Özgün Çalışma / Original Article

Ankara Eğt. Arş. Hast. Derg., 2025 ; 58(1) :11-15
DOI: 10.20492/aeahtd.1602750

Larenks skuamöz hücreli karsinomunda tedavi öncesi trombosit/lenfosit oranı, ortalama trombosit hacmi ve trombosit dağılım genişliğinin prognostik değeri: 594 hastanın analizi

Prognostic value of the pretreatment platelet-to-lymphocyte ratio, mean platelet volume and platelet distribution width in laryngeal squamous cell carcinoma: Analyses of 594 patients

Sümeyra DOLUOĞLU(1), Gökhan TOPTAŞ(1), Ömer BAYIR(1), Emel C. TATAR(2), M. Hakan KORKMAZ(2), Güleser SAYLAM(3)

ÖZET

AMAÇ: Larenks skuamöz hücreli kanserli (LSCC) hastalarda tedavi öncesi tespit edilen trombosit-lenfosit oranı (PLR), ortalama trombosit hacmi (MPV) ve trombosit dağılım genişliğinin (PDW) hastalığın prognozu üzerine etkisini değerlendirmek

GEREÇ VE YÖNTEM: Çalışma popülasyonu iki gruba ayrıldı: sağ kalanlar (Grup 1) ve sağ kalmayanlar (Grup 2). Daha sonra, iki grup arasında yaş, cinsiyet, sigara içme durumu, lezyon lokalizasyonu, ön komissür tutulumu, tümör T evresi, N evresi, M evresi, erken/ileri evre ve tümör patolojik derecesi dahil olmak üzere çok sayıda değişken açısından kapsamlı bir karşılaştırma yapıldı. Genel sağkalımı (OS) tahmin etmek için ROC eğrisi analizi gerçekleştirildi. Daha sonra, kesme değerlerine göre gruplar oluşturuldu ve bu gruplar 3 ve 5 yıllık genel sağkalım (OS) oranları açısından karşılaştırıldı.

BULGULAR: Çalışmaya dahil edilme kriterlerini karşılayan 594 hasta alındı. Sağ kalan grup yaş ortalaması 59.8±9.18 yıl olan 419 (%70.5) hastadan (Grup 1) ve sağ kalmayan grup yaş ortalaması 62.4±11.17 yıl olan 175 (%29.5) hastadan (Grup 2) oluşuyordu. PDW (kesme değeri 16,35 fL) %78,3 duyarlılık ve %52,2 özgüllük ile kanser prognozunu öngörme potansiyeline sahipti. Ayrıca, PLR (kesme değeri 123.64) kanser prognozunu %70.2 duyarlılık ve %51.1 özgüllük ile öngörebildi.

SONUÇLAR: Tanı anında PDW >16.35 fL ve PLR >%123.64 olan LSCC hastalarının tedavi seçimi ve takibinde dikkatli olunmalıdır.

Anahtar Kelimeler: Kan Trombositleri, Laringeal neoplazmlar, Ortalama trombosit hacmi, Trombosit dağılım genişliği, Sağkalım Analizi

ABSTRACT

AIM: The objective of this study was to evaluate the effect of platelet-to-lymphocyte ratio (PLR), mean platelet volume (MPV) and platelet distribution width (PDW) determined before treatment on the prognosis of patients with laryngeal squamous cell carcinoma (LSCC).

MATERIAL AND METHOD: The study population was divided into two groups: survivors (Group 1) and non-survivors (Group 2). Subsequently, we conducted a comprehensive comparison between the two groups with respect to a multitude of variables, including age, gender, smoking status, lesion localization, anterior commissure involvement, tumor T stage, N stage, M stage, early/advanced stage, and tumor pathological grade. ROC curve analysis was performed to estimate overall survival (OS). Then, groups were formed according to cut-off values and these groups were compared in terms of 3- and 5-year overall survival (OS) rates.

RESULTS: The study included 594 patients who met the inclusion criteria. The survivor group consisted of 419 (70.5%) patients with a mean age of 59.8±9.18 years (Group 1) and the non-survivor group consisted of 175 (29.5%) patients with a mean age of 62.4±11.17 years (Group 2). PDW (cut-off value 16.35 fL) demonstrated the potential to predict cancer prognosis with a sensitivity of 78.3% and specificity of 52.2%. Furthermore, PLR (cut-off 123.64) was able to predict cancer prognosis with a sensitivity of 70.2% and specificity of 51.1%.

CONCLUSION: It was suggested that LSCC patients with PDW >16.35 fL and PLR >123.64% at the time of diagnosis should be careful in treatment selection and follow-up.

