Journal of Current Research in Oral Surgery
2026, Volume 6, Issue 1, Page No: 78-89

Available online at: www.tsdp.net

ISSN: 3062-3480

Original Article

Prognostic Value of Systemic Inflammatory Indices in Oropharyngeal Cancer: A Retrospective Cohort Study

Chinedu Okafor[1]*, Amina Bello[1]

[1]Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, University of Lagos, Lagos, Nigeria.

***E-mail** ✉ chinedu.okafor@gmail.com

Received: 05 November 2025; **Revised:** 24 February 2026; **Accepted:** 28 February 2026

ABSTRACT

Inflammation has historically been a cornerstone of clinical recognition and therapeutic approaches to malignant disease, presumably influencing tumor onset, staging, and progression. Systemic inflammatory responses, in particular, frequently become heightened before a cancer manifests and persist throughout its evolution. In cancer detection and surveillance, systemic inflammatory activity is quantified using indices such as the systemic inflammatory response index (SIRI), plasma-to-lymphocyte ratio (PLR), systemic immune inflammation index (SII), and neutrophil-to-lymphocyte ratio (NLR). Our objective was to ascertain the connection between pre- and post-treatment concentrations of these inflammatory metrics and the prognosis and clinical outcomes of oropharyngeal cancer (OPC). A retrospective review of medical records was undertaken for 172 individuals diagnosed with OPC who received therapeutic intervention at University Medical Center in Lubbock, TX, from May 2013 through May 2023. Primary tumor locations were extracted from clinical documentation. The HPV infection status and degree of tumor differentiation were documented for each subject. Therapeutic strategies were divided into surgery, radiotherapy, chemotherapy, or a combination of concurrent chemotherapy and radiation. Clinical outcomes were stratified by disease recurrence and mortality attributable to the malignancy. Associations between treatment outcomes and the aforementioned inflammatory indices were analyzed. Given the extensive array of variables, suitable parametric statistical tests were employed. Pre-treatment values of SIRI and albumin showed a positive predictive relationship with locoregional recurrence ($P = 0.031$ and $P = 0.039$). Measurements of NLR, SII, and SIRI obtained at the three-month post-treatment mark likewise demonstrated positive predictive values for locoregional recurrence ($P = 0.005$, $P < 0.0005$, and $P = 0.007$, respectively). SIRI readings collected at six months after treatment were also positively predictive of locoregional recurrence ($P = 0.008$). SII levels at the six-month post-treatment interval were positively predictive of overall survival ($P = 0.027$). The findings of this investigation suggest that post-treatment concentrations of several inflammatory indices, particularly SIRI, NLR, and SII, may be useful for predicting long-term prognosis and recurrence risk in head and neck cancer following therapy.

Keywords: SIRI, Oropharyngeal cancer, Prognosis, Inflammatory markers

How to Cite This Article: Okafor C, Bello A. Prognostic Value of Systemic Inflammatory Indices in Oropharyngeal Cancer: A Retrospective Cohort Study. J Curr Res Oral Surg. 2026;6(1):78-89. https://doi.org/10.51847/gdu5EObv5k

Introduction

The role of inflammation has been firmly established as a fundamental element in the diagnostic workup and therapeutic management of malignant tumors, with a probable influence on disease emergence, tumor staging, and advancement [1, 2]. Heightened systemic inflammatory activity, in particular, is commonly observed both before the onset of cancer and during the course of the disease [1]. Across the landscape of cancer diagnosis and longitudinal monitoring, systemic inflammation is evaluated through multiple inflammatory ratios, including the systemic inflammatory response index (SIRI), plasma-to-lymphocyte ratio (PLR), systemic immune inflammation index (SII), and neutrophil-to-lymphocyte ratio (NLR). A substantial body of

published evidence documents elevated diverse inflammatory indices across a spectrum of malignancies.

Numerous studies in the scientific literature have examined the interplay between the aforementioned inflammatory markers and various cancer-related endpoints. The neutrophil-to-lymphocyte ratio (NLR) has repeatedly been identified in research as a biomarker associated with poorer survival and adverse prognostic trajectories across several solid tumor types [3]. Superior NLR figures have been correlated with accelerated tumor expansion and poorer outlook in multiple cancers affecting the gastrointestinal tract [4-6]. Raised NLR has additionally been recognized as a harbinger of unfavorable outcomes in squamous cell carcinoma of the head and neck [7]. Increased platelet-to-lymphocyte ratios (PLR) have similarly been linked with inferior prognosis across a broad range of neoplastic conditions, encompassing melanoma, rectal carcinoma, and hepatocellular carcinoma [6, 8, 9].

SIRI constitutes an inflammatory metric formulated from the proportional relationship between neutrophil, monocyte, and lymphocyte counts [10]. Several investigations have demonstrated the significance of SIRI as an influential inflammatory parameter in the progression pathways of numerous tumors [10]. The index was verified to act as an autonomous predictor of outcome in gallbladder carcinoma [11]. It likewise emerged as a prognostic biomarker in head and neck squamous cell carcinoma [12].

An elevated systemic immune inflammation index (SII) signals a poor prognosis among patients undergoing immune checkpoint inhibitor therapy [13]. Increased SII has been associated with worse prognostic outcomes in a variety of malignant diseases, among them bladder cancer and non-small cell lung cancer [14, 15]. Oropharyngeal cancer stands among the most frequently encountered malignancies on a global scale and represents the 7th most common cause of cancer-related mortality worldwide [16]. The development of OPC is connected to tobacco consumption, alcohol use, and infection with human papillomavirus (HPV) [16]. In addition, OPC, particularly the variant linked to HPV, has exhibited rising incidence within the United States [16]. While the literature on the relationship between various inflammatory indices and the prognosis of different malignancies is extensive, oropharyngeal cancer (OPC) has received relatively limited scrutiny in this domain. Furthermore, the task of investigating and contrasting which inflammatory indices provide the most reliable determination of clinical course and prognosis in OPC constitutes a nascent field of inquiry that we resolved to examine.

We aimed to establish relationships between the SIRI, PLR, SII, and NLR inflammatory indices and the prognosis and clinical outcomes of OPC. Beyond this, we sought to identify which indices carry the greatest prognostic weight in OPC. We performed a single-institution retrospective analysis of medical records from 172 patients diagnosed with OPC and assessed their inflammatory index measurements.

