

COMPARISON OF PATIENTS WITH MALIGNANT OR BENIGN LARYNGEAL LESIONS AND HEALTHY INDIVIDUALS IN TERMS OF HEMATOLOGICAL INFLAMMATORY PARAMETERS

Abstract

Purpose: Recent studies have shown a relationship between cancer and inflammatory response. The aim of this study is to compare NLR and PLR values, which are inflammatory parameters, in precancerous and cancerous lesions and to determine whether there is a parameter that can be used in the early diagnosis of laryngeal squamous cell carcinoma.

Methods: 174 patients who were benign as a result of pathology, 122 patients who were malignant, 39 patients who were premalignant (335 patients in total) and 117 normal individuals were included in the study. Data groups were divided into 4 groups as Benign Laryngeal Lesion(BLL), Precancerous Laryngeal Lesion(PLL), Malignant Laryngeal Lesion(MLL) and Control Group(CG). In addition, the PLL group was subdivided into Mild Dysplasia(MiD), Moderate Dysplasia(MoD) and Severe dysplasia-carcinoma in situ (SeD/CIS). NLR, PLR and other parameters were calculated.

Results: NLR and PLR values were significantly different between the groups. ($p = 0.000$, $p = 0.002$) The mean NLR was higher in the MLL and PLL groups, and was lower in the BLL and control groups. The mean PLR was also higher in the MLL and PLL groups. When the groups were compared in pairs, there was a significant difference between BLL and MLL ($p = 0.001$) and MLL and CG. ($p = 0.006$) The PLL group was subdivided into MiD, MoD and SeD / CIS. There was a significant difference in NLR when CG and other subgroups were compared. ($p = 0.027$) Significant differences were found between CG and SeD when the groups were compared in pairs. ($p = 0.007$) There was no significant difference between the groups in terms of PLR and dysplasia. ($P = 0.516$)

Conclusion: As revealed in this study, these rates were low in the CG and BLL groups and high in the MLL group, so they could be used as markers to differentiate malignant lesions.

Keywords: larynx, neutrophil / lymphocyte ratio, platelet / lymphocyte ratio

What is already known about this topic?

- Inflammation has been shown to be effective in the development of many tumors and proliferation of cancer cells, angiogenesis and tumor response to treatment.
- Neutrophils, lymphocytes and platelets are thought to play an important role in the formation of these processes.

What does this article add?

- Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio are low cost and easy to reach. These rates were high in the malign lesion group.

1. Background

The larynx has functions such as prevention of aspiration during swallowing and sound production, which is very important for social communication. Inflammatory, traumatic, benign and malignant lesions of the larynx can be seen at any time in life as in other organs.^{1,2} Ninety percent of malignant laryngeal lesions are composed of squamous cell carcinomas, which predominantly consist of precancerous epithelial lesions.³

Laryngeal squamous cell carcinoma (LSCC) is one of the most common malignant tumors of the head and neck. It is estimated that 12,410 new cases of laryngeal cancer will be diagnosed in the United States in 2019, and approximately 3,760 of them will die.⁴

In the treatment of LSCC, chemoradiotherapy is applied before or after total laryngectomy for advanced stage tumors, whereas partial laryngeal surgery or radiotherapy is applied for earlier stage tumors.^{5,6} Treatment-related causes, comorbidities, secondary cancers, and psychosocial factors are responsible for the morbidity and mortality of LSCC.⁷ Therefore, in order to reduce morbidity and mortality, the detection of premalignant lesions and the detection and treatment of malignant lesions at an early stage will prevent many voice disorders, respiratory and swallowing disorders and many of the mental problems associated with these diseases.

Recent studies have shown a relationship between cancer and inflammatory response. Inflammation has been shown to be effective in the development of many tumors and proliferation of cancer cells, angiogenesis and tumor response to treatment. Neutrophils, lymphocytes and platelets are thought to play an important role in the formation of these processes. When the literature is reviewed, it is seen that neutrophil / lymphocyte ratio (NLR) and platelet / lymphocyte ratio (PLR) calculated from complete blood count are studied in various inflammatory diseases, precancerous lesions and malignancies.⁸⁻¹¹ NLR and PLR values were found to be significant in the early diagnosis and prognosis of laryngeal squamous cell carcinoma.¹²⁻¹⁵ The aim of this study is to compare NLR and PLR values, which are inflammatory parameters, in precancerous and cancerous lesions and to determine whether there is a parameter that can be used in the early diagnosis of laryngeal squamous cell carcinoma.

