Dynamic changes of inflammatory markers and their effects on the prognosis of patients with laryngeal and hypopharyngeal cancer submitted to total pharyngolaryngectomy

Original Article

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Abstract

Introduction: The use of prognostic markers to decide the most appropriate therapies to perform in each case is assumed as one of the pillars of the approach to the patient with squamous cell carcinoma (SCC) of the hypopharynx and larynx. In addition to the clinical and pathological stage determined by the classification system TNM, there is evidence that the tumor-related systemic inflammatory response (SIR) has implications for tumor aggressiveness and progression. However, its value as an independent prognostic factor remains ambiguous.

Aims: To analyze the tumor SIR, its perioperative dynamic changes and after adjuvant treatment and its prognostic value in patients with SCC of the larynx and hypopharynx undergoing total pharyngolaryngectomy.

Methods: Retrospective analysis of clinico-pathological data of patients undergoing total pharyngolaryngectomy between January 2013 and December 2018 in a tertiary-level hospital. SIR was assessed using the following parameters: lymphocyte-monocyte ratio (LMR), platelets-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR) and systemic immuno-inflammatory index (SII). Kaplan-Meier analysis and Cox regression were used to analyze survival outcomes and associated risks.

Results: 59 patients were included in the study, with a mean age of 59.2 years. The mean follow-up time was 49.2 months. Preoperative PLR was the best predictor of overall survival (OS) at 5 years (area under the curve (AUC) 0.796, $p<0.005$). The optimal cutoff value was determined for each inflammatory parameter analyzed preoperatively, postoperatively and after adjuvant treatment (LMR: 2.6, 2.8 and 2.2, respectively; PLR: 125.0, 162.6 and 57.2, respectively; NLR: 2.3, respectively; 2.3, 2.8 and 3.9, respectively; SSI: 931.4, 732.8 and 931.43, respectively). Multivariate survival analysis showed that OS and distant metastasis-free survival

(MFS) were statistically lower in patients with preoperative PLR >125.0 (HR 4.39, p<0.005 and HR 17.65, p <0.005, respectively). There was a significant decrease in SIR after complete treatment with surgery with or without adjuvant chemoradiation. However, the pattern of parameters variation with treatments had no influence on OS or MFS. Patients with preoperative LPR >125.0 tend to have higher NLR and SII (p<0.005), although these did not prove to be independent predictors of survival. Conclusions: A high preoperative PLR was significantly associated with worse OS and MFS in patients undergoing total pharyngolaryngectomy. Still, the use of this marker in our current clinical practice to predict postoperative outcomes must be performed in a critical way.
Keywords: Systemic inflammatory response; laryngeal carcinoma; hypopharyngeal carcinoma; platelet-lymphocyte ratio; survival

Introduction

Carcinoma of the head and neck region is the sixth most common cancer globally, and squamous cell carcinoma is the most prevalent histological type[1,2]. The estimated annual incidence of carcinomas of the larynx and hypopharynx in Europe is 5.9 cases per 100,000 people, and the associated 5-year survival rate is estimated to be 60%[3]. The use of prognostic markers to plan the optimal treatment strategy for each case (surgery, chemoradiotherapy, and/or radiotherapy) is one of the pillars of management of these patients.

There are several predictive factors for the outcome in patients with cancer of the larynx and hypopharynx, which are related to the characteristics of the patient, tumor, and treatment. The tumor's location, clinical and pathological TNM staging, and histological type and grade are universally recognized as determinants of prognosis and are used to select the most adequate treatment[4]. However, these clinical parameters are insufficient for a comprehensive characterization of this type of cancer because they do not consider the biological aggressiveness of the tumor or the host's immune response[4]. In this context, the concept of tumor microenvironment considers the cancer cells and non-malignant cells in a surrounding extracellular matrix (which includes several types of lymphocytes, macrophages, neutrophils, endothelial cells, and fibroblasts) along with their interactions, which play a fundamental role in tumor growth and progression[2,5]. Understanding the mechanism of invasion of the host's immune system in the tumor microenvironment and its role may allow the development of new diagnostic and treatment tools to help improve the care provided to these patients. There has been a significant progress in the study of several solid tumors, including those of the head and neck region—regarding the identification of inflammatory markers that are easily obtained in clinical practice and may explain tumor aggressiveness and the risk of tumor progression—thereby contributing to the early prediction of clinical outcomes[1].