Materials and Methods

After securing authorization from the Texas Tech University Health Sciences Center Internal Review Board, a retrospective examination of patient records uncovered 172 individuals who underwent therapy for oropharyngeal cancer spanning the period from 9 May 2013 to 9 May 2023. Individuals were excluded from the analysis if they lacked available pre- or post-treatment hematological studies for review or if their post-treatment surveillance period was less than 3 months.

Baseline demographic characteristics—including sex, age, BMI, and ethnicity—alongside documented risk factors such as tobacco use and alcohol intake were collected **(Table 1)**. The anatomical sites of the primary tumors were established through record inspection and grouped into tonsil, base of tongue, soft palate, posterior pharyngeal wall, and overlapping subsites. In addition, HPV infection status (positive, negative, n/a) and tumor differentiation (well, moderate, poor, undifferentiated) were recorded for each subject. Disease staging was recorded according to both the 7th and 8th editions of the American Cancer Society's oropharyngeal cancer staging criteria. The therapeutic goal was designated as either curative or palliative, while the primary treatment approaches were sorted into the following categories: surgery, radiotherapy, chemotherapy, or concurrent chemoradiation. Subjects who received adjuvant regimens were similarly documented. Surgical margin status after treatment was classified as negative, positive, or n/a, and oncologic outcomes were stratified by disease recurrence and mortality attributable to the malignancy. Among cases with recurrence, its anatomical location was further specified as the original tumor site, the cervical region, both areas, or not otherwise indicated. The associations between therapeutic outcomes and pre- and post-treatment concentrations of inflammatory indices—namely, the systemic inflammatory response index (SIRI), plasma-to-lymphocyte ratio (PLR), systemic immune inflammation index (SII), and neutrophil-to-lymphocyte ratio (NLR)—were systematically investigated.

Journal of Current Research in Oral Surgery
2026, Volume 6, Issue 1, Page No: 78-89

Available online at: www.tsdp.net

ISSN: 3062-3480

Table 1. Patient demographics.

Category	Subgroup	Percentage	Count
Gender	Male	79.1%	136
	Female	20.9%	36
Ethnicity	Caucasian	86.0%	148
	Black	2.9%	5
	Hispanic or other	11.0%	19
Smoking status	No history of smoking	39.5%	68
	< 10 pack-years	14.0%	24
	> 10 pack-years	46.5%	80
Alcohol consumption	Non-drinker	48.3%	83
	Social drinking	30.8%	53
	Heavy drinking	20.9%	36
Tumor site	Tonsil	27.9%	48
	Base of tongue (BOT)	44.2%	76
	Soft palate	5.2%	9
	Posterior region	6.4%	11
	Overlapping sites	16.3%	28
HPV status	Positive	37.7%	66
	Negative	30.3%	53
	Not available (N/A)	30.3%	53
Tumor differentiation	Well differentiated	6.4%	11
	Moderately differentiated	36.0%	62
	Poorly differentiated	27.3%	47
	Undifferentiated	30.2%	52

Abbreviations: BOT = Base of Tongue, HPV = Human Papillomavirus.

The entire statistical analysis was conducted in SPSS (Version 23, IBM, Armonk, NY, USA). Given the broad array of variables studied, a multiple-testing plan was implemented. Group means for variables split into two categories were compared through independent t-tests and the Mann–Whitney U-test. When variables consisted of three or more categories, a one-way ANOVA (analysis of variance) was applied. Chi-squared and Fisher's exact tests were used to examine categorical variables. Survival probability curves for univariate analysis were plotted using the Kaplan–Meier method, with group comparisons performed using the log-rank test. For multivariate survival analysis, the Cox proportional hazards regression model was employed, and any variable approaching significance ($P < 0.2$) was included to adjust for potential confounders. A two-sided design was used for all tests, and the threshold for statistical significance was set at $P = 0.05$.

Results and Discussion

The preliminary screen identified 263 patients, of whom 91 were excluded from the final study group because blood work was unavailable or the follow-up duration was insufficient. The demographic breakdown of the ultimate cohort of 172 patients is summarized in **Table 1**: 79.1% (n = 136) were male, and 20.9% (n = 36) were female. The overwhelming majority of subjects identified as Caucasian (86%, n = 148), while 2.9% (n = 5) identified as Black. Regarding smoking history, 46.5% (n = 80) of the cohort had accumulated more than 10 pack-years, 14% (n = 24) had fewer than 10 pack-years, and 39.5% (n = 68) had no prior history of tobacco use. With respect to alcohol consumption, 48.3% (n = 83) denied any intake, 30.8% (n = 53) characterized their drinking as social, and 20.9% (n = 36) reported heavy alcohol use. The base of the tongue represented the single most frequently encountered primary site, at 44.2% (n = 76), with the tonsil ranking second (27.9%, n = 48), followed by overlapping subsites (16.3%, n = 28), posterior pharyngeal wall (6.4%, n = 11), and soft palate (5.2%, n = 9). When stratified by HPV status, 37.7% (n = 66) tested positive,

30.3% (n = 53) tested negative, and 30.3% (n = 53) had an unrecorded or not applicable status. Tumor differentiation was distributed as follows: well differentiated (6.4%, n = 11), moderately differentiated (36.0%, n = 62), poorly differentiated (27.3%, n = 47), and undifferentiated (30.2%, n = 52).

Tumor stage classifications, based on the 7th and 8th editions of the American Cancer Society staging manuals, are detailed in **Table 2**. **Table 3** displays the therapeutic intent and resulting outcomes, illustrating that a curative aim underpinned treatment in 94.2% (n = 162) of cases. Surgery was the predominant primary intervention (57.6%, n = 99), followed by combined chemotherapy and radiation (39.0%, n = 67). The combination of chemotherapy and radiation was the most frequently used adjuvant strategy (50%, n = 86). Following completion of therapy, disease recurrence was documented in 23.8% (n = 41) of the entire group, with the cervical region being the most prevalent site of locoregional failure (35%, n = 14), followed by the original primary site (32.5%, n = 13), both the primary and the neck simultaneously (25%, n = 10), and locations that were not specified (7.5%, n = 3). A total of 59 patients (34.3%, n = 59) died during the study period, and among these, 26 patients (44.1%, n = 26) succumbed to their disease.

Table 2. Tumor stages.