2. Methods

This study was approved by the ethics committee of xx University Faculty of Medicine with decision number 183 dated 22.11.2018. The study was started after the approval of the ethics committee. In this study, the records of 335 patients (174 benign lesion, 122 malignant lesion, 39 premalignant lesion) who presented to the otorhinolaryngology outpatient clinic between May 2013 and October 2018 with complaints of respiratory distress, hoarseness, difficulty in swallowing, and who had laryngeal pathological sampling were retrospectively analyzed. 117 patients who were admitted to our clinic for any reason, who did not have any systemic inflammatory disease or malignancy in any organ and whose hemogram test was requested at follow-up were included as control group in the study. Informed consent was obtained from children and parents who volunteered to participate in the study.

Data groups were divided into 4 groups as Benign Laryngeal Lesion (BLL), Precancerous Laryngeal Lesion (PLL), Malignant Laryngeal Lesion (MLL) and Control Group (CG). In addition, the PLL group was subdivided into Mild Dysplasia (MiD), Moderate Dysplasia (MoD) and Severe dysplasia-carcinoma in situ (SeD / CIS). Patients with any cardiovascular disease, diabetes mellitus, hypercholesterolemia, hypertension, thyroid diseases, malignancy in any organ other than laryngeal region and presence of local or systemic infection were excluded from the study.

Peripheral venous blood was collected from the patients before surgery and from normal subjects who agreed to participate in the study. Complete blood count was calculated by Cell-Dyn 3700 (optical scatter laser method, Abbott Diagnostics, Chicago, USA). Sex, age, lymphocyte count, leukocyte count, neutrophil count, NLR and PLR values of the patients and control group were recorded. NLR was calculated by dividing the neutrophil count by lymphocyte count. PLR value was calculated by dividing the platelet count by lymphocyte count.

SPSS 21.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The data were subjected to Kolmogorav-Smirnov test and Nonparametric tests were used in statistical analysis since they did not correspond to normal distribution. Kruskal-Wallis test was used to compare multiple groups with independent variables. $p < 0.05$ was considered statistically significant. Bonferroni correction was performed and Mann Whitney U test was performed for pairwise comparison of groups.

3. Results

When the demographic data of the groups were examined (Table 1), the mean age was 48.3 ± 12.3 years in the BLL group of 174 patients. The control group consisted of 32 (27.4%) women and 85 (72.6%) men. The mean age of the control group was 51.21 ± 14.0 years. (Table 1)

NLR and PLR were calculated separately for each group (Table 2). Kruskal-Wallis test was performed because the data did not correspond to the normal distribution. Nonparametric Bonferroni test was used for pairwise comparisons. NLR values were significantly different between the groups ($p = 0.000$), mean values were higher in MLL and PLL groups, but lower in BLL and CG groups. Significant differences were found between the BLL and MLL groups ($p = 0,000$) and between MLL and CG ($p = 0,000$). There was a significant difference between the groups in terms of PLR value ($p = 0.002$). PLR values were higher in MLL and BLL groups as in NLR. When the groups were compared in pairs, there was a significant difference between BLL and MLL ($p = 0.001$) and MLL and CG ($p = 0.006$). (Table 2)

The PLL group was subdivided into MiD, MoD and SeD / CIS. There was a significant difference in NLR when CG and subgroups were compared ($p = 0.027$). Significant differences were found between CG and SeD when the groups were compared in pairs. ($p = 0.007$). There was no significant difference between the groups in terms of PLR and dysplasia. ($P = 0.516$). (Table 3)

4. Discussion

LSCC is very common among head and neck tumors. The morbidity and mortality rates increase when the diagnosis and treatment are late. Diagnosis and treatment of precancerous lesions will prevent a number of advanced laryngeal surgical procedures that increase morbidity, especially since the majority of these patients have precancerous lesions.

Given that many cancers occur at sites of infection, chronic irritation and inflammation, recent data suggest that inflammation plays a critical role in tumor development, and that inflammatory cells are indispensable elements of the neoplastic process.⁹ There are studies showing that lymphocyte infiltration in the tumor microenvironment is associated with good prognosis, neutrophil predominance in tumoral tissue is associated with poor prognosis, and high neutrophil and platelet values correlate with angiogenesis and metastasis risk.¹⁶⁻¹⁹

In this study, the NLR and PLR values calculated from the patients were compared with the control group consisting of healthy individuals. In the literature, there are very few studies using the control group in studies investigating the relationship between laryngeal lesions and NLR-PLR. In our study, the NLR and PLR values were significantly higher in the LSCC group than in the CG and BLL group. Recent articles on this subject suggest that there may be a strong relationship between malignancy and NLR and PLR. When the relationship between NLR-PLR values and degree of dysplasia is examined, there is no significant difference in similar studies in the literature. In this study, the NLR value in severe dysplasia was found to be significantly higher than in the control group.