Keywords: Blood Platelets, Laryngeal neoplasms, Mean platelet volume, Platelet distribution width, Survival Analysis

1 Department of Otorhinolaryngology Head and Neck Surgery, Ankara Etlik City Hospital, University of Health Sciences, Ankara, Turkey
2 Private Clinic, Ankara, Turkey
3 Department of Otorhinolaryngology Head and Neck Surgery, Akay Hospital, University of Lokman Hekim, Ankara, Turkey.

Makale geliş tarihi / Submitted: Aralık 2024 / December 2024

Makale kabul tarihi / Accepted: Mart 2025 / March 2025

Sorumlu Yazar / Corresponding Author:
Sümeyra DOLUOĞLU
Address: Department of Otorhinolaryngology Head and Neck Surgery, Ankara Etlik City Hospital, University of Health Sciences Ankara, Turkey
Varlık Mahallesi, Halil Sezai Erkut Caddesi, No:5, Yenimahalle, Ankara, Turkey.
Phone: +90 530 466 23 97
E-Mail: sumeyradoluoglu@gmail.com
ORCID: 0000-0002-7264-6578

Yazar bilgileri:
Gökhan TOPTAŞ: ORCID ID: 0000-0003-2444-4450, E-mail: drgokhantoptas@gmail.com
Omer BAYIR: ORCID ID: 0000-0001-9445-6129, E-mail: bayiromer@hotmail.com
Emel C. TATAR: ORCID ID: 0000-0003-3365-6308, E-Mail: ectatar@gmail.com
M. Hakan KORKMAZ: ORCID ID: 0000-0001-8732-3061, E-Mail: mhkorkmaz@hotmail.com
Güleser SAYLAM: ORCID ID: 0000-0002-6499-7140, E-mail: guleserkilic@yahoo.com

INTRODUCTION

Laryngeal cancer is one of the most common head and neck cancers (HNC). According to the 2018 cancer statistics, the estimated number of new laryngeal cancer cases annually is 177,000, approximately half of which die due to the laryngeal cancer (1) Although diagnosis and treatment options for laryngeal cancer have been improved in recent years, the increase in the 5-year relative survival rate over the past thirty years from 59.6% to 66.8% is not at a sufficient level (2) The current TNM staging system has been reported to be insufficient as patients with laryngeal squamous cell cancer (LSCC) at high-risk recurrence and prognosis are described purely on the anatomic extent of LSCC (3) Although many prognostic factors have been identified to predict the prognosis in LSCC, such as tumor size, grade, lymph node metastasis, and immunohistochemical marker, these factors can only be evaluated after surgical treatment (4) Therefore, there is a need for a simple, rapid, reliable and low-cost pre-treatment prognostic marker for LSCC.

Carcinogenesis is a multifactorial process and inflammation is known to play a role in tumorigenesis and tumor progression (5,6) Peripheral inflammatory cells, such as neutrophils, platelets (PLT), lymphoctes and monocytes have been shown to have prognostic value for the inflammation-tumorigenesis relationship in head and neck squamous cell cancers (HNSCC). Platelets (PLT) can stimulate tumor growth by increasing angiogenesis, microvascular permeability, and the extravasation of cancer cells. Mean platelet volume (MPV), the most commonly used measure of platelet size, is a surrogate marker of platelet activation (7) Altered MPV levels have been reported in gastric cancer, ovarian cancer, lung cancer, and breast cancer (8-11) In a study of 96 oral cavity squamous cell carcinoma patients and 96 healthy individuals, Anand et al. found no significant difference in PLR, MPV and PDW between the groups (12) In a retrospective study of 87 medullary thyroid cancer patients, Li et al. found that both PLR, MPV and PDW were significant in terms of clinicopathological features and postoperative calcitonin elevation (13) Platelet distribution width (PDW), another platelet index, indicates variation in platelet size, with increased levels having been shown to be significantly associated with poorer overall survival (OS) in LSCC patients (14) Many recent studies have stated that the pre-treatment neutrophil-to lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are closely associated with prognosis in patients with LSCC (15) Therefore, the aim of this study was to evaluate the effects of pre-treatment PLR, MPV, and PDW on the prognosis of patients with LSCC.