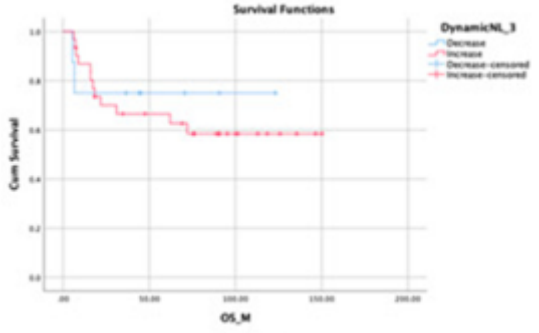
	Number	Percentage
T staging (7th edition)		
T1	24	14.0%
T2	44	25.6%
T3	62	36.0%
T4	42	24.4%
N staging (7th edition)		
N0	31	18.0%
N1	36	20.9%
N2a	23	13.4%
N2b	39	22.7%
N2c	16	9.3%
N3a	20	11.6%
N3b	7	4.1%
M staging (7th edition)		
M0	119	69.2%
M1	11	6.4%
M2	42	24.4%
T staging (8th edition)		
T1	24	14.0%
T2	44	25.6%
T3	62	36.0%
T4	42	24.4%
N staging (8th edition)		
N0	31	18.0%
N1	24	14.0%
N2a	10	5.8%
N2b	24	14.0%
N2c	10	5.8%
N3a	11	6.4%
N3b	3	1.7%
N11	20	11.6%
N22	27	15.7%
N33	9	5.2%
N44	3	1.7%
M staging (8th edition)		
M0	119	69.2%
M1	11	6.4%
M2	42	24.4%

Abbreviations: T = Tumor (size of primary tumor), N = Node (positive spread to lymph node(s)), M = Metastasis (to different area of body).

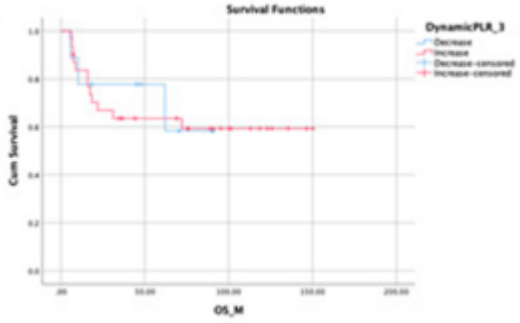
Table 3. Treatments and oncologic outcomes.

Category	Subgroup	Number	Percentage
Treatment intent	Curative approach	162	94.2%
	Palliative approach	10	5.8%
Primary treatment modality	Chemoradiation	67	39.0%
	Surgery	99	57.6%
	Radiotherapy alone	4	2.3%
	Chemotherapy alone	2	1.2%
Adjuvant therapy	No adjuvant treatment	66	38.4%
	Chemoradiation	86	50.0%
	Surgery	9	5.2%
	Radiotherapy	7	4.1%
	Chemotherapy	4	2.3%
Surgical margin status	Negative margins	32	18.6%
	Not available (N/A)	79	45.9%
	Positive margins	61	35.5%
Recurrence status	No recurrence	78	45.3%
	Recurrence present	41	23.8%
	Unknown (?)	53	30.8%
Site of local recurrence	Primary tumor site	13	32.5%
	Neck region	14	35.0%
	Both sites	10	25.0%
	Not specified	3	7.5%
Mortality status	Deceased	59	34.3%
	Alive	113	65.7%
Disease-specific death	Yes	26	44.1%
	No	33	55.9%

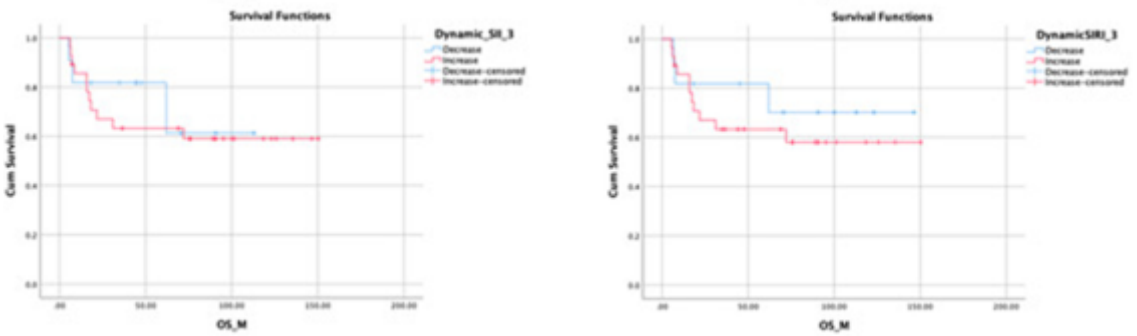
Table 4 summarizes the average readings of the inflammatory biomarkers SIRI, PLR, SII, NLR, and PNI collected at baseline, at three months post-treatment, and at six months post-treatment, categorized according to sex, ethnicity, smoking and drinking history, primary tumor site, HPV status, histological grade, AJCC stage (both 7th and 8th editions), treatment intent, main intervention, adjuvant modality, surgical margin outcome, recurrence status, site of recurrence, and mortality. Based on these findings, it was established that both baseline SIRI and albumin concentrations had positive predictive values for locoregional recurrence (P = 0.031 and P = 0.039, respectively). Levels of NLR, SII, and SIRI measured three months after the end of therapy were likewise positive predictors of locoregional recurrence (P = 0.005, P < 0.0005, and P = 0.007), together with SIRI recorded at the six-month post-therapy follow-up (P = 0.008). In addition, SII, assessed 6 months after completing treatment, was positively associated with overall survival (P = 0.027). The survival-related data are illustrated in **Figures 1-4** as Kaplan–Meier plots. A general pattern of better survival corresponded to decreasing concentrations of inflammatory biomarkers on these curves. Despite this, the sole marker to retain significance within the Cox proportional hazards framework was the six-month post-treatment SII value (P = 0.027).



a)