In a study conducted by Kum et al. on 209 patients, NLR values in benign, malignant and precancerous lesions were evaluated and it was reported that NLR was significantly higher in the malignancy group compared to the other two groups. In the study, precancerous lesions were divided into three groups as mild to moderate and severe dysplasia, and no significant differences were found between NLR and dysplasia degree.¹²

Duzlu et al found that the NLR value was significantly higher in LSCC patients than in the control group.²⁰ In a study comparing benign, precancerous and malignant lesions, Kara et al. found that NLR and PLR were significantly higher in malignant lesions. In the same study, precancerous lesions were divided into three groups as mild, moderate and CIS / severe dysplasia, and no significant differences were found between the groups in terms of NLR and PLR.²¹

Bulgurcu et al. found that NLR and PLR values were significantly higher in LSCC patients compared to premalign laryngeal lesions in their study with 98 patients.²² In our study, no significant difference was found between these two groups in terms of NLR and PLR.

NLR and PLR have been studied in various tumors and significant differences were found in favor of malignancy. In their study of 100 healthy individuals and 100 patients with oropharyngeal squamous cell carcinoma, Phularuri et al. reported a significantly higher NLR in the malignancy group compared to healthy subjects.²³

Kemal et al compared small-cell lung cancer patients and healthy individuals in terms of NLR and PLR and found that these rates were significantly higher in lung cancer patients.²⁴ Hsueh et al reported that preoperative NLR, PLR values were significantly associated with cancer progression and survival. They stated that these hematological parameters could be

considered as independent prognostic values for patients with LSCC.²⁵ In addition, Wong et al. Reported that NLR could be used as a prognostic factor in LSCC.²⁶

5. Conclusion

NLR and PLR values are low cost and easy to reach because they are obtained with complete blood count. As revealed in this study, these rates were low in the CG and BLL groups and high in the MLL group, so they could be used as markers to differentiate malignant lesions. However, the retrospective nature of this study and its single-centeredness constitute its main limitations. Prospective studies involving multicenter tumor-specific lymphocytes and neutrophils will contribute to this issue.

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Table 1: Demographic Data of Groups

		BLL	PLL	MLL	CONTROL	
Age(mean±SD,year)		48,3±12,3	56,63±10,8	63,02±11,4	51,21±14,0	
		n(%)	n(%)	n(%)	n(%)	
Gender	Female	48 (%27,6)	7(%17,9)	11(%9)	32(%27,4)	
	Male	126(%72,4)	32(82,1)	111(91)	85(72,6)	
Total		174	39	122	117	452

Benign Laryngeal Lesion (BLL), Precancerous Laryngeal Lesion (PLL), Malignant Laryngeal Lesion (MLL), SD: Standard deviation

Table 2: Comparison of Groups in terms of NLR, PLR

	BLL ¹ (n=174)	PLL ² (n=38)	MLL ³ (n=122)	CONTROL ⁴ (n=117)	
	(mean±SD)	(mean±SD)	(mean±SD)	(mean±SD)	<i>P</i> [#]
NLR	2,25±1,2	2,92±2,6	4,40±6,8	2,02±1,1	0,000*
PLR	109,60±38,7	126,83±64,1	158,83±127,8	119,19±50,5	0,002**

Benign Laryngeal Lesion (BLL), Precancerous Laryngeal Lesion (PLL), Malignant Laryngeal Lesion (MLL), SD: Standard deviation, NLR: Neutrophil / lymphocyte ratio, PLR: Platelet / lymphocyte ratio, *P*[#] : Kruskal-Wallis test , Mann Whitney U test was performed for pairwise comparison ^{*3-4} *P*=0,000 , ^{*1-3} *p*=0,000, ^{**1-3} *p*=0,001 , ^{**3-4} *p*=0,006

Table 3: Comparison of Precancerous Lesions in terms of NLR, PLR

	MI¹(n=15) (mean±SD)	MoD²(n=7) (mean±SD)	SeD³(n=15) (mean±SD)	CIS(n=2) (mean±SD)	CONTROL⁴(n=117) (mean±SD)	P[‡]
NLR	2,35±1,1	3,78±3,5	3,53±3,5		2,01±1,13	0,027*
PLR	109,84±38,2	133,99±64,8	140,89±78,0		119,19±50,55	0,516

Mild Dysplasia :MI¹, Moderate Dysplasia: MoD, Severe dysplasia: SeD, carcinoma in situ: CIS, NLR: Neutrophil / lymphocyte ratio, PLR: Platelet / lymphocyte ratio, SD: Standard deviation, , **P** : Kruskal-Wallis test , Mann Whitney U test was performed for pairwise comparison *³⁻⁴ P=0,007