***Original Article / Çalışma - Araştırma***

# Assessment of patients with nasal polyposis by the neutrophil-to-lymphocyte ratio and eosinophil-to-lymphocyte ratio

## Nazal polipozisli hastaların nötrofil/lenfosit oranı ve eozinofil/lenfosit oranı ile değerlendirilmesi

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***ABSTRACT***

**Objectives:** This study aims to investigate the neutrophil-to-lymphocyte ratio (NLR) and eosinophil-to-lymphocyte ratio (ELR) levels in recurrent and non-recurrent nasal polyposis, and identify how the NLR and ELR reflect the inflammatory status in this specific diagnosis preoperatively.

**Patients and Methods:** A total of 158 patients (102 males, 56 females; mean age 29.40±5.44 years; range 14 to 48 years) were included in the study. The patients were divided into two groups: group 1 included 80 recurrent nasal polyposis patients (44 males, 36 females; mean age 30.0±9.4 years; range 14 to 47 years) and group 2 included 78 non-recurrent nasal polyposis patients without allergic or atopic backgrounds (58 males, 20 females; mean age 28.8±10.1 years; range 17 to 48 years). The NLR and ELR values for each patient were calculated from the complete blood counts taken before surgery. The values of preoperative white blood cell, neutrophil, lymphocyte, eosinophil, NLR and ELR were compared for each group, and also in between the two groups.

**Results:** The preoperative neutrophil, eosinophil, NLR and ELR values of group 1 were significantly higher than group 2 (p=0.042, p=0.013, p=0.019, and p=0.0001 respectively).

**Conclusion:** Neutrophil-to-lymphocyte and ELR measurements can be used effectively in patients with nasal polyposis as an auxiliary method in deciding for the necessity of recurrence follow-ups.

***Keywords:*** Eosinophil; inflammation; lymphocyte; nasal polyp; neutrophil.

***ÖZ***

**Amaç:** Bu çalışmada reküren ve nonreküren nazal polipoziste nötrofil/lenfosit oranı (NLO) ve eozinofil/lenfosit oranı (ELO) düzeyleri araştırıldı ve NLO ile ELO'nun bu spesifik tanıda ameliyat öncesi enflamatuvar durumu nasıl yansıttığı belirlendi.

**Hastalar ve Yöntemler:** Çalışmaya toplam 158 hasta (102 erkek, 56 kadın; ort. yaş 29.40±5.44 yıl; dağılım 14-48 yıl) dahil edildi. Hastalar iki gruba ayrıldı: grup 1'e 80 reküren nazal polipozis hastası (44 erkek, 36 kadın; ort. yaş 30.0±9.4 yıl; dağılım 14-47 yıl) ve grup 2'ye alerjik veya atopik geçmişi olmayan 78 nonreküren nazal polipozis hastası (58 erkek, 20 kadın; ort. yaş 28.8±10.1 yıl; dağılım 17-48 yıl) dahil edildi. Her hasta için NLO ve ELO değerleri cerrahi öncesi alınan tam kan sayımlarından hesaplandı. Her grup için ve iki grup arasında ameliyat öncesi beyaz kan hücresi, nötrofil, lenfosit, eozinofil, NLO ve ELO değerleri karşılaştırıldı.

**Bulgular:** Grup 1'in ameliyat öncesi nötrofil, eozinofil, NLO ve ELO değerleri grup 2'den anlamlı olarak yüksekti (sırasıyla, p=0.042, p=0.013, p=0.019 ve p=0.0001).

**Sonuç:** Nötrofil/lenfosit ve ELO ölçümleri nazal polipozisli hastalarda reküren takiplerin gerekliliğine karar vermede yardımcı bir yöntem olarak etkili bir şekilde kullanılabilir.