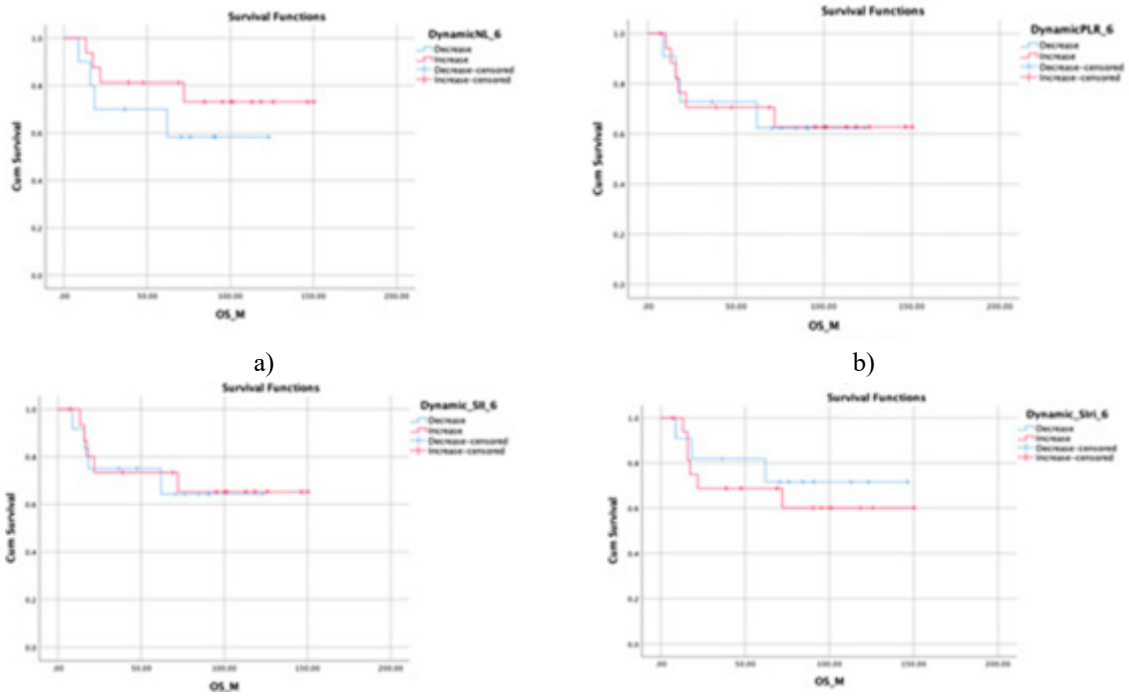


b)



c) d)

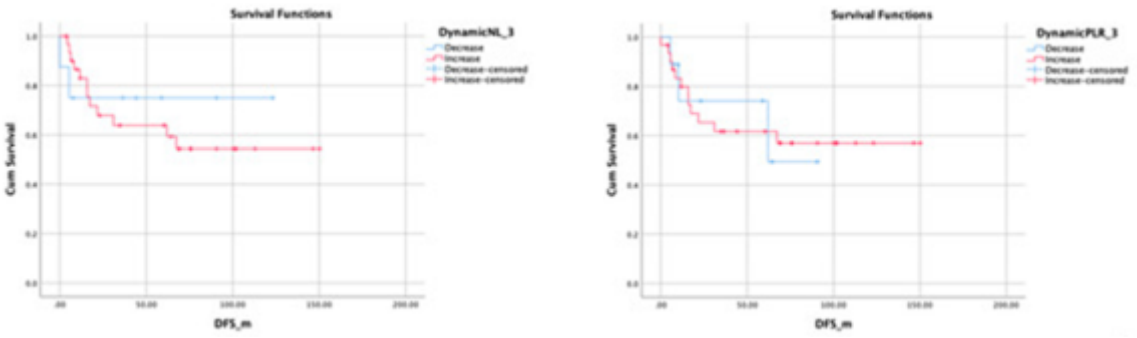
Figure 1. Kaplan–Meier curves showing overall survival by the three-month changes in the relevant inflammatory markers. Improved survival is associated with reduced levels of these inflammatory markers.



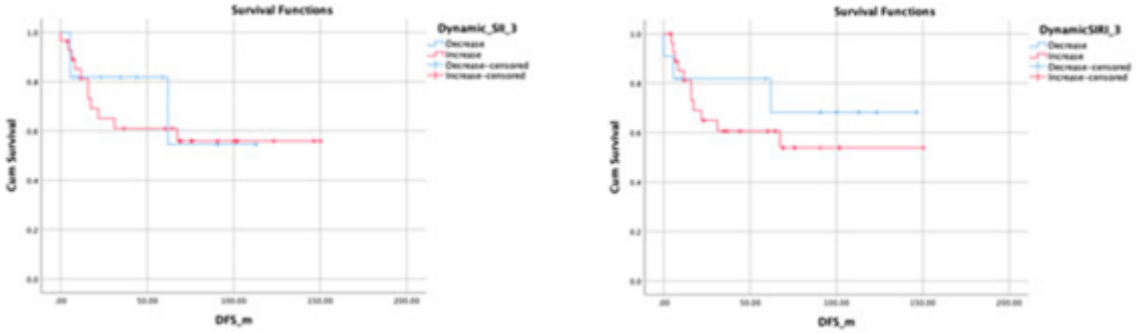
a) b)

c) d)

Figure 2. Kaplan–Meier graphs illustrating overall survival outcomes in association with changes in inflammatory markers at 6 months.