In this sense, ongoing clinical research has indicated that tumor-related systemic inflammatory response (SIR), assessed by the lymphocyte-monocyte ratio (LMR), neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII), reflects tumor aggressiveness and risk of tumor progression and has an impact on the patients' prognosis. These correlations have been confirmed for many tumor types and locations, including head and neck tumors[6-11].

These ratios of analytical values, which are easily calculated from the complete blood count, reflect the complex interactions between the local immune response to the tumor and the associated systemic response and are expected to vary after elective treatment with surgery. However, their dynamic variation with the treatment and clinical impact remain unknown in patients with squamous cell carcinoma (SCC) of the larynx and hypopharynx. Therefore, this study aimed to analyze and perform a longitudinal characterization of the tumor-related SIR, clarify its dynamic variation perioperatively and after adjuvant treatment, and establish its prognostic value in patients with SCC of the larynx and hypopharynx undergoing total pharyngolaryngectomy.

Materials and Methods

Sample

This was a retrospective analysis of the clinical and histopathological data of patients who underwent total pharyngolaryngectomy for SCC of the larynx and hypopharynx between January 2013 and December 2018 in a tertiary hospital. The following patients were excluded from the study: (1) those who received neoadjuvant treatment; (2) who had immune diseases; (3) who did not undergo laboratory testing for the complete blood count (CBC) in the pre- and postoperative periods; (4) who had an acute infectious complication at the time of laboratory testing; (5) who had a second primary tumor or distant metastasis at diagnosis; (6) who had incomplete or inaccurate clinical records; (7) who were lost to follow-up after surgery.

The characterization of the sample regarding postoperative tumor staging was performed according to the guidelines of the National Comprehensive Cancer Network (NCCN Guidelines®) for head and neck tumors[12].

Analysis of inflammatory markers

LMR, NLR, PLR, and SII were calculated for the analysis of SIR using the absolute values of lymphocytes (L), neutrophils (N), monocytes (M), and platelets (P) obtained from the CBC. SII results were obtained from the equation $(N \times P)/L$. SIR was evaluated at various stages of the sample's follow-up: (1) preoperatively, by laboratory testing performed in the seven days before surgery; (2) postoperatively, by laboratory testing performed before the administration of adjuvant treatment (if applicable) or up to six weeks after surgery; (3) after the adjuvant treatment.

The analysis of the variation in the markers' values with the chosen treatments only compared the values after the adjuvant treatment with the pre- and postoperative values in the same patient (n=49).

Statistical analysis

To obtain the ideal cutoff values of the selected ratios to determine SIR, receiver operating characteristic (ROC) curve analysis was performed for the 5-year overall survival at each evaluation time-point (preoperatively, postoperatively, and after adjuvant treatment). The cutoff values obtained for each ratio and at each evaluation time-point were used to categorize the patients into two groups to determine their prognostic significance.

The proportions of the categorical variables between the two groups were analyzed and compared using the chi-square test or Fisher's exact test. The t-student test for paired samples or analysis of variance for repeated measures were used to compare the quantitative variables at different time-points of follow-up.

The Kaplan-Meier method and Cox regression were used to analyze the survival and associated risks, respectively.

Descriptive and inferential statistical analyses were performed using the Statistical Package for the Social Science software (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp®) and statistical significance was set at $p < 0.05$.

Results

Characterization of the sample

This study included 59 patients, of which 56 (94.9%) were men, and 3 (5.1%) were women. The mean age was 59.2 ± 10.9 years. The mean follow-up time was 49.2 months. Regarding the disease features, most patients (86.4%) had a primary tumor of the larynx, and 13.6% had a tumor originating in the hypopharynx. With regard to the TNM staging, five patients (8.5%) were in stage II, 10 patients (16.9%) in stage III, 40 patients (67.8%) in stage IVa, and four patients (6.8%) in stage IVb. Forty-nine patients (83.1%) received adjuvant treatment, mostly (71.4%) chemoradiotherapy.

Determination of the cutoff values of inflammatory markers

The optimal cutoff value was determined through ROC curve analysis for each evaluated inflammation parameter (LMR, PLR, NLR, and SII) in the preoperative and postoperative

periods and after adjuvant treatment. The following values were obtained: LMR - 2.6, 2.8, and 2.2; LRP - 125.0, 162.6, and 57.2; NLR - 2.3, 2.8, and 3.9; SII - 931.4, 732.8, and 931.4, respectively. Preoperative LRP was the best predictor of overall survival (OS) at 5 years (area under the curve [AUC] 0.796, p<0.005).

