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The significance of the systemic inflammation response index and panimmune inflammation value in differentiating benign, premalignant, and malignant laryngeal lesions

Benign, premalign ve malign larenks lezyonlarını ayırt etmede sistemik enflamasyon yanıt indeksi pan-immün enflamasyon değerinin önemi

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ABSTRACT

Objectives: This study aimed to compare the levels of systemic inflammation response index (SIRI) and panimmune inflammation value (PIV) in patients with benign, premalignant, and malignant laryngeal lesions and to determine the potential role of these indices in the differential diagnosis of laryngeal pathologies.

Patients and Methods: This retrospective study was conducted with patients who underwent laryngeal biopsy between January 1, 2018, and June 1, 2023. Patients were categorized into three groups according to histopathological evaluation of the laryngeal lesion: benign, premalignant, and malignant. The SIRI and PIV were calculated for each patient. The groups were statistically compared in terms of age, complete blood count parameters, SIRI, and PIV.

Results: Data from a total of 206 male patients (mean age: 58.8±12.9 years; range, 22 to 95 years) were analyzed. Of these 206 patients, 85 (41.3%) had malignant laryngeal lesions, 55 (26.7%) had premalignant laryngeal lesions, and 66 (32%) had benign laryngeal lesions. Despite the lack of statistical significance, the highest values for both indices were observed in the malignant group, while the lowest values were found in the benign group.

Conclusion: Although the SIRI and PIV tended to be higher in cases with malignant laryngeal lesions, this difference was not statistically significant. We propose that systemic inflammation indices should not be used as standalone diagnostic tools, but rather should be evaluated in conjunction with clinical, histopathological, and radiological findings.

Keywords: Benign neoplasms, inflammation, inflammatory markers, laryngeal neoplasms, malignant neoplasms, precancerous conditions.

ÖZ

Amaç: Bu çalışmada benign, premalign ve malign larenks lezyonlarına sahip hastalarda sistemik enflamasyon yanıt indeksi (SIRI) ve pan-immün enflamasyon değeri (PIV) düzeylerinin karşılaştırılarak bu indekslerin larenks lezyonlarının ayırıcı tanısındaki olası rolünün belirlenmesi amaçlandı.

Hastalar ve Yöntemler: Bu retrospektif calışma, 1 Ocak 2018 - 1 Haziran 2023 tarihleri arasında larengeal biyopsi yapılan hastalar ile yürütüldü. Hastalar larengeal lezyonun histopatolojik inceleme sonucuna göre üç gruba ayrıldı: Benign, premalign ve malign. Her hasta için SIRI ve PIV hesaplandı. Gruplar; yaş, tam kan tetkiki parametreleri, SIRI ve PIV açısından istatistiksel olarak karşılaştırıldı.

Bulgular: Çalışma kapsamında 206 hastanın (ort. yaş: 58.8±12.9 yıl; dağılım, 22-95 yıl) verileri analiz edildi. Bu 206 hastadan 85'i (%41.3) malign, 55'i (%26.7) premalign ve 66'sı (%32) benign larengeal lezyona sahipti. İstatistiksel olarak anlamlı bulunmamasına rağmen her iki indeks için en yüksek değerler malign grupta, en düşük değerler ise benign grupta gözlendi.

Sonuç: Sistemik enflamasyon yanıt indeksi ve PIV malign larengeal lezyonlarda daha yüksek seyretse de, bu fark istatistiksel olarak anlamlı bulunmadı. Sistemik enflamasyon indekslerinin tek başına tanısal araçlar olmayıp, klinik, histopatolojik ve radyolojik bulgularla birlikte değerlendirilmesi gerektiğini önermekteyiz.

Anahtar sözcükler: Benign neoplazi, enflamasyon, enflamasyon belirteçleri, larenks neoplazmları, malign neoplazi, prekanseröz durumlar.

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Laryngeal lesions encompass a wide spectrum with distinct biological and clinical characteristics, including benign, premalignant, and malignant entities. The differential diagnosis of these lesions is generally established through clinical examination, imaging modalities, and histopathological evaluation. Certain lesions clinically assessed as benign can be managed with medical therapy and monitored without the need for biopsy. However, there is currently no additional diagnostic tool available to support this decision. In recent years, the role of systemic inflammation in tumor development and progression has been better understood. Inflammation indices derived from peripheral blood parameters have been considered as potential diagnostic and prognostic markers for malignancy, as they reflect immune responses.[1-11] One of these indices, the systemic inflammation response index (SIRI), is calculated using neutrophil, monocyte, and lymphocyte counts and has been suggested to be associated with immunosuppression and inflammation levels in cases with solid tumors. Another parameter, the panimmune inflammation value (PIV), incorporates neutrophil, monocyte, platelet, and lymphocyte counts to provide a more comprehensive profile of systemic inflammation.[7,9] Although some studies have evaluated the diagnostic and prognostic significance of inflammatory markers in laryngeal malignancies, comparative analyses involving benign, premalignant, and malignant lesions remain limited in the literature.[1,10] In this study, we aimed to compare SIRI and PIV levels in patients with benign, premalignant, and malignant laryngeal lesions to assess whether these indices reflect systemic inflammation associated with laryngeal pathology and to evaluate their potential roles in differential diagnosis.