***Anahtar Sözcükler:*** Eozinofil; enflamasyon; lenfosit; nazal polip; nötrofil.

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Nasal polyps are usually bilateral, multiple and freely movable protrusions of benign edematous mucosa. They are glistening, pale-grey smooth and semi translucent in appearance.[1] The frequency of nasal polyps is approximately 4-25% of the population. Nasal polyps cause considerable morbidity including nasal obstruction, rhinorrhea and anosmia.[2,3] The etiology and pathophysiology of nasal polyposis are still mainly unknown though significant knowledge has been obtained about nasal physiology and nasal polyposis with scientific advances in the fields of biochemistry, microbiology, and immunology.[3] Histopathologically, mucosal swelling induced by inflammation is caused by basal membrane thickening, atypical gland formation, goblet cell hyperplasia, inflammatory cell infiltration and subepithelial edema.[4]

The edema, which is seen in nasal polyposis, is an inflammation rather than an edema caused by inflammation mediators, cytokines, adhesion molecules, and endothelial counter receptors. Eosinophils are the most seen inflammatory cells. The reason of the eosinophilia may be the increase in migration and the extension of the lifetime of eosinophil.[5]

According to previous studies, the overall inflammatory status of the body is reflected by thrombocytosis, peripheral lymphopenia and neutrophilia.[6-8] The neutrophil to lymphocyte ratio (NLR) is a low cost, reproducible and readily available test, which has been identified as a systemic inflammatory marker.[9] The integrating deleterious effects of lymphopenia and neutrophilia are also defined as systemic inflammatory markers. The poor clinical results in cardiac disease and several malignancies are correlated with an increase in the NLR.[10,11]

This study aimed to investigate whether NLR and eosinophil-to-lymphocyte ratio (ELR), as a recently proposed inflammatory marker, would be helpful in indicating ongoing systemic reaction and inflammation in patients with nasal polyposis.

## PATIENTS AND METHODS

This was a cross sectional retrospective study, approved by the local clinical research ethics commission on 25.12.2013 with 2013/19 meeting number and 2013/371 decision number. One hundred fifty-eight patients (102 males, 56 females; mean age 29.40±5.44 years; range 14 to 48 years) were included in the study as the sample population, who had undergone surgery during October-December 2012, at the ear nose and throat clinic. A single surgeon performed all of the surgical procedures.

All cases had their preoperative complete blood counts (CBCs) in their charts. Those cases that were lost to follow-up, or lacked postoperative CBC results were not included in the study.

*Criteria for excluding subjects from this study were as follows:* chronic lung disease, hypothyroidism, chronic kidney disease, craniofacial anomalies, cerebral palsy, malnutrition, neuromuscular diseases, chronic allergic rhinitis, mental and/or physical retardation due to various illnesses such as Down syndrome, cystic fibrosis, cardiac disease, active infection, parasitic infections, various atopic conditions (i.e. allergic rhinitis, asthma) or family histories of allergy or atopy, recent systemic steroid use, including preoperative oral steroids, and cigarette smoking.

Patients were divided into two groups based on their diagnoses-group 1, recurrent nasal polyposis (44 males, 36 females; mean 30.0±9.4; range 14 to 47 years) and group 2, non-recurrent nasal polyposis without allergic or atopic backgrounds (58 males, 20 females; mean 28.8±10.1; range 17 to 48 years). Patients who did not develop polyposis in the postoperative year were included in the non-recurrent group; those who developed polyposis at least once were included in the recurrent group.

The diagnosis of nasal polyposis according to the European position paper on rhinosinusitis and nasal polyps consensus depends on the presence of two or more nasal symptoms one of which should be either nasal blockage or nasal discharge, and/or reduction/loss of smell, and/or facial pain for more than 12 weeks, and the presence of either nasal polyps by nasal endoscopy or mucosal changes within the ostiomeatal complex and/or paranasal sinuses by computed tomography (CT) scan.[12]

These patients had applied to our clinic with complaints of nasal blockage, reduction in odor sensation, headache, and open-mouth breathing while sleeping. These patients were