Analysis of the prognostic value of SIR and its dynamic variation with the selected treatment

Univariate analysis of the SIR of the analyzed sample (Table 1) showed that OS and distant metastasis-free survival (MFS) were statistically lower in patients with preoperative PLR ≥ 125.0 (hazard ratio [HR] 4.13, p=0.001 and HR 8.27, p=0.006, respectively). In the Kaplan-Meier analysis, patients with a PLR higher than 125 had a significantly worse long-term prognosis (OS of 32.6% at 5 years and MFS of 57.2%) than patients with a low PLR (OS of 78.8% at 5 years and MFS of 93.9%) (p<0.001) (Figures 1 and 2, respectively).

Univariate analysis also showed that a preoperative SII ≥ 931.4 was predictive of a worse MFS (HR 4.5, p=0.023) (Table 1). Analysis of the remaining inflammatory parameters in the preoperative period, postoperative period, and after adjuvant treatment revealed that they were not predictive of survival.

After obtaining the above results, we included preoperative PLR and SII in a multivariate model in which we considered other factors that can have an impact on OS and MFS—age at diagnosis, primary location, and TNM disease staging (Table 2). We observed that only preoperative PLR remained a significant independent predictor of OS and MFS (HR 5.78, p=0.001 and HR 14.49, p=0.008, respectively). Additionally, stage IVb was also an independent predictor of worse OS than stage II (HR 16.26, p=0.025).

Subsequently, we analyzed the variation of SIR with the selected treatments (surgery and adjuvant treatment), as shown in Figure 3. The LMR decreased with treatment

Figure 1
Association between preoperative platelet-lymphocyte ratio (PLR) and overall survival