MATERIAL AND METHOD

Approval for the study was granted by the Local Ethics Committee (decision no: 70/09, dated: 26.08.2019). A retrospective analysis was made of the data of patients who were diagnosed with LSCC and treated in our clinic between 2010- 2020. Venous blood samples were collected from all patients after a 12-hour overnight fast within 3 days prior to the diagnostic suspension-laryngoscopy procedure. The blood samples were withdrawn into EDTA-containing tubes and then processed within 30 minutes. White blood cell (WBC), haemoglobin, and platelet indices were measured by an autoanalyzer (Sysmex XE-2100, Kobe, Japan).The study inclusion criteria were as follows: (1) primary LSCC confirmed by pathology and classified according to the TNM-UICC/AJCC stage classification- 8th edition; (2) patients with a diagnosis of LSCC of any stage with the data available of a hemogram taken prior to diagnostic suspension-laryngoscopy procedure; (3) pre-treatment hemogram parameters (PLT, MPV, PDW, and PLR, which may be easily calculated); (4) complete clinical, imaging, and follow-up data.

The exclusion criteria were as follows: (1) patients with any inflammatory, autoimmune, acute or chronic infectious disease, hematological disorder, history of corticosteroid therapy or chronic renal insufficiency, medical treatment with anticoagulants, statins, or acetylsalicylic acid; (2) cancer of uncertain origin or probable metastatic LSCC determined on CT or MRI scans; (3) patients with unavailable pre-treatment hemogram parameters.
The patients were separated into two groups as survivors (Group 1) and non-survivors (Group 2). These groups were compared in respect of age, gender, smoking status, lesion localization, anterior commissure involvement, tumor T stage, N stage, M stage, early/ advanced stage, and tumor pathological grade. Groups were then formed according to cut-off values and were compared in terms of 3 and 5-year overall survival (OS) rates.

Statistical Analysis

Data obtained in the study were analyzed statistically using IBM SPSS for Windows version 22.0 software. Continuous variables were presented as mean ± standard deviation values and categorical variables as frequency and percentage. Conformity of the numerical variables to normal distribution was assessed with the Kolmogorov-Smirnov test. Differences in quantitative data between the groups were determined using the Student's t-test. The Pearson chi-square test was applied to determine the associations between categorical variables. Survival analyses were performed with Kaplan Meier product limit estimation, and the Log rank test was used to determine the differences between groups. Cut off value was determined by ROC analysis to evaluate the effect of PLR and PDW on overall survival. A value of p<0 (05) was considered statistically significant.

RESULTS

From a retrospective scan of the data of 620 patients, diagnosed with LSCC and treated in our clinic between 2010- 2020, 594 patients who met the inclusion criteria were included in the study. The survivors group comprised 419 (70 (5)%) patients with a mean age of 59 (8)±9 (18) years (Group 1), and the non-survivors group comprised 175 (29 (5)%) patients with a mean age of 62 (4)±11 (17) years (Group 2). The patients in Group 2 were seen to be significantly older (p=0.011). The data of both groups related to gender, smoking status, tumor localization, anterior commissure involvement, tumor stage (T1-4), lymph node stage (N0-3), presence of metastasis (M0-1), clinical stage (early/advanced), histopathology, PLT, MPV, PDW, lymphocyte, and PLR values, primary treatment (surgery/ chemotherapy [CT] and/or radiotherapy [RT]), and the recurrence rates of the groups are presented in Table 1.

Table 1: Demographic data of the patients

Parameters	Group 1 (n=419)	Group 2 (n=175)	p value
Age (years)	59.8± 9.18	62.4± 11.17	0.011
Gender (Male/Female)	392(66%)/ 27(4.5%)	161(27.1%)/ 14(2.4%)	0.49
Smoking status (smoker/non-smoker)	409(68.9%)/ 10(1.7%)	160(26.9%)/ 15(2.5%)	0.001
Tumor localization (supraglottic/glottic/transglottic/ hypopharynx)	34(5.7%)/ 235(39.6%) /124(20.9%)/ 26(4.4%)	13(2.2%)/ 46(7.7%) /83(14%)/ 33(5.6%)	0.0001
Anterior commissure involvement (absent/present)	268(45.1%)/ 151(25.4%)	87(14.6%)/ 88(14.8%)	0.001
Tumor stage (T1/T2/T3/T4a/T4b)	190(32%)/ 79(13.3%) /108(18.2%)/ 39(6.6%)/ 3(0.5%)	34(5.7%)/ 29(4.9%) / 84(14.1%)/ 24(4%)/ 4(0.7%)	0.0001
Lymph node stage (N0/N1/N2a/N2b/N2c/N3)	353(59.4%)/ 23(3.9%)/ 6(1%)/ 14(2.4%)/ 19(3.2%)/ 4(0.7%)	115(19.4%)/ 24(4%)/ 4(0.7%)/ 8(1.3%)/ 21(3.5%)/ 3(0.5%)	0.0001
Metastasis (M0/M1)	414(69.7%)/ 5(0.8%)	166(27.9%)/ 9(1.5%)	0.002
Clinical stage (Early/Advanced)	255(42.9%)/ 164(27.6%)	51(8.6%)/124(20.9%)	0.0001
Histopathology (CIS/ well differentiated SCC/ moderately diff SCC/ poorly diff SCC)	58(9.8%)/ 123(20.7%) /150(25.3%)/ 88(14.8%)	6(1%)/ 44(7.4%) /69(11.6%)/ 56(9.4%)	0.0001
Platelet (x10^3/µL)	256.7± 63.7	275± 79.5	0.0001
Mean Platelet Volume (MPV)(fL)	8.7± 1.1	8.3± 1.01	0.29
Platelet Distribution Width (PDW)(fL)	16.1± 1.7	16.7± 0.75	0.0001
Lymphocytes (x10^3/µL)	2.08± 0.6	1.78± 0.7	0.056
Platelet-to-Lymphocyte Ratio (PLR) (%)	140.3± 76.1	195.8± 136.2	0.0001
Primary treatment (surgery/ CT and/or RT)	241(40.6%)/ 178(30%)	56(9.4%)/ 119(20%)	0.0001
Recurrence (absent/present)	350(58.9%)/ 69(11.6%)	98(16.5%)/ 77(13%)	0.0001