**Table 1.** Demographics of the groups

| Variables | Group 1 | | Group 2 | | |
|---|---|---|---|---|---|
| | n | Mean±SD | n | Mean±SD | *p* |
| Sex | | | | | |
| Male | 44 | | 58 | | >0.05 |
| Female | 36 | | 20 | | >0.05 |
| Age | | 30.03±9.36 | | 28.77±10.07 | >0.05 |

SD: Standard deviation; Tukey HSD test; p<0.05; p<0.01.

diagnosed with recurrent and non-recurrent nasal polyposis through endoscopic examination and paranasal sinus tomography; and functional endoscopic sinus surgery had been performed on these patients. At the control examination a year after surgery from October-December 2012, the patients were examined by endoscopy and paranasal sinus tomography for recurrence of polyposis.

In all cases, white blood cell (WBC), neutrophil, eosinophil and lymphocyte counts, NLR and ELR values were recorded from their preoperative CBC differentials. The preoperative WBC, neutrophil, eosinophil, lymphocyte, NLR and ELR values were compared in each group and between the two groups.

**Calculating the NLR and ELR**

Blood samples were obtained from all patients for preoperative CBC. The CBCs had automated differential counts, measured by Sysmex XT 2000i (Sysmex Corporation, Kobe, Japan), and showed total WBC, neutrophil, eosinophil and lymphocyte counts per microliter. The NLR was calculated for each patient twice, simply by dividing the number of neutrophils by the number of lymphocytes: NLR= neutrophils ($10^3$ mcL)/lymphocytes ($10^3$ mcL). The ELR was calculated for each patient twice, simply by dividing the number of eosinophils by the number of lymphocytes: ELR= eosinophils ($10^3$ mcL)/lymphocytes ($10^3$ mcL).

**Statistical analysis**

The NCSS (Number Cruncher Statistical System) 2007 & PASS (Power Analysis and Sample Size) 2008 Statistical Software (Statistical Software, Utah, USA) program were employed for evaluating the data gathered in the study. Besides using descriptive statistics (mean, standard deviation) in evaluating the data, the two sample T-test was used for comparing the quantitative data, for comparing the normally distributed parameters between the groups. The significance level was set at p<0.001 and p<0.05.

## RESULTS

Demographic characteristics of the patients are shown in Table 1. There was no statistically significant difference between the average ages of the groups (p>0.05).

There was a statistically significant difference between the preoperative neutrophil, eosinophil, NLR and ELR measurements of the groups (p<0.05). The two sample T-test showed that the

**Table 2.** Laboratory data of the groups

| Variables | Group 1 | Group 2 | |
|---|---|---|---|
| | Mean±SD | Mean±SD | *p* |
| White blood cell | 7.0±1.6 | 7.4±1.5 | 0.32 |
| Neutrophil ($10^3$ mcL) | 4.7±1.1 | 4.1±1.3 | 0.042* |
| Eosinophil ($10^3$ mcL) | 6.6±0.9 | 5.5±1.0 | 0.013* |
| Lymphocyte ($10^3$/u) | 2.0±0.6 | 2.2±0.6 | 0.28 |
| Neutrophil-to-lymphocyte ratio | 2.5±1.0 | 1.8±0.9 | 0.019* |
| Eosinophil-to-lymphocyte ratio | 3.3±1.5 | 1.9±1.6 | 0.0001** |

SD: Standard deviation; Two Sample t-test; * p<0.05; ** p<0.01.

levels of preoperative neutrophil, eosinophil, NLR and ELR in the patients of the group 1 were significantly higher than those patients in the group 2 (p=0.042, p=0.013, p=0.019, and p=0.0001 respectively). On the other hand, the preoperative WBC and lymphocyte levels of the groups did not show any significant difference (p=0.32, p=0.28) (Table 2).

The level change in preoperative NLR and ELR in the group 1 was significantly lower than those in the group 2 (Figure 1, 2).