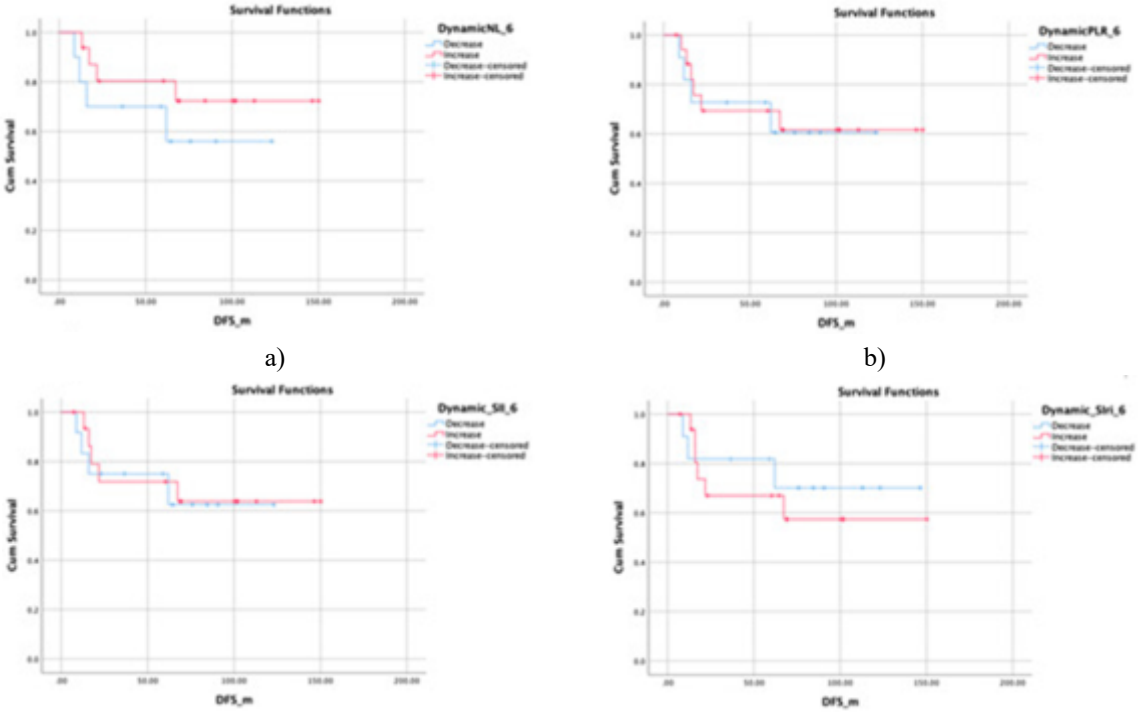


a) b)



c) d)

Figure 3. Kaplan–Meier curves showing disease-free survival by changes in the three-month inflammatory markers.



a) b)

c) d)

Figure 4. Kaplan-Meier curves of disease-free survival outcomes associated with changes in the relevant inflammatory markers at 6 months.

Table 4. Pre-treatment and post-treatment values of SIRI, PLR, SII, NLR, and PNI.

		SIRI			PLR			SII			NLR			PNI
		Pre-treatment	3 months	6 months	Pre-treatment	3 Months	6 Months	Pre-Treatment	3 Months	6 Months	Pre-Treatment	3 Months	6 Months	Pre-treatment
Sex	Male	24.02	45.60	32.49	97.68	256.11	201.77	1199.37	2768.84	2382.91	4.78	10.47	9.38	25.50
	Female	25.70	19.39	29.83	192.44	242.84	112.38	2361.78	1764.03	1145.61	7.87	6.17	5.07	25.58
Ethnicity	Caucasian	24.29	40.86	33.25	117.49	275.14	199.92	1374.44	2443.75	2332.70	5.32	8.96	9.25	27.33
	Black	24.04	33.07	26.87	13.36	8.48	5.97	871.19	550.10	390.07	2.60	3.09	2.89	22.73
	Hispanic	24.99	42.58	18.26	154.50	85.49	73.23	2156.84	4238.48	737.31	7.51	17.67	2.89	12.33
Smoking	No	26.14	58.19	29.57	74.50	154.08	130.45	1497.93	2463.81	2380.28	5.79	12.52	12.15	24.69