ROC curve analysis was applied to estimate overall survival (OS). Using the cut-off value of 16 (35) fL

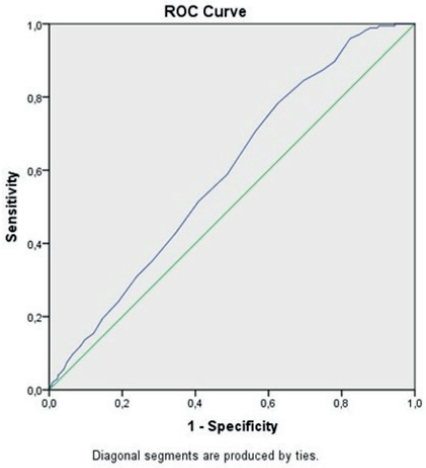

Figure 1: ROC curve for OS prediction, PDW (fL) (AUC=0.591, 95% CI: 0.543-0.638)

PDW was seen to be able to predict the cancer prognosis with 78 (3)% sensitivity and 52 (2)% specificity (AUC=0.591, 95% CI: 0.543-0.638, p<0.0001). The patients were separated into 2 groups of PDW≤16 (35) fL (n=195, 32 (8)%) and PDW>16 (35) fL (n=399, 67 (2)%). In the group with PDW≤16 (35) fL, 3-year OS was determined to be 84 (3)% and 5-year OS, 77 (2)%. In the patient group with PDW>16 (35) fL, these rates were determined to be 75 (1)% for 3-year OS and 63 (5)% for 5-year OS. The difference between these groups formed according to the cut-off value was determined to be statistically significant (p=0.006)

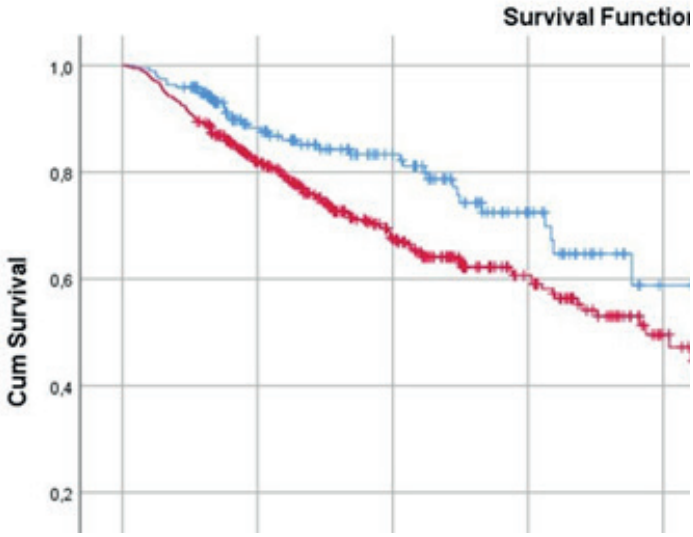

Figure 2: OS Kaplan-Meier curve according to the PDW cut-off value of 16.35 fL

In the ROC curve analysis for OS using the optimal cut-off value for PLR of 123 (64)%