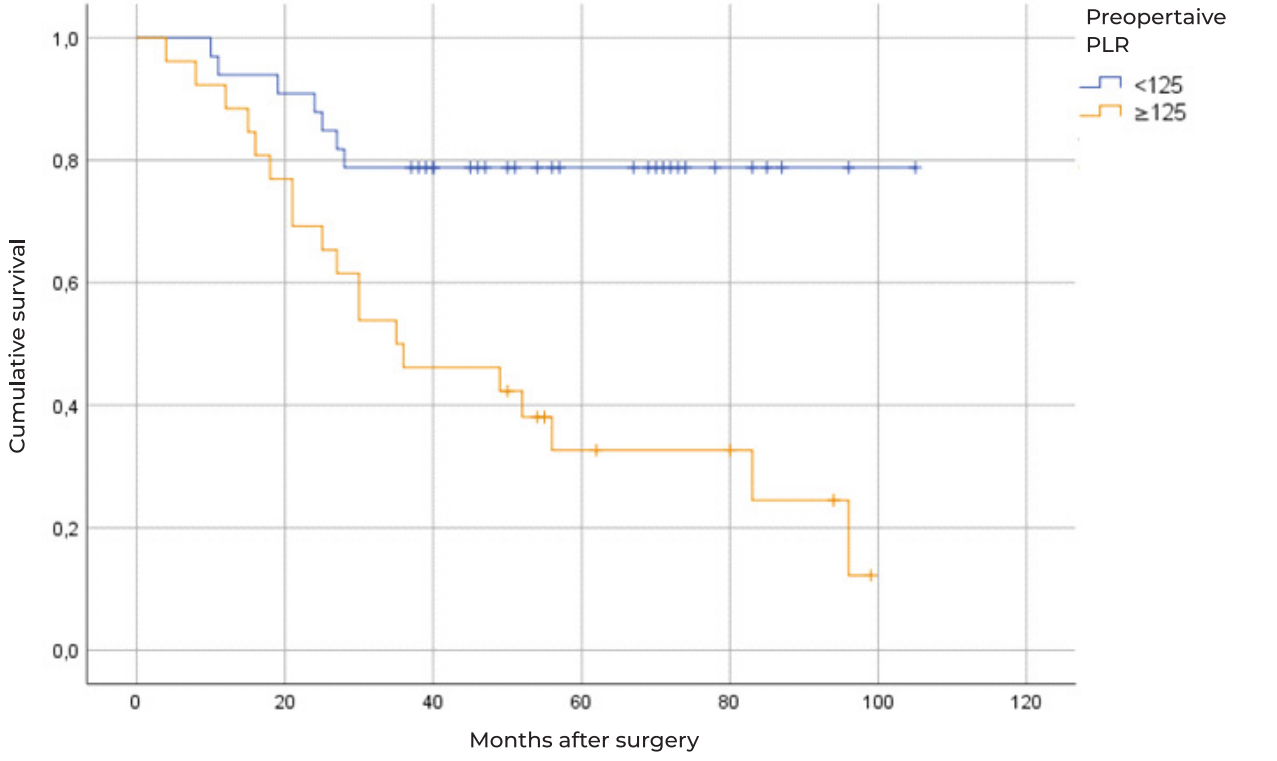
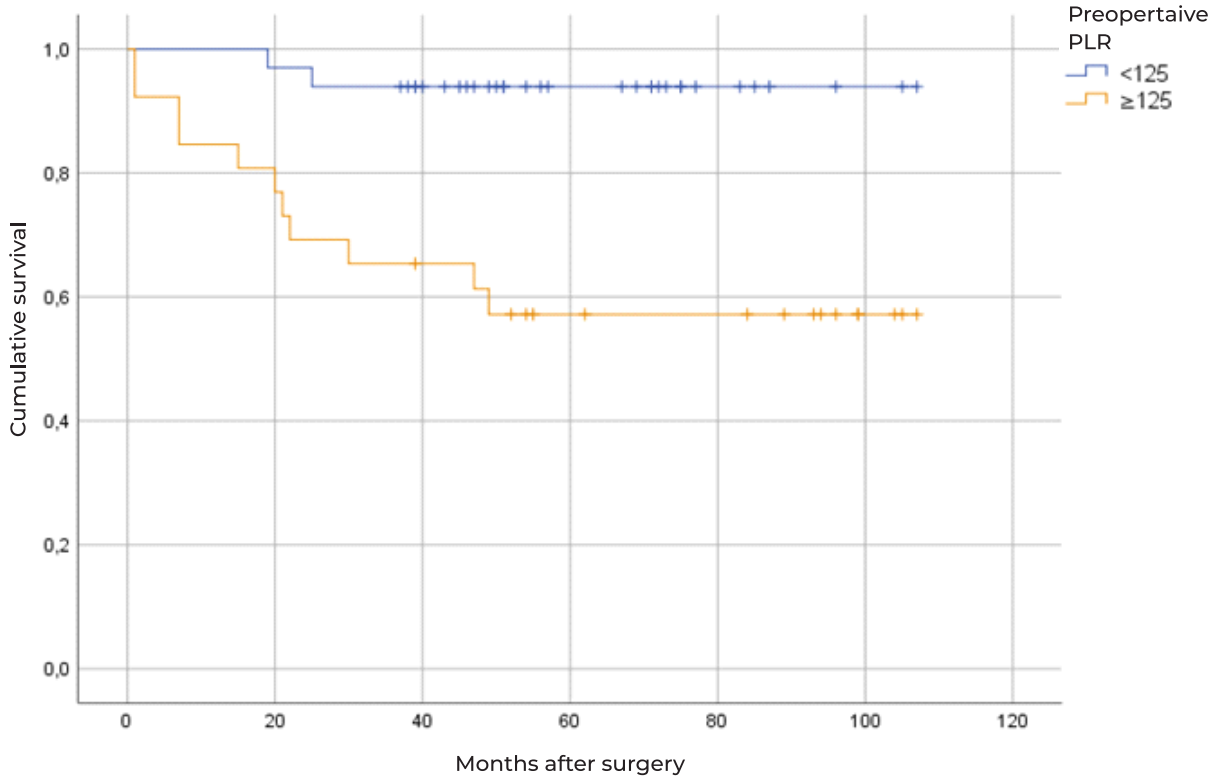


Figure 2
Association between preoperative platelet-lymphocyte ratio (PLR) and distant metastasis-free survival



(Figure 3a), and this reduction was significant after complete treatment with surgery and adjuvant therapy. The PLR increased and decreased (Figure 3b) after surgery and adjuvant therapy, respectively, and these values varied significantly relative to the initial status ($p<0.05$). Regarding NLR and SII values (Figures 3c and 3d, respectively), although they decreased significantly after surgery, the ratios after complete treatment did not vary significantly relative to the preoperative period.