	Age ≤ 60	42.67	24.07	22.30	81.93	258.79	88.04	1585.58	2757.72	916.68	6.74	9.56	4.11	25.35
	Age > 60	19.21	34.96	34.54	143.63	304.79	229.24	1326.05	2626.25	2229.28	4.80	8.33	7.39	26.25
Alcohol	No Alcohol	29.23	60.87	43.60	57.79	158.41	86.25	1398.34	2733.73	1434.51	5.71	11.04	5.92	23.21
	Social	29.05	28.94	20.11	137.16	252.52	266.81	1334.03	2210.38	3598.18	5.31	9.34	13.77	25.35
	Heavy	13.58	18.39	26.73	168.58	445.44	259.73	1501.55	2824.19	1894.26	4.91	7.65	7.76	30.94
Location Of Tumor	Tonsil	17.00	37.12	33.24	66.70	198.38	117.00	763.31	1661.65	1130.60	3.18	7.50	5.47	23.86
	BOT	15.50	38.36	30.87	126.10	189.46	192.35	1025.94	2126.21	2825.55	3.87	9.30	10.56	26.54
	Soft Palate	40.46	25.33	28.89	67.00	338.34	7.28	1313.13	2055.45	488.15	6.47	10.56	3.28	22.04
	Pharyngeal wall	35.99	99.31	31.37	194.31	312.01	278.25	3489.36	8285.52	1615.26	12.13	23.67	7.03	23.75
	Overlap	41.03	31.60	37.14	127.81	579.27	452.68	2169.05	3695.78	3532.29	7.75	8.11	13.72	27.27
Hpv	Positive	25.12	37.28	27.75	100.77	189.38	170.72	1376.81	1696.25	2285.45	5.73	7.02	9.28	28.01
	Negative	28.62	46.87	39.48	75.22	329.76	154.66	1256.59	3490.03	1538.60	5.06	12.24	6.39	23.51
	n/a	17.78	41.04	35.52	184.46	289.60	257.41	1658.75	3317.86	2538.07	5.26	12.12	9.39	24.51
Differentiation	Well	62.30	7.98	.3636	75.94	1392.63	155.45	2459.24	6017.02	310.91	9.15	4.50	1.82	32.03
	Moderate	28.71	37.46	29.44	116.78	103.07	187.14	1646.38	1495.39	3124.95	6.49	5.60	11.80	21.27
	Poor	18.73	50.83	41.57	95.20	252.88	154.50	1205.46	2881.12	1719.40	4.50	11.02	6.81	23.78
	Undiff	14.85	38.32	27.68	137.21	256.19	222.52	1081.09	2933.54	1596.62	3.95	13.13	7.11	30.79
Ajcc 7 Staging	T1	37.53	34.45	32.72	86.59	428.64	12.51	3057.45	2544.49	835.32	28.33	4.68	3.50	13.81
	T2	6.34	33.34	12.77	131.98	185.00	162.98	797.70	2251.12	682.30	3.52	8.58	3.99	28.33
	T3	29.58	46.59	44.46	97.09	163.27	125.39	1264.57	2156.40	2832.00	4.87	9.60	12.18	27.28
	T4	24.21	45.75	33.05	135.52	373.51	373.49	1527.93	3672.62	3256.58	5.28	14.23	10.07	26.79
	N0	29.75	23.77	32.89	95.57	522.64	113.56	1512.05	2870.39	6088.58	5.90	6.15	30.28	25.34
	N1	24.99	16.57	13.18	131.94	285.60	163.20	1712.47	1691.06	786.07	6.37	6.59	4.36	27.47
	N2a	11.54	44.93	33.54	99.86	94.17	235.17	795.79	1225.86	2370.51	3.42	5.92	6.35	18.52
	N2b	22.95	44.66	15.78	140.03	178.07	312.86	1392.75	3041.01	2016.61	5.11	14.69	7.60	25.04
	N2c	33.07	68.57	84.92	102.17	44.39	31.50	1579.58	2189.85	2529.08	5.55	7.49	9.09	29.87
	N3a	24.03	70.00	27.41	105.88	493.27	221.04	1314.31	6382.21	1580.05	4.93	20.30	7.14	30.37
	Nx	21.10	24.07	19.07	126.49	341.33	147.16	1439.00	1156.37	1025.47	6.86	4.75	5.03	17.86
	M0	20.98	29.86	33.77	117.54	298.81	202.49	1349.87	2026.73	1715.13	5.23	7.57	7.16	27.43
	M1	41.20	158.62	28.41	38.96	169.04	7.48	1013.05	9684.81	492.24	5.18	29.81	3.29	25.51
	Mx	26.06	62.22	27.73	144.46	71.39	169.99	1824.58	3421.94	3765.54	5.84	14.44	13.82	20.19
Ajcc 8 Staging	T1	37.54	34.45	32.72	86.59	428.64	12.51	3057.45	2544.49	835.32	11.98	4.68	3.50	13.81
	T2	6.34	33.34	12.77	131.98	185.00	162.98	797.70	2251.12	682.30	3.52	8.58	3.99	28.33
	T3	29.58	46.59	44.46	97.09	163.27	125.39	1264.57	2156.40	2832.00	4.87	9.60	12.18	27.28
	T4	24.21	45.75	33.05	135.52	373.51	373.49	1527.93	3672.62	3256.58	5.28	14.23	10.07	26.79
	N0	29.75	23.77	32.89	95.57	522.64	113.56	1512.05	2870.39	6088.58	5.90	6.15	30.28	25.34
	N1	12.50	15.07	14.19	220.35	355.47	252.51	1246.60	2009.14	1110.16	3.81	7.76	6.40	22.60
	N2a	10.41	47.67	41.52	64.33	91.21	153.71	1080.14	1444.49	1637.63	4.23	6.00	5.57	11.56
	N2b	25.59	60.31	11.15	128.07	221.06	652.08	1462.76	4558.55	4060.68	5.33	22.25	14.11	27.60
	N2c	29.68	56.42	104.46	152.48	58.29	44.35	1921.61	1916.73	3673.00	6.42	6.08	11.45	27.86
	N3a	36.28	195.58	60.44	22.42	261.00	35.23	1161.97	14,162.25	2927.39	4.39	40.45	9.44	28.22
	Nx	-	29.83	19.20	-	7.32	6.08	-	466.76	376.52	-	2.76	2.28	15.00
	N1	36.11	36.54	25.15	36.23	37.53	33.45	1834.10	820.64	551.32	7.84	4.25	2.65	24.25
	N2	19.85	43.06	32.35	125.45	126.61	213.07	818.66	1605.68	2157.33	3.27	6.74	6.41	29.43
	N3	3.62	28.14	19.15	244.98	570.70	267.49	1568.20	3788.86	1243.22	5.84	13.59	6.56	33.00
	N	21.10	21.19	18.95	126.49	508.33	288.23	1439.00	1501.17	1674.43	6.86	5.74	7.77	26.68
	M0	20.98	29.86	33.77	117.54	298.81	202.49	1349.87	2026.73	1715.13	5.23	7.57	7.16	27.43
	M1	41.20	158.62	28.41	38.96	169.04	7.48	1013.05	9684.81	492.24	5.18	29.81	3.29	25.51
	Mx	26.06	62.22	27.73	144.46	71.39	169.99	1824.58	3421.94	3765.54	5.84	14.44	13.82	20.19

Treatment Intent	Curative	24.51	42.30	32.07	106.10	249.51	187.40	1344.55	2523.72	2184.06	5.20	9.61	8.69	25.53
	Palliative	22.36	8.73	-	210.43	350.29	-	2145.17	4134.33	-	7.05	12.02	-	25.32
Primary Treatment	Chemoradiation	24.96	40.97	32.85	130.96	278.00	236.48	1648.40	3098.54	2966.08	6.22	11.13	11.34	29.40
	Surgery	22.23	41.90	31.29	102.16	236.28	138.33	1200.21	2214.22	1402.03	4.36	8.72	6.03	22.71
	RT	53.70	-	-	11.82	-	-	884.54	-	-	6.13	-	-	22.03
	Chemo	16.19	0.80	-	114.40	140.95	-	974.36	456.69	-	4.28	1.54	-	38.55
Adjuvant Treatment	None	25.63	32.91	33.86	122.93	253.69	239.40	1644.82	2119.68	3056.96	6.16	8.13	11.69	27.65
	CRT	20.38	43.03	32.00	113.75	248.34	143.20	1202.04	2309.15	1438.63	4.25	9.05	6.18	20.54
	Surgery	62.15	140.38	16.71	112.51	244.76	9.13	1844.93	10,391.99	506.74	9.73	31.90	1.86	40.56
	RT	30.63	23.79	-	13.60	425.88	-	1009.05	4091.68	-	4.38	16.67	-	37.33
	Chemotherapy	2.45	1.53	1.04	133.02	213.35	155.38	707.88	1638.09	419.54	3.08	5.80	2.08	40.27
Margin	Negative	24.52	23.77	19.02	99.02	318.56	168.88	1150.93	1367.67	895.73	4.17	5.41	4.26	31.32
	n/a	24.45	55.13	41.95	122.66	161.32	171.17	1571.42	3133.41	2847.21	5.85	12.33	10.97	25.28
	Positive	23.92	25.02	21.55	106.02	383.01	225.86	1203.28	2252.86	1695.84	4.96	7.32	7.01	22.68
Recurrence	No	14.73	30.17	30.93	113.48	164.98	191.79	1044.07	1227.30	2267.51	4.17	6.17	9.06	27.74
	Yes	28.79	48.27	18.99	167.81	500.54	210.18	1468.14	4531.35	1222.10	5.21	15.03	5.91	28.12
	n/a	36.86	118.27	91.94	72.02	201.41	48.68	1990.49	8565.98	4194.39	7.48	24.14	12.66	20.16
Location Of Recurrence *	Primary Site	21.85	38.79	26.04	252.40	437.04	98.01	1322.54	3557.62	909.84	3.95	10.47	4.48	27.72
	Neck	55.07	61.77	32.67	19.19	57.32	11.62	1427.66	1354.85	775.20	5.86	7.33	3.36	26.98
	Both	4.02	62.65	4.94	240.94	839.74	380.83	1603.75	7847.63	1913.25	5.97	25.04	8.38	24.51
	n/a	33.52	13.02	19.85	21.38	244.35	241.36	1676.14	1959.92	1070.04	5.41	8.15	6.68	41.02
Death **	Yes	28.84	54.42	42.70	143.79	342.88	255.44	1650.57	3726.64	4025.86	5.97	13.53	15.00	25.79
	No	21.40	33.45	26.61	95.24	205.23	152.47	1256.99	1961.08	1238.27	4.95	7.60	5.44	25.38
Death Of Disease	Yes	29.72	32.11	18.70	205.28	600.45	392.34	1857.69	5031.72	3361.56	6.34	16.03	7.73	32.61
	No	27.96	76.73	56.69	77.90	85.32	175.58	1443.46	2421.55	4413.37	5.60	11.03	19.25	20.07