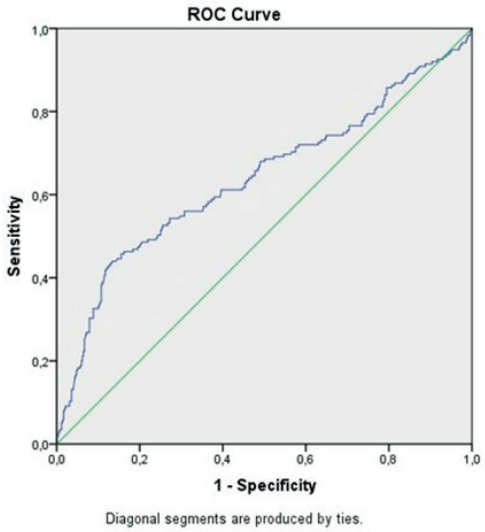

Figure 3: ROC curve for OS prediction, PLR (%) (AUC=0.639, 95 % CI: 0.586-0.692)

cancer prognosis was predicted with 70 (2)% sensitivity and 51 (1)% specificity (AUC=0.639, 95 % CI: 0.586-0.692, p<0.0001). The patients were divided into 2 groups of PLR≤123 (64)% (n=266, 44 (8)%) and PLR>123 (64)% (n=328, 55 (2)%). In the group with PLR≤123 (64)%, 3-year OS was 86 (1)%, and 5-year OS was 76 (3)%. In the group with PLR>123 (64) %, these rates were 71 (3)% for 3-year OS, and 60 (7)% for 5-year OS. The difference between these groups formed according to the PLR cut-off value was determined to be statistically significant (p=0.0001)

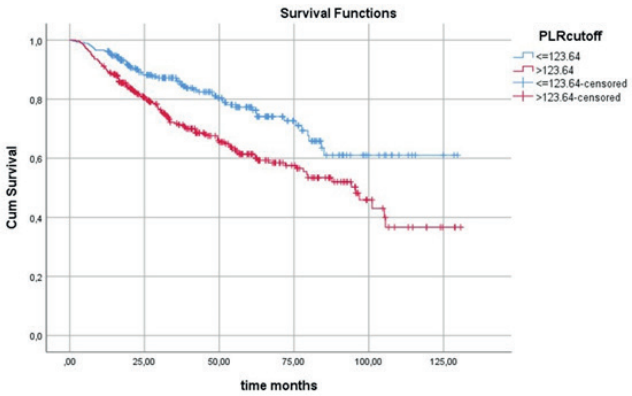

Figure 4: OS Kaplan-Meier curve according to the PLR cut-off value of 123.64%

DISCUSSION

The results of this study demonstrated differences between the survivors and non-survivors groups in respect of the increase in platelet count, the increase in PDW showing platelet activation, and the increase in PLR increasing morbidity and mortality. This indicates that the disease course can be evaluated using hemogram examination, a low-cost, simple, and routinely used method in patients with laryngeal cancer. The aim of this study was to show that OS can be predicted at the time of first diagnosis of the disease, and that the treatment to be selected and follow-up can be provided with a preoperative hemogram test.

PLT plays a significant role in the emergence and development of malignant tumors (16) It has been stated that 30% to 60% of malignant tumors are associated with a rise in PLT, especially in the late stages of tumors, even when accompanied by thrombotic diseases (16,17) PLT can promote carcinogenesis through various means, such as providing mechanical protection to tumor cells during

transport in the circulation and promoting the transport and release of tumor molecules from their particles by enriching various biological activities in the tumor microenvironment (17)
Mean platelet volume (MPV), the most commonly used measurement of platelet size, is an important marker of platelet activation (18) MPV reflects platelet volume size, megakaryocyte proliferation, and platelet formation. Platelet distribution width (PDW), caused by fragmentation of megakaryocytes in varying sizes, is a measure of platelet heterogeneity and reflects the uniformity of platelet volume and the distribution of platelet volume in the blood (19,20)

Many studies have reported the role of platelet parameters in the progression and prognosis of LSCC. Ye et al (21) showed that pre-treatment PLT>248×109/L was a promising indicator of prognosis in patients with operable HNSCC. Pardo et al (22) reported that PLT was significantly associated with survival in univariate analysis, although prognostic capacity was lost in multivariate analysis, limiting its use as a prognostic marker in patients with HNSCC. Zhang et al (14) reported that PDW elevation may be a new prognostic marker in laryngeal cancer. Fu et al (23) stated that MPV decreased and PDW increased in patients with laryngeal cancer compared to patients without laryngeal cancer patients with laryngeal cancer. Additionally, MPV and PDW have been shown to play different roles in laryngeal cancer and benign laryngeal disease. Guo et al (24) reported that elevated PDW and decreased MPV may serve as independent biomarkers for worse survival in laryngeal cancer, while Sheng et al (25) came to the opposite conclusion that increased preoperative MPV was associated with decreased prognosis in patients with LSCC. Kara et al (26) concluded that caution should be exercised when using these new hematological parameters as they can be affected by many factors. In the current study, MPV was determined to be 8.7±1.1fL in the survivors group, and 8.3±1.01fL in the non-survivors group, and the difference between the groups was not found to be statistically significant (p=0.29). The PDW value was determined to be 16.1±1.7fL in the survivors group and this was seen to be statistically significantly increased to 16.7±0.75fL in the non-survivors group (p=0.0001). In the ROC curve analysis, the PDW cut-off value to be able to predict OS was found to be 16.35 fL, with 78.3% sensitivity and 52.2% specificity. Using this cut-off value, the 594 patients were grouped as 195(32.8%) with PDW≤16.35 fL, and 399(67.2%) with PDW>16.35 fL. A statistically significant difference was determined between these two groups in respect of the 3 and 5-year OS values (p=0.006). According to these results, it can be recommended that greater care should be taken in the treatment selection and follow-up of LSCC patients with PDW >16.35 fL at the time of diagnosis.

