Ethics Committee of Adnan Menderes University (Approval Date: January 18, 2018; Approval Number: 2018/1293).

Informed Consent: Informed consent was not obtained due to the nature of the study.

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