As preoperative PLR was the only inflammatory marker affecting OS and MFS in the multivariate analysis, and its values changed significantly after surgery and adjuvant therapy, we explored the effect of its dynamic variation on the prognosis of these patients. Therefore, considering the cutoff values previously determined for the preoperative and postoperative periods and after adjuvant therapy, we divided the patients into the following groups: (1) elevated preoperative PLR - elevated PLR after complete treatment; (2) high preoperative PLR after complete treatment; (3) low preoperative PLR - high PLR after complete treatment; (4) low preoperative PLR – low PLR after complete treatment. However, the trend of PLR variation with the selected treatment did not have a significant impact on OS or MFS.

Association of PLR with clinical and laboratory variables

Finally, the correlations of the clinical and laboratory variables with the preoperative PLR were analyzed. The patients with a preoperative PLR >125 tended to be in a more advanced stage (stage IV) ($p<0.05$) and had higher levels of inflammatory parameters (NLR and SII) ($p<0.05$) (Table 3).

Discussion

The 5-year overall survival rate in carcinomas of the larynx and hypopharynx varies mainly according to the location and stage of the

Table 1
Univariate analysis (with relative risk) of the systemic inflammatory parameters at various evaluation time-points for overall survival, disease-free survival, and metastasis-free survival

	OS			DFS		MFS	
	Univariate analysis			Univariate analysis		Univariate analysis	
	n	HR (CI 95%)	p value	HR (CI 95%)	p value	HR (CI 95%)	p value
Preoperative							
LMR							
<2.6	19	Ref.	0.229	Ref.	0.969	Ref.	0.260
≥2.6	40	1.75 (0.70-4.42)		0.34 (0.08-1.54)		0.54 (0.18-1.59)	
PLR							
<125	33	Ref.	0.001*	Ref.	0.108	Ref.	0.006*
≥125	26	4.13 (1.73-9.85)		2.51 (0.82-7.67)		8.27 (1.83-37.34)	
NLR							
<2.3	20	Ref.	0.088	Ref.	0.070	Ref.	0.411
≥2.3	39	0.51 (0.23-1.11		0.37 (0.12-1.09)		1.72 (0.47-6.25)	
SII							
<931.4	32	Ref.	0.500	Ref.	0.825	Ref.	0.023*
≥931.4	27	1.30 (0.60-2.82)		1.13 (0.38-3.37)		4.50 (1.24-16.36)	
Postoperative							
LMR							
<2.8	24	Ref.	0.194	Ref.	0.157	Ref.	0.376
≥2.8	35	1.75 (0.75-4.07)		2.54 (0.70-9.24)		0.61 (0.21-1.82)	
PLR							
<162.6	30	Ref.	0.120	Ref.	0.425	Ref.	0.155
≥162.6	29	0.53 (0.23-1.18)		0.63 (0.21-1.94)		0.43 (0.11-1.38)	
NLR							
<2.8	38	Ref.	0.205	Ref.	0.650	Ref.	0.397
≥2.8	21	0.63 (0.26-1.50)		0.76 (0.23-2.47)		1.60 (0.54-4.78)	
SII							
<732.8	32	Ref.	0.300	Ref.	0.494	Ref.	0.485
≥732.8	27	0.65 (0.29-1.47)		1.56 (0.49-4.35)		1.48 (0.50-4.40)	
After adjuvant treatment							
LMR							
<2.2	30	Ref.	0.262	Ref.	0.65	Ref.	0.386
≥2.2	19	0.60 (0.24—1.47)		0.76 (0.22-2.58)		0.56 (0.15-2.10)	
RPL							
<57.2	23	Ref.	0.080	Ref.	0.975	Ref.	0.749
≥57.2	26	0.46 (0.19-1.10)		0.98 (0.20-3.22)		1.21 (0.37-3.98)	
NLR							
<3.9	24	Ref.	0.245	Ref.	0.656	Ref.	0.366
≥3.9	25	1.66 (0.71-3.93)		1.31 (0.40-4.29)		1.76 (0.52-6.02)	
SII							
<931.4	28	Ref.	0.071	Ref.	0.335	Ref.	0.335
≥931.4	21	2.30 (0.93-5.40)		1.79 (0.46-5.89)		1.79 (0.55-5.89)	

Abbreviations: OS, overall survival; DFS, disease-free survival; MFS, metastasis-free survival; HR, hazard ratio (relative risk); CI, confidence interval; LMR, lymphocyte-monocyte ratio; PLR, platelet-lymphocyte ratio; NLR, neutrophil-lymphocyte ratio; SII, systemic immune-inflammation index