The increase of PLR value was first related to the increase of platelet ratio. A large body of evidence has shown that tumor cells can induce platelet activation, and thus, activated platelets can also promote the growth of tumor cells (27) The mechanisms of this are that platelets can induce tumor dissemination and invasion by increasing angiogenesis, microvascular permeability and promoting tumor cell extravasation,7,28 while the interaction between platelets and tumor cells can also promote the proliferation of tumor cells and protect tumor cells from apoptosis (29) From another perspective, high PLR levels in peripheral blood may also indicate a decrease in lymphocyte ratio. Lymphocytes and neutrophils constitute the majority of total leukocytes and play an important role in systemic inflammation. They can inhibit or promote the progression of malignant tumors by regulating immune interactions in the microenvironment. It is well known that lymphocytes play an important role in the immune surveillance of malignant tumors, and can inhibit the proliferation and metastasis of tumor cells. The relative decrease of lymphocytes will create an immunosuppressive state in the body, which inhibits the proliferation and metastatic activity of tumor cells, while the relative increase of neutrophils can provide the host with a microenvironment to promote tumor growth. Changes in either of these may indicate that the body has an inadequate immune response to the tumors. Several studies have reported the prognostic value of preoperative evaluation of the PLR, with a high PLR level has been shown to be associated with poor CSS and DFS (15,30) The cut off value for PLR varies from 106 to 193.55 Kara et al (31) reported that pretreatment high PLR is a predictive factor of survival rates in patients with LSCC, and a high PLR increases mortality in these patients. Wang et al (32) stated that PLR was a reliable prognostic factor in patients with LSCC, and Zhong et al (33) reported that change in the PLR may be a useful prognostic marker for patients with T3-T4 LSCC. In the current study, the PLR was determined to be 140.3±76.1% in the survivors group and 195.8±136.2% in the non-survivors group (p=0.0001). In the ROC analysis the cut-off value for PLR to be able to determine OS was found to be 123.64% with 70.2% sensitivity and 51.1% specificity. According to this cut-off value the 594 patients were grouped as 266 (44.8%) with PLR≤123.64% and 328 (55.2%) with PLR>123.64%. The difference in the 3 and 5-year OS values of these two groups separated according to the cut-off value was determined to be statistically significant (p=0.0001). Similarly, greater attention should be paid to the treatment and follow-up of LSCC patients with a PLR value >123.64% at the time of diagnosis.

There are still limitations to research on this subject, primarily the fact that the majority of studies in the literature are retrospective, single-center and small-sample studies may lead to bias in retrospective studies. Although detailed data and follow-up results have been recorded in many studies, prospective studies will help to better evaluate the prognostic factors of patients with laryngeal cancer. Therefore, the current study results still need to be confirmed by prospective studies with larger sample sizes. A second limitation of this study could be said to be that since many other factors, such as acute undetected infections and hematological diseases, affect hematological markers, this may affect the accuracy of prognosis prediction based on hematological markers. In addition, there is a lack of a clear method to obtain the best cut-off value of hematological markers, and the current recommended critical values are empirical and determined by the simplicity of the calculation and the relatively good balance between the number of patients in the upper and lower groups. Therefore, there is a need to develop uniform classification criteria with consensus for the use of these hematological markers in clinical settings. Based on the observations of this retrospective study, there can be seen to be a need for further large prospective studies on this topic to be able to further investigate the relationship between hematological markers and laryngeal squamous cell carcinoma.

CONCLUSION

It can be recommended that greater care should be taken in the treatment selection and follow-up of LSCC patients with PDW >16.35 fL at the time of diagnosis. In the same way as for PDW, greater attention should be paid to treatment and follow-up for LSCC patients with a PLR value >123.64% at the time of diagnosis. For these patients, closer follow-up and more aggressive treatment should be chosen.