PATIENTS AND METHODS

In this retrospective study, patients who underwent laryngeal biopsy under microlaryngoscopic suspension at Süleyman Demirel University Faculty of Medicine, Department of Otorhinolaryngology between January 01, 2018, and June 01, 2023, were included. Inclusion criteria were age ≥18 years, availability of preoperative complete blood count results, and definitive histopathological diagnosis. Exclusion criteria included the presence of inflammatory or autoimmune diseases, history of additional malignancies, presence of active infectious pathologies, use of medications known to affect complete blood count parameters, histopathological diagnosis of malignancy other than squamous cell carcinoma, and incomplete access to required data in archived records. Written informed consent was obtained from each patient. The study protocol was approved by the Süleyman Demirel University Faculty of Medicine Clinical Research Ethics Committee (Date: 29.12.2023, No: 362). The study was conducted in adherence with the principles of the Declaration of Helsinki.

The following data for patients who underwent laryngeal biopsy within the specified time frame were included in the study: age, sex, medical history, findings from anamnesis and physical examination, operative notes, and complete blood count results obtained during preoperative evaluation. These data were retrieved from the hospital's electronic medical record system. Based on histopathological evaluation, patients were categorized into three groups: benign, premalignant, and malignant. Findings such as vocal cord nodule, vocal cord cyst, vocal cord polyp, and contact granuloma were classified as follows: benign; low-grade and high-grade dysplasia and hyperkeratosis as premalignant lesions; and carcinoma *in situ*, microinvasive carcinoma, and squamous cell carcinoma as malignant lesions.

From the complete blood count results, leukocyte count, neutrophil count, lymphocyte count, monocyte count, and platelet count were extracted. Using these parameters, PIV and SIRI values were calculated for each patient. The PIV was calculated using the following formula: (neutrophil × monocyte × platelet) / lymphocyte. The SIRI was calculated using the following formula: (neutrophil × monocyte) / lymphocyte. The groups were statistically compared in terms of age, complete blood count parameters, and PIV and SIRI values.

Statistical analysis

Statistical analyses were performed using IBM SPSS version 30 software (IBM Corp., Armonk, NY, USA). Data were initially evaluated for entry errors and distribution characteristics. The one-way analysis of variance was employed to compare continuous variables among the groups. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation. Correlation analyses were conducted using the Pearson correlation test. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 233 patients (206 males, 27 females) who met the inclusion criteria were enrolled in the

Table 1
Mean values for complete blood count parameters and inflammation indices across the groups

	Malignant group (n=85)	Premalignant group (n=55)	Benign group (n=66)	Total (n=206)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Leukocyte	7.93±2.70	7.96±2.04	7.73±2.14	7.87±2.35
Neutrophil	5.08±2.40	4.97±1.60	4.59±1.77	4.89±2.02
Lymphocyte	1.98±0.64	2.13±0.76	2.24±0.68	2.10±0.69
Monocyte	0.62±0.24	0.61±0.21	0.62±0.19	0.62±0.22
Platelet	242.90±84.59	234.38±54.53	246.68±63.10	241.83±70.71
PIV	520.67±615.16	404.68±338.11	370.31±294.67	441.53±466.15
SIRI	1.92±1.63	1.71±1.35	1.46±1.00	1.72±1.39

SD: Standard deviation; PIV: Panimmune inflammation value; SIRI: Systemic inflammation response index.

Table 2
Statistical analysis of mean complete blood count parameters and inflammatory index values between groups

	Malignant-premalignant-benign groups	Malignant-premalignant groups	Malignant-benign groups	Premalignant-benign groups
Leukocyte	0.840	0.996	0.872	0.858
Neutrophil	0.328	0.943	0.310	0.573
Lymphocyte	0.077	0.457	0.064	0.642
Monocyte	0.952	0.954	0.972	0.997
Platelet	0.627	0.767	0.944	0.609
PIV	0.114	0.319	0.120	0.913
SIRI	0.130	0.650	0.108	0.587

PIV: Panimmune inflammation value; SIRI: Systemic inflammation response index.

study. Due to the low number of female patients, the asymmetric distribution of female patients across the groups, and the potential effects of hormonal variations on complete blood count parameters, the data from female patients were excluded from the statistical analyses. The intention was to achieve more homogeneous and standardized results with this approach. Among the 206 male patients (mean age: 58.8±12.9 years; range, 22 to 95 years) included in the final analysis, 85 (41.3%; mean age: 62.5±10.2 years) had malignant laryngeal lesions, 55 (26.7%; mean age: 60.9±13.0 years) had premalignant laryngeal lesions, and 66 (32%; mean age: 52.4±13.6 years) had benign laryngeal lesions. A statistically significant difference in age was observed among the three groups ($p<0.001$). In pairwise comparisons, no significant difference in age was found between the malignant and premalignant groups ($p=0.746$), whereas the differences for all other group combinations were statistically significant ($p<0.001$).