Table 2
Multivariate analysis (with relative risk) of the clinical and laboratory variables associated with overall survival and metastasis-free survival

	OS			MFS	
	Multivariate analysis			Multivariate analysis	
Clinical and laboratory variables	**n**	**HR (CI 95%)**	**p value**	**HR (CI 95%)**	**p value**
Age					
< 60 years	34	Ref.	0.100	Ref.	0.820
≥ 60 years	25	1.99 (0.88-4.53)		0.87 (0.27-2.84)	
Tumor location					
Larynx	51	Ref.	0.830	Ref.	0.189
Hypopharynx	8	1.12 (0.40-3.10)		2.30 (0.67-7.92)	
Disease staging					
II	5	Ref.		Ref.	
III	10	4.81 (0.49-46-81)	0.176	1.42 (0.21-10.92)	0.865
IVa	40	2.47 (0.31-19.76)	0.394	1.89 (0.12-6.43)	0.765
IVb	4	16.26 (1.43-184.72)	0.025*	5.40 (0.31-14.53)	0.654
Preoperative PLR					
<125	33	Ref.	0.001*	Ref.	0.008*
≥125	26	5.78 (2.15-15.51)		14.49 (2.01-104.46)	
Preoperative SII					
<931.4	32	-	-	Ref.	0.476
≥931.4	27	-		1.72 (0.39-7.67)	

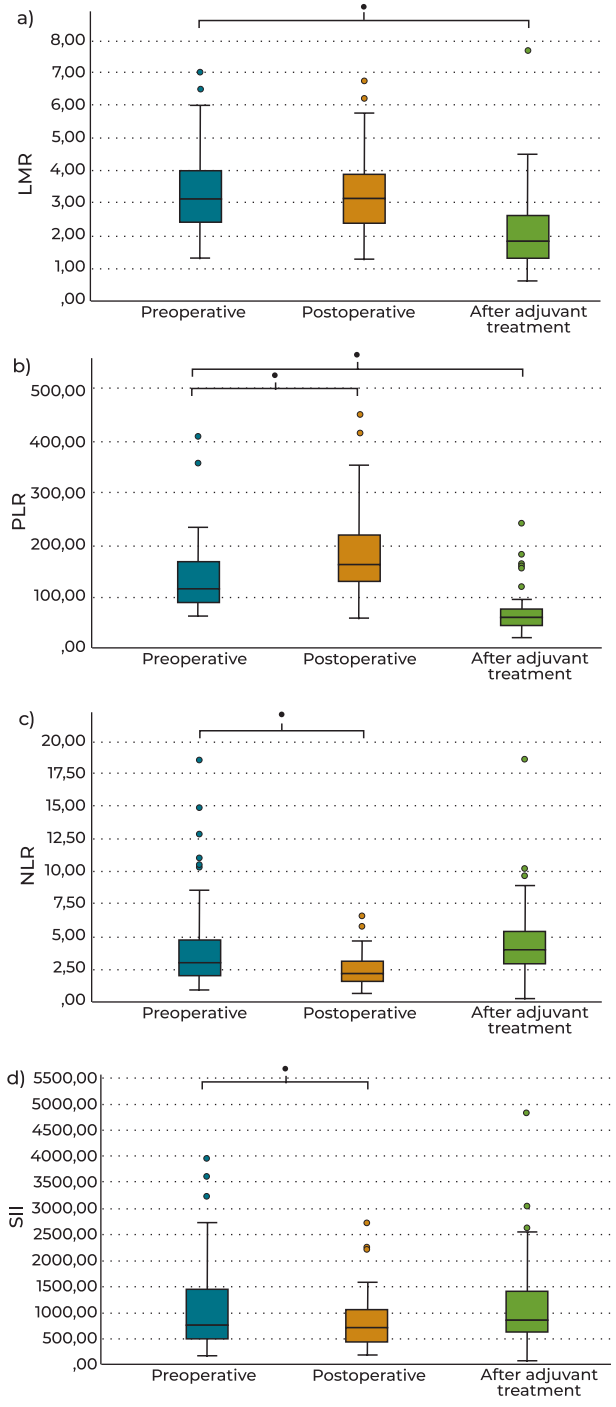
Abbreviations: OS, overall survival; MFS, metastasis free survival; HR, hazard ratio (relative risk); CI, confidence interval; PLR, platelet-lymphocyte ratio; SII, systemic immune-inflammation index