Conflict of interest: The authors disclose no conflicts of interest.
Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
Author Contributions: Conception: SD, OB; Design: SD; Supervision MHK, ECT, GS; Fundings: SD; Materials: SD; Data Collection and/or Processing: SD, GT; Analysis and/or Interpretation: SD; Literature Review: SD; Writing: SD; Critical Review: SD, GT, OB
Acknowledgments: Our article was evaluated and approved by linguist Caroline Walker. We thank her for her contributions.

REFERENCES

1. Bray F, Ferlay J, Soarjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018 Nov; 68(6): 394-424. https://doi.org/10.3322/caac.21492
2. Howlader N, Noone A, Krapcho M, Miller D, Bishop K, Altekruse S. www.impactjournals.com/oncotarget 60526 Oncotarget Mariotto A. SEER Cancer Statistics Review, 1975-2013, National Cancer Institute.
3. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017 Mar;67(2):93-99. doi: 10.3322/caac.21388
4. Çelik EK, Han Ü, Mutlu M, Saylam G, Keseroğlu K, Bayır Ö, et al. Expression of Estrogen Receptor Beta 2 in Laryngeal Cancer and Its Relationship with Lymph Node Metastasis. B-ENT

2022;18(3),184-189.
5. Balkwill F, Mantovani A. Inflammation and cancer: back to Virchow? Lancet. 2001; 357: 539–45. https://doi.org/10.1016/S0140-6736(00)04046-0
6. Coussens LM, Werb Z. Inflammation and cancer. Nature. 2002; 420:860–67. https://doi.org/10.1038/nature01322
7. Sabrkhany S, Griffioen AW, Oude Egbrink MGA. The role of blood platelets in tumor angiogenesis. Biochim Biophys Acta 2011; 1815: 189–196. https://doi.org/10.1016/j.bbcan.2010.12.001
8. Shen XM, Xia YY, Lian L, Zhou C, Li XL, Han SG, et al. Mean platelet volume provides beneficial diagnostic and prognostic information for patients with resectable gastric cancer. Oncol Lett. 2016; 12: 2501-6. https://doi.org/10.3892/ol.2016.4913
9. Kemal Y, Demirağ G, Ekiz K, Yücel I. Mean platelet volume could be a useful biomarker for monitoring epithelial ovarian cancer. J Obstet Gynaecol. 2014; 34: 515-8. https://doi.org/10.3109/01443615.2014.912620
10. Kumagai S, Tokuno J, Ueda Y, Marumo S, Shoji T, Nishimura T, et al. Prognostic significance of preoperative mean platelet volume in resected non-small-cell lung cancer. Mol Clin Oncol. 2015; 3: 197-201. https://doi.org/10.3892/mco.2014.436
11. Tanriverdi O, Menekse S, Teker F, Oktay E, Nur Pilanc K, Gunaldi M, et al. The mean platelet volume may predict the development of isolated bone metastases in patients with breast cancer: a retrospective study of the Young Researchers Committee of the Turkish Oncology Group (TOG). J BUON. 2016; 21: 840-50. (PMID: 27685904)
12. Anand A, Raju K, Azeem Mohiyuddin SM. Significance of platelet parameters in squamous cell carcinoma of oral cavity - A case-control study. J Cancer Res Ther. 2022 Jul-Sep;18(4):1036-1041. doi: 10.4103/jcrt.jcrt_786_21
13. Li C, Zhang H, Li S, Zhang D, Li J, Dionigi G, et al. Prognostic Impact of Inflammatory Markers PLR, LMR, PDW, MPV in Medullary Thyroid Carcinoma. Front Endocrinol (Lausanne). 2022 Mar 8;13:861869. doi: 10.3389/fendo.2022.861869.
14. Zhang H, Liu L, Fu S, Liu YS, Wang C, Liu T, et al. Higher platelet distrubition width predicts poor prognosis in laryngeal cancer. Oncotarget 2017; 8(29): 48138-44. https://doi.org/10.18632/oncotarget.18306
15. Hsueh C, Tao L, Zhang M, Cao W, Gong H, Zhou J, et al. The prognostic value of preoperative neutrophils, platelets, lymphocytes, monocytes and calculated ratios in patients with laryngeal squamous cell cancer. Oncotarget. 2017 Mar 15;8(36):60514-60527. https://doi.org/10.18632/oncotarget.16234
16. Zhang X, Lv Z, Yu H, Zhu J. The clinicopathological and prognostic role of thrombocytosis in patients with cancer: a meta-analysis. Oncol Lett. 2017;13:5002–8. https://doi.org/10.3892/ol.2017.6054