Abbreviations: SIRI: Systemic Inflammatory Response Index, PLR: Platelet-to-Lymphocyte Ratio, SII: Systemic Immune-Inflammation Index, NLR: Neutrophil-to-Lymphocyte Ratio, PNI: Prognostic Nutritional Index, AJCC: American Joint Committee on Cancer; notable significance emerged for baseline SIRI, the three-month post-therapy NLR, SII, and SIRI measurements, and the SIRI value at the six-month post-treatment follow-up; significance was also detected for the SII level collected six months after treatment.

The central purpose of this retrospective analysis was to examine the impact of the inflammatory indices—SIRI, PLR, SII, NLR, and PNI—on predicting outcomes in head and neck cancer. The scientific record contains ample documentation of these markers in relation to both the emergence of cancer and its subsequent course [1, 2, 8]. Even so, a unified consensus surrounding their precise function in head and neck malignancy has not yet formed [17]. Among the other well-validated determinants of outcome in this disease category are TNM (Tumor, Node, Metastasis) classification and HPV-positive disease [18].

To compute SIRI, one multiplies the absolute neutrophil count by the ratio of monocytes to lymphocytes [12]. Published data have identified SIRI as a standalone predictor of disease-specific survival in head and neck squamous cell carcinoma [12]. The same index was also found to anticipate local, regional, and distant recurrence-free survival [12], and it is considered a meaningful prognostic instrument in head and neck tumors [18]. Consistent with this, our results regarding SIRI were particularly compelling for locoregional failure. Pre-treatment SIRI was positively predictive of locoregional recurrence (P = 0.031). At the three-month post-treatment interval, SIRI again demonstrated positive predictive capacity for locoregional recurrence (P = 0.007). Finally, this pattern persisted for SIRI collected six months after therapy, which also maintained positive predictive value for locoregional relapse (p = 0.008). These observations align with previously published work showing that baseline SIRI concentrations foretell local and regional recurrence-free survival [12]. The current investigation extends those earlier contributions by confirming that SIRI readings taken at both three-month and six-month landmarks following treatment remain significantly associated with locoregional recurrence.

The formula underpinning SII multiplies the platelet count by the neutrophil-to-lymphocyte ratio [19]. Investigators have deployed this metric as a predictor of prognosis in a spectrum of malignancies, among them cervical, colorectal, bladder, pulmonary, and

hepatic cancers [19]. In head and neck cancer, an elevated SII before initiating treatment has been connected to shorter overall survival and more advanced disease burden [12]. Our dataset did not yield a meaningful signal regarding the prognostic utility of pre-treatment SII. That said, statistically significant relationships emerged when we evaluated post-treatment levels: the three-month value was associated with recurrence ($p < 0.0005$), and the six-month value was associated with survival ($P = 0.027$).

NLR, denoting the ratio of neutrophils to lymphocytes, and PLR, indicating the platelet-to-lymphocyte ratio, are surrogates of the inflammatory state that have repeatedly shown prognostic relevance across numerous cancer types [20]. Superior pre-treatment PLR and NLR results are linked with worse survivorship in pancreatic, gastrointestinal, bladder, and ovarian malignancies [20]. In the head and neck cancer population, higher baseline PLR and NLR levels correspond to inferior survival regardless of the chosen therapeutic route, be it surgical or chemotherapeutic [20]. In our evaluation, NLR readings secured three months after treatment were also positively predictive of locoregional recurrence ($P = 0.005$). We did not detect statistical relevance for baseline NLR, which diverges from the primary emphasis of much of the current body of research. However, we observed the relevance of post-treatment NLR at the three-month juncture. Of note, our analysis revealed no significant relationships for PLR at either the pre-treatment or post-treatment time points.

Finally, the prognostic nutritional index (PNI) is derived from serum albumin and the total count of circulating lymphocytes [21]. A depressed PNI has been correlated with worse overall survival in esophageal cancer cohorts [21]. Further evidence indicates that a low PNI bears a significant association with poorer overall survival in head and neck cancer. However, it did not emerge as a meaningful marker for disease-specific survival [22].

Several limitations temper the interpretation of this study. Its design is that of a single-center retrospective record review encompassing only 172 subjects. The sample lacked sufficient statistical power to detect significance for pre-treatment levels of various inflammatory indices in relation to locoregional recurrence and overall survival. Notwithstanding these constraints, this work constitutes a meaningful contribution to the published literature, demonstrating the utility of post-treatment inflammatory marker concentrations as indicators of prognosis and recurrence in head and neck cancer.

The present study advances the existing literature by demonstrating how inflammatory indices can inform prognosis in head and neck cancer. While a large share of previous investigations has emphasized pre-treatment marker levels, this project is distinct in that it scrutinized both pre-treatment and post-treatment values at defined intervals of three and six months. It further illustrates the application of these indices in appraising the risk of locoregional tumor reappearance in head and neck cancer. According to our findings, SIRI collected at both three and six months after treatment, together with NLR and SII measured at the three-month mark, proved capable of forecasting locoregional recurrence. Separately, SII was the only inflammatory index to show a significant association between post-treatment levels and overall survival. In summary, we have specifically highlighted the potential importance of post-treatment inflammatory markers as prognostic and locoregional indicators for head and neck cancer.