Table 3
Correlation between preoperative PLR and clinical and laboratory variables

	Preoperative NLR (*cutoff* 125)				
	Low (n=33)		Elevated (n=26)		
Clinical and laboratory variables	**n**	**%**	**n**	**%**	**p value**
Age					
< 60 years	20	60.6	14	53.8	0.791
≥ 60 years	13	39.4	12	42.4	
Tumor location					
Larynx	30	90.9	21	80.8	0.284
Hypopharynx	3	9.1	5	19.2	
Disease staging					
II or III	12	36.4	3	11.5	0.038*
IV	21	63.6	23	88.5	
Preoperative LMR					
<2.6	9	27.3	10	38.5	0.410
≥2.6	24	72.7	16	61.5	
Preoperative NLR					
<2.3	15	45.5	5	19.2	0.032*
≥2.3	18	54.4	21	80.8	
Preoperative SII					
<931.4	25	75.8	7	26.9	<0.001*
≥931.4	8	24.2	19	73.1	

Abbreviations: n, number of patients; PLR, platelet-lymphocyte ratio; LMR, lymphocyte-monocyte ratio; NLR, neutrophil-lymphocyte ratio; SII, systemic immune-inflammation index.

Figure 3
Dynamic variation of LMR (a), PLR (b), NLR (c), and SII (d) after surgical treatment and after adjuvant therapy in patients with carcinoma of the larynx and hypopharynx undergoing total laryngopharyngectomy. LMR, lymphocyte-monocyte ratio; PLR, platelet-lymphocyte ratio; NLR, neutrophil-lymphocyte ratio; SII, systemic immune-inflammation index.



tumor (determined by the TNM system). However, age, patient's general condition and nutritional status, and associated comorbidities—immunosuppression—also appear to have an impact on the clinical prognosis[4]. The staging systems currently used in clinical practice to decide and guide treatment are mainly anatomical and do not consider the abovementioned factors, tumor aggressiveness, or the host's immune response. Thus, the ability of these staging systems to predict the long-term outcomes accurately for each individual case remains limited and has been questioned. In this context, studies have been conducted more recently to identify new markers that can aid in prognostic assessment and therapeutic decision-making, identify factors potentially modifiable by an early intervention, and aid in the development of targeted immunotherapy as a complementary treatment approach. The value of using inflammatory markers in the evaluation of these patients is that, in addition to reflecting the host's response to cancer, confirmed by the fact that immunodepressed patients are at a higher risk of developing cancer[13,14], they are inexpensive, easily obtained, and routinely available.

In this study, the clinical impact of the systemic inflammatory response was assessed using inflammatory markers obtained by quantitative evaluation of the CBC. Although there is some evidence on this topic in the literature, the mechanisms by which these biomarkers impact prognosis and predict the outcomes of these patients remain confusing and unclear as a result of the heterogeneity of the studies conducted on this theme[1,6,8]. Among the analyzed inflammatory parameters (LMR, PLR, NLR, and SII), preoperative PLR was found to be the best predictor of 5-year OS, with a ratio >125 being an independent predictor of worse OS and DFS (HR 5.8 and 14.5, respectively), as demonstrated in the multivariate analysis. In fact, there is scientific evidence that the immune status has a significant effect on the prognosis of patients with solid tumors of

the head and neck region, and the analyzed ratios reflect the SIR of the host in the tumor microenvironment[1,5]. Regarding PLR in head and neck tumors, including those of the larynx and hypopharynx, numerous studies have correlated high preoperative levels with worse OS—two recent meta-analyses on the topic[1,15]. In these, the cutoff value of PLR to estimate OS ranged between 111 and 186, an interval that includes the cutoff value obtained in this study (125). Tumor infiltration by lymphocytes, especially cytotoxic $CD8^+$ T lymphocytes, appears to be associated with a better response to treatment and increased survival[16,17]. Conversely, lymphopenia, which occurs when the ability of the immune system to neutralize tumor progression is compromised, is associated with worse survival[17,18]. However, neutrophils and platelets provide the necessary bioactive molecules, including angiogenic, epithelial, and stromal growth factors and remodeling enzymes of the extracellular matrix, responsible for tumor progression[9]. Hence, the inflammatory markers neutrophils, platelets, and lymphocytes have been identified as independent prognostic factors[17,20,21]. Thus, patients with immune and acute inflammatory diseases were excluded from this study because these conditions could alter the significance of the changes in leukocytes and platelet counts.