17. Meikle CK, Kelly CA, Garg P, Wuescher LM, Ali RA, Worth RG. Cancer and thrombosis: the platelet perspective. Front Cell Dev Biol. 2016;2012 4:147. https://doi.org/10.3389/fcell.2016.00147
18. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation. Curr Pharm Des. 2011;17:47–58. https://doi.org/10.2174/138161211795049804
19. Wiwanitkit V. Plateletcrit, mean platelet volume, platelet distribution width: its expected values and correlation with parallel red blood cell parameters. Clin Appl Thromb Hemost. 2004;10:175–8. https://doi.org/10.1177/107602960401000208
20. Bambace NM, Holmes CE. The platelet contribution to cancer progression. J Thromb Haemost. 2011;9:237–49. https://doi.org/10.1111/j.1538-7836.2010.04131.x
21. Ye J, Liao B, Jiang X, Dong Z, Hu S, Liu Y, et al. Prognosis value of platelet counts, albumin and neutrophil-lymphocyte ratio of locoregional recurrence in patients with operable head and neck squamous cell carcinoma. Cancer Manag Res. 2020;12:731–41. https://doi.org/10.17.2147/CMAR.S234618
22. Pardo L, Valero C, López M, García J, Camacho M, Quer M, et al. The prognostic value of pretreatment platelet count in patients with head and neck squamous cell carcinoma. Auris Nasus Larynx 2017;44:313–8. https://doi.org/10.1016/j.anl.2016.06.009
23. Fu S, Liu L, Zhang X, Liu ZP, Wang RT. Platelet indices in laryngeal cancer. Cancer Biomark. 2018;21:675–80. https://doi.org/10.3233/CBM-170751
24. Guo E, Zhang C, Guo L, Song K, Wang G, Duan C, et al. Prognostic value of platelet distribution width and mean platelet volume in patients with laryngeal cancer. Future Oncol. 2021;17:1025–37. https://doi.org/10.2217/fon-2020-0658
25. Sheng X, Zhang H, Ge P, Chen L, Zhang S. A retrospective study of the prognostic significance of preoperative plasma fibrinogen, mean platelet volume, and the neutrophil-to-lymphocyte ratio in patients with laryngeal squamous cell carcinoma. Med Sci Monit. 2019;25:4527–34. https://doi.org/10.12659/MSM.914426
26. Kara A, Guven M, Demir D, Yilmaz MS, Gundogan ME, Genc S. Are calculated ratios and red blood cell and platelet distribution width really important for the laryngeal cancer and precancerous larynx lesions. Niger J Clin Pract. 2019;22:701–6. https://doi.org/10.4103/njcp.njcp_478_18
27. Sierko E, Wojtukiewicz MZ. Platelets and angiogenesis in malignancy. Semin Thromb Hemost. 2004;30:95–108. https://doi.org/10.1055/s-2004-822974
28. Suzuki K, Aiura K, Ueda M, Kitajima M. The influence of platelets on the promotion of invasion by tumor cells and inhibition by antiplatelet agents. Pancreas. 2004;29:132–40. https://doi.org/10.1097/00006676-200408000-00008
29. Jain S, Harris J, Ware J. Platelets: linking hemostasis and cancer. Arterioscler Thromb Vasc Biol. 2010;30:2362–7. https://doi.org/10.1161/ATVBAHA.110.207514
30. Atasever Akkas E, Yucel B. Prognostic value of systemic immune inflammation index in patients with laryngeal cancer. Eur Arch Otorhinolaryngol. 2021;278:1945–55. https://doi.org/10.1007/s00405-021-06798-2
31. Kara M, Uysal S, Altinisik U, Cevizci S, Güclü O, Dereköy FS. The pre-treatment neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and red cell distribution width predict prognosis in patients with laryngeal carcinoma. Eur Arch Otorhinolaryngol. 2017;274:535–42. https://doi.org/10.1007/s00405-016-4250-8
32. Wang J, Wang S, Song X, Zeng W, Wang S, Chen F, et al. The prognostic value of systemic and local inflammation in patients with laryngeal squamous cell carcinoma. Onco Targets Ther. 2016;9:7177–85. https://doi.org/10.2147/OTT.S113307
33. Zhong B, Gu DY, Du JT, Chen F, Liu YF, Liu SX. May the change of platelet to lymphocyte ratio be a prognostic factor for T3–T4 laryngeal squamous cell carcinoma: a retrospective study. PLoS One. 2018;13:e0210033. https://doi.org/10.1371/journal.pone.0210033