## DISCUSSION

Nasal polyposis in the nose or paranasal sinuses is characterized by chronic inflammation causing stromal edema.[3] Although the frequency of nasal polyposis in America and Europe is approximately 4.3%, the cause of the condition has not been identified yet. It has been suggested that many exogenic and endogenic factors result in the formation of nasal polyps including bacterial and viral infections.[13-15]

Although the prevalence of nasal polyps is 1-4%,[16] an endoscopic autopsy study has shown that this value may increase up to 32%.[17] Nasal polyposis affects adults in the majority of cases and is generally observed in subjects older than 20 years old. Although nasal polyposis is not frequently observed in children under the age of 10, ciliary disorders such as cystic fibrosis come to mind when it is observed in this age group. One in three patients with nasal polyps are also diagnosed with asthma, but only 7% of asthma patients are diagnosed with nasal polyps.[18]

A study detected 60-70% presence of *Staphylococcus aureus* in mucin samples obtained from patients diagnosed with nasal polyposis.[19] Staphylococcus and staphyloccal exotoxins cause clonal hyperplasia in lymphocytes by showing super antigen activity, and immunoglobulin E (IgE) is increased in serum against these toxins. In particular, the increased type 1 helper T cells (Th-1) and type 2 helper T cells (Th-2), cytokines produced by lymphocytes cause nasal mucosa damage and they increase nasal polyposis inflammation.[19-22] Recently, it has been focused that NLR is an independent predictor of mortality in patients with acute heart failure.[23,24] The NLR was defined as a novel-potential marker to determine inflammation in cardiac and non-cardiac disorders.[25,26] The NLR was created as a marker for mortality a long-time after chronic kidney disease and percutaneous coronary interventions in patients;[27,28] however, more NLRs were associated with less survival rates in patients who had coronary artery bypass grafting.[29] According to some studies focusing on cancer survival, NLR can be an important factor determining the disease-specific and all survival rates of cancer patients.[26,27] Systemic inflammation was also found to be another main determinant in the survival of cancer patients. It is still a question of debate whether systemic inflammation is associated with malignancy itself or induced by any of the accompanying comorbid conditions. According to recent researches seeking a reliable biomarker, it has been proposed that

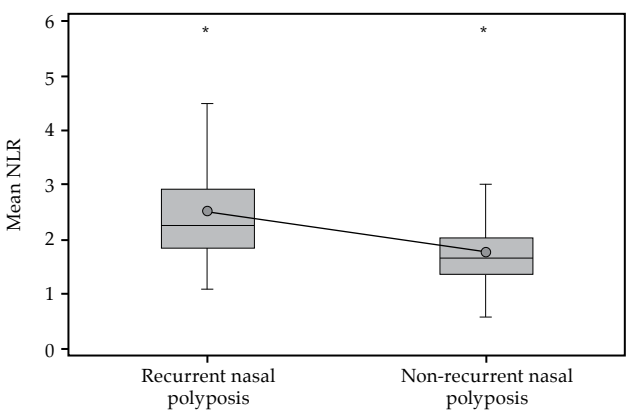


***Figure 1.*** *Neutrophil-to-lymphocyte ratio (NLR) values of the groups.*

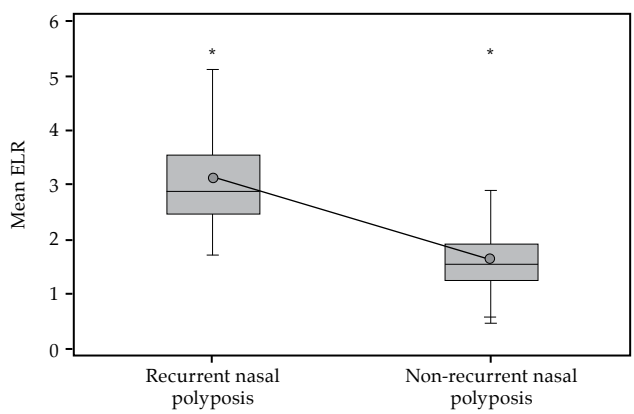


***Figure 2.*** *Eosinophil-to-lymphocyte ratio (ELR) values of the groups.*

survival is commonly focused on systemic inflammation.[27]

The NLR can simply be simply calculated from the lymphocyte and neutrophil counts of routine CBC measurements at no extra cost unlike other inflammation biomarkers such as tumor necrosis factor alpha (TNF-α), interleukin 6 (IL-6), IL-1α and other inflammatory cytokines-- in which lymphocyte count is associated with stress and nutritional conditions of the body, whereas neutrophil count shows the inflammatory status.[28] Several studies accept NLR as a reliable biomarker predicting adverse clinical outcomes in oncology.[26,27] and cardiology (heart failure, acute coronary syndromes and coronary revascularization procedures). In addition, it is also a significant biomarker for some other diseases such as Alzheimer accompanied by systemic inflammation.[29]

Nasal polyp epithelia cells generate various inflammatory cytokines and growth hormones including IL-8, granulocyte-macrophage colony stimulating factor (GM-CSF), IL-6 and IL-1β, tumor necrosis factor TNF-α and vascular endothelial growth factor (VEGF). These cytokines lead to eosinophilia by increasing peripheral circulation of eosinophils.[30] Mediators, hidden by eosinophils, result in increased eosinophilia life time and eosinophil aggregation at the same location.[30]

In previous studies, it was detected that protein kinase C inhibitors were absent in the nasal polyposis that regulates apoptosis of eosinophils.[31] Protein kinase C causes eosinophil infiltration by blocking eosinophil apoptosis. Therefore, it increases collagen synthesis that forms matrix besides resulting in eosinophil inflammation and contributing to polyp development.[31] Vogel et al.[32] examined total serum IgE and eosinophil values in 39 patients and 11 healthy individuals, demonstrating that total serum IgE and eosinophil values were higher in the patient group compared to the healthy control group, and that the difference between these two groups was statistically significant. Di Lorenzo et al.[33] indicated in their study that serum eosinophil values in the patients with nasal polyposis were significantly higher than healthy individuals. Matsuwaki et al.[34] suggested that high peripheral blood eosinophil count is associated with the recurrence of chronic rhinosinusitis. In our study, we observed that serum eosinophil and ELR values were significantly higher in recurrent nasal polyposis patients compared to the non-recurrent nasal polyposis group (Table 2).

Steroids are the most effective drugs known for nasal polyps. Topical or systemic steroids block the inflammatory signal that gets activated by vasoactive mediators.[35] Steroids decrease eosinophilia by decreasing the synthesis of GMCSF and increasing the apoptosis of eosinophils.[36] The treatment of nasal polyposis requires a long time period, so the patient needs to be observed and treated closely. Recurrence of polyposis is seen often after medical or surgery treatments. For this reason, we aimed here to show the relationship between NLR and ELR in recurrent nasal polyposis.

Ours is a preliminary study describing the relationship between NLR and ELR and recurrent nasal polyposis. The main limitation of our study is lack of C-reactive protein and other established markers of inflammation as a reference for comparison. Larger studies incorporating inflammatory markers would shed additional light on this subject. Postoperative NLR values would be valuable to determine the role of nasal polyposis in systemic inflammation.

The results of our study suggest that the NLR and ELR increase as a consequence of systemic inflammatory response in recurrent nasal polyposis. We believe this study is the first in the literature that reveals the significant value of NLR and ELR in recurrent nasal polyposis cases.

We demonstrated higher NLR and ELR in patients with recurrent nasal polyposis when compared with the non-recurrent nasal polyposis. To the best of our knowledge, this is the first study demonstrating the relationship between high NLR and ELR levels and recurrent nasal polyposis. Neutrophil to lymphocyte ratio and ELR calculation may be used as an easy and readily available tool at no extra cost and can be successfully employed in recurrent nasal polyposis cases for determining the timing of surgical intervention and for postoperative recurrence follow-ups. More advanced studies are necessary to fully clarify the mechanism of NLR and ELR in recurrent nasal polyposis.

**Declaration of conflicting interests**

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