Conclusion

This investigation suggests that post-treatment concentrations of a select group of inflammatory indices—SIRI, NLR, and SII chief among them—may serve a practical role in estimating the long-term trajectory and recurrence risk of head and neck cancer following therapeutic intervention. More specifically, SIRI recorded at both the three- and six-month post-treatment time points, as well as NLR and SII obtained at the three-month milestone, were shown to predict locoregional recurrence. Beyond that, SII was the only inflammatory index to show a significant association between post-treatment levels and overall survival. These insights build on a foundational literature that has primarily focused on pre-treatment index values and their relationship to overall survival prognosis. The work further underscores the necessity for forthcoming studies to delve more deeply into how post-treatment inflammatory index levels shape the likelihood of future recurrence and influence the broader prognosis of head and neck cancer.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: This study was exempt from formal IRB review by the Institutional Review Board for the protection of human subjects at Texas Tech Health Science Center, Lubbock/Odessa IRB. IRB number:

L20-102. This research meets the criteria for exemption from formal review by the IRB, in accordance with 45 CFR 46.104(d)(4)(iii). The investigator has provided the information required to make this determination. A waiver of individual HIPAA authorization has been requested and found to be appropriate. This application was screened for exempt status in accordance with TTUHSC policies and applicable federal regulations. The study was found not to require formal IRB review because it falls into one of the categories specifically designated as exempt under 45 CFR 46.104(d).

References

1. Nøst TH, Alcala K, Urbarova I, Byrne KS, Guida F, Sandanger TM, et al. Systemic inflammation markers and cancer incidence in the UK Biobank. Eur J Epidemiol. 2021;36:841-8.
2. Diakos CI, Charles KA, McMillan DC, Clarke SJ. Cancer-related inflammation and treatment effectiveness. Lancet Oncol. 2014;15:e493-e503.
3. Templeton AJ, McNamara MG, Šeruga B, Vera-Badillo FE, Aneja P, Ocaña A, et al. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst. 2014;106:dju124.
4. Lin N, Li J, Yao X, Zhang X, Liu G, Zhang Z, et al. Prognostic value of neutrophil-to-lymphocyte ratio in colorectal cancer liver metastasis: a meta-analysis of results from multivariate analysis. Int J Surg. 2022;107:106959.
5. Miyamoto R, Inagawa S, Sano N, Tadano S, Adachi S, Yamamoto M. The neutrophil-to-lymphocyte ratio (NLR) predicts short-term and long-term outcomes in gastric cancer patients. Eur J Surg Oncol. 2018;44:607-12.
6. Schobert IT, Savic LJ, Chapiro J, Bousabarah K, Chen E, Laage-Gaupp F, et al. Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios as predictors of tumor response in hepatocellular carcinoma after DEB-TACE. Eur Radiol. 2020;30:5663-73.
7. Ferrandino RM, Roof S, Garneau J, Haidar Y, Bates SE, Park YHA, et al. Neutrophil-to-lymphocyte ratio as a prognostic indicator for overall and cancer-specific survival in squamous cell carcinoma of the head and neck. Head Neck. 2020;42:2830-40.
8. Li B, Zhou P, Liu Y, Wei H, Yang X, Chen T, et al. Platelet-to-lymphocyte ratio in advanced cancer: review and meta-analysis. Clin Chim Acta. 2018;483:48-56.
9. Zhang F, Gong W. Prognostic value of the platelet-to-lymphocyte ratio in patients with melanoma: a meta-analysis. Front Oncol. 2020;10:1116.
10. Sun L, Hu W, Liu M, Chen Y, Jin B, Xu H, et al. High systemic inflammation response index (SIRI) indicates poor outcome in gallbladder cancer patients with surgical resection: a single institution experience in China. Cancer Res Treat. 2020;52:1199-210.
11. Xu Y, He H, Zang Y, Yu Z, Hu H, Cui J, et al. Systemic inflammation response index (SIRI) as a novel biomarker in patients with rheumatoid arthritis: a multi-center retrospective study. Clin Rheumatol. 2022;41:1989-2000.
12. Valero C, Pardo L, Sansa A, Lorenzo JG, López M, Quer M, et al. Prognostic capacity of systemic inflammation response index (SIRI) in patients with head and neck squamous cell carcinoma. Head Neck. 2020;42:336-43.
13. Tian BW, Yang YF, Yang CC, Yan LJ, Ding ZN, Liu H, et al. Systemic immune-inflammation index predicts prognosis of cancer immunotherapy: systematic review and meta-analysis. Immunotherapy. 2022;14:1481-96.
14. Li J, Cao D, Huang Y, Xiong Q, Tan D, Liu L, et al. The prognostic and clinicopathological significance of systemic immune-inflammation index in bladder cancer. Front Immunol. 2022;13:865643.
15. Liu J, Li S, Zhang S, Liu Y, Ma L, Zhu J, et al. Systemic immune-inflammation index, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio can predict clinical outcomes in patients with metastatic non-small-cell lung cancer treated with nivolumab. J Clin Lab Anal. 2019;33:e22964.
16. Bosetti C, Carioli G, Santucci C, Bertuccio P, Gallus S, Garavello W, et al. Global trends in oral and pharyngeal cancer incidence and mortality. Int J Cancer. 2020;147:1040-9.
17. Yamahara K, Mizukoshi A, Lee K, Ikegami S. Pretherapeutic nutritional/inflammatory factors as predictors for survival of both early and advanced staged head and neck cancer patients. Auris Nasus Larynx. 2021;48:731-7.
18. Bossi P. Prognostic nutritional index: an easy nutritional screening for patients with head and neck cancer? ESMO Open. 2018;3:e000449.
19. Wang YT, Kuo LT, Weng HH, Hsu CM, Tsai MS, Chang GH, et al. Systemic immune-inflammation index as a predictor for head and neck cancer prognosis: a meta-analysis. Front Oncol. 2022;12:899518.

20. Abelardo E, Davies G, Kamhieh Y, Prabhu V. Are inflammatory markers significant prognostic factors for head and neck cancer patients? ORL J Otorhinolaryngol Relat Spec. 2020;82:235-44.
21. Okadome K, Baba Y, Yagi T, Kiyozumi Y, Ishimoto TM, Iwatsuki MM, et al. Prognostic nutritional index, tumor-infiltrating lymphocytes, and prognosis in