Additionally, we investigated the dynamic variation in these inflammatory parameters over time and according to the selected treatment and observed that LMR and PLR were statistically lower after complete treatment (surgery plus adjuvant treatment). However, the pattern of PLR variation according to treatment was not shown to be a predictor of clinical prognosis—the most important predictor of survival was preoperative PLR but its variation over time (decrease or increase in the ratio after the treatments) did not influence patient survival. Nevertheless, this study is one of the first to assess and analyze the dynamic variation in these markers according to the treatment used in head and neck tumors. In fact, the literature on the variation in these indices during and after treatment is considerably scarce. It is not yet clear how the treatments (surgery and chemoradiotherapy) modify the tumor microenvironment and the associated systemic inflammatory response and affect the clinical prognosis.

Moreover, we concluded that higher levels of preoperative PLR tended to occur mainly in patients with advanced stages of the disease (IV) and higher preoperative NLR and IIS, although the latter were not shown to be independent predictive factors of survival. Nevertheless, there is evidence that an elevated pretreatment NLR is a negative predictive factor for tumors of the head and neck[21,22]. The significant heterogeneity that exists in the literature regarding the definition of the ideal cutoff values for high and low ratios that determine survival may contribute to this difference[6]. This variation may be attributed to the different methods used in the studies. In a study on laryngeal cancer conducted by Du et al. [21], in which an association between a high NLR and worse prognosis was demonstrated by survival analysis, the CART (classification and regression tree) method was used, and a value of 3.18 was obtained as the cutoff. Regarding the SII, a similar score that reflects increased levels of circulating neutrophils and monocytes (SIRI - systemic inflammation response index) has been shown to be associated with increased mortality in patients with head and neck tumors (HR of 3.3) [18].

Although there appears to be a correlation between SIR and the clinical prognosis of these patients, these markers should be used carefully in the prediction of prognosis, once these inflammatory markers reflect the immune system's activity at an exact and unique moment in time and, therefore, do not reflect the dynamic variations that occur over time. Additionally, it is important to consider that the immune profile analyzed is a systemic and overall evaluation of the inflammatory response and may not necessarily reflect the tumor microenvironment and the specific subpopulations of cells involved in the

immune process.

The major limitation of this study was the small sample size of each analyzed subgroup, which did not allow us to show that the tumor location (hypopharynx versus larynx) influences the clinical prognosis of the patients, as previously demonstrated[18]. Further, we could not make inferences about the possibility of the remaining analyzed inflammatory markers being predictors of survival, as other authors have done. Moreover, the fact that it was a retrospective study prevented rigorous collection timings for the laboratory tests (pre- and post-treatment). Additionally, the variety of treatments performed made the sample heterogeneous, which could, by itself, influence the clinical outcomes of the patients. Despite the abovementioned limitations, we concluded that a high PLR is a negative prognostic factor, as is the case for many other cancers, including lung, esophageal, and renal cancers[23-25]. This shows some coherence and strengthens the idea that the tumor microenvironment and, consequently, the associated systemic inflammatory response have an impact on tumor aggressiveness and progression.

It would be pertinent to conduct a multicenter prospective study in the future to further determine which inflammatory marker or combination of markers better predicts the clinical outcomes of these patients, in addition to assessing its dynamic variation accurately with the selected treatments and determining the statistic reliability (test-retest) of the inflammatory parameters. It would also be important to define fixed cutoff values to evaluate their applicability in clinical practice. Finally, it would be interesting to analyze other factors—albumin and the albumin/globulin ratio—which reflect the patient's nutritional status[21] and have been shown to be predictors of clinical outcomes in tumors of the head and neck and other cancers[18].

Conclusion

The results of this study indicate that preoperative PLR, as an index of SIR, may predict the prognosis of patients with carcinoma of the larynx and hypopharynx undergoing total pharyngolaryngectomy. Therefore, this marker, which is accessible and easily obtained, in combination with other markers that have been shown in previous studies to have an impact on the clinical prognosis of patients, may become an additional tool for risk stratification and therapeutic decision-making in patients with head and neck tumors—those of the larynx and hypopharynx.

Conflicts of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Data Confidentiality

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the 2013 Helsinki Declaration of the World Medical Association.

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Availability of scientific data

There are no datasets available, publicly related to this work.

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