The mean values for complete blood count parameters and inflammation indices in each group are presented in Table 1. The results of the statistical analysis of these parameters are shown

Table 3
Results of correlation analysis between age and inflammatory index values

	Age	
	r	*p*
PIV	0.106	0.129
SIRI	0.129	0.065

PIV: Panimmune inflammation value; SIRI: Systemic inflammation response index; r: Pearson correlation coefficient.

in Table 2. No correlation was found between age and inflammation index values in the correlation analysis (Table 3).

DISCUSSION

Early detection of lesions with malignant transformation potential has a direct impact on treatment success and disease prognosis. In most cases, definitive diagnosis requires biopsy under general anesthesia. However, the application of general anesthesia carries numerous risks, particularly in elderly patients with comorbidities. Therefore, there is a need for additional parameters that will help predict the histopathological nature of the detected lesion in these patients. In this context, the potential diagnostic utility of noninvasive and easily obtainable inflammatory indices has gained attention. Although results in the literature are often conflicting, various associations were identified between clinical characteristics of patients with laryngeal cancer and these inflammatory indices. In a study conducted by Atasever Akkas and Yücel[2] in 2021, the prognostic and clinical features of 118 patients with laryngeal cancer were evaluated in terms of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII). In this study, high SII values were identified as a negative prognostic factor for overall survival. Additionally, high NLR, PLR, and SII values were also associated with reduced disease-free survival. Significant correlations were found between high NLR values and local recurrence, as well as between high SII values and perineural invasion.[2] In a study by Shen et al.,[3] SII levels were associated with the N stage and tumor differentiation in patients with laryngeal cancer; however, no association was found for NLR or PLR. Kawano et al.[4] reported an association between lymphocyte-to-monocyte ratio (LMR) and survival in laryngeal cancer patients, whereas no significant relationship was observed for NLR or PLR. In a study by Chen et al.,[5] high preoperative NLR, PLR, and monocyte-to-lymphocyte ratio (MLR) were associated with poorer survival and increased disease progression. Koca et al.[6] evaluated inflammation indices in patients with laryngeal cancer who received definitive radiotherapy. Their study included NLR, PLR, MLR, SII, and PIV. Significant associations were found between many of these indices and clinical parameters. The authors emphasized there were particularly strong correlations between PIV with progression-free survival, overall survival, and lymphatic metastasis. Shi et al.[7] investigated PIV in patients with laryngeal and pharyngeal cancers and concluded that PIV was associated with poor prognosis in both tumor types. In a study by Wang et al.,[9] high SIRI values were linked to worse overall and disease-free survival in patients with laryngeal cancer. Demir et al.[11] identified a relationship between SII and tumor recurrence in laryngeal cancer. Topuz et al.[10] aimed to determine the predictive value of NLR, PLR, and SII in laryngeal pathologies. Similar to our study, their patients were categorized into benign, premalignant, and malignant groups. They found statistically significant differences for all three indices, with the strongest association observed for SII. Therefore, they emphasized the relationship between SII and the malignant potential of laryngeal lesions.[10] Sivrice et al.[1] also examined patients who underwent laryngeal biopsy, dividing them into three groups. However, unlike other studies, they did not find any significant relationships for NLR, PLR, or SII. The authors attributed this to the altered immune response in the elderly population included in their study. Fang et al.,[8] on the other hand, evaluated NLR, PLR, and MLR in patients with vocal cord leukoplakia and reported associations between these indices and the development of leukoplakia. They also found significant correlations between NLR with recurrence and malignant transformation.[8]

In contrast to most studies in the literature that focused on inflammation indices in laryngeal cancer, our study did not identify a statistically significant association for either PIV or SIRI. This may be due to the fact that patients in our study were evaluated at the time of diagnosis, before a systemic inflammatory response could be fully established. Interestingly, although no statistically significant differences were found, the mean values for both indices were highest in the malignant group and lowest in the benign group. This trend suggests that, similar to previous studies, inflammatory indices tend to increase in malignant processes. The absence of statistical significance is likely related to the limited sample size. Indeed, statistical significance and clinical significance do not always align. The trends observed for the index levels may become statistically significant with larger and more homogeneous patient populations.

This study was limited by its retrospective design, limited sample size, lack of staging data for malignant cases, and the exclusion of female patients from the final analysis.

In conclusion, although SIRI and PIV values were higher in cases with malignant laryngeal lesions, this difference was not statistically significant.

This finding is thought to be attributable to the limited sample size. Future studies with larger cohorts are needed to better clarify the diagnostic and prognostic value of these indices. We recommend that systemic inflammation indices should not be used as standalone diagnostic tools, but rather interpreted in conjunction with clinical, histopathological, and radiological findings.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, design, literature review, writing the article, control/supervision, critical review: F.Y., H.Y., E.O., V.A., Y.Ç.K. M.E.S.; Data collection and/or processing: F.Y., H.Y., V.A.; Analysis and/or interpretation: F.Y., E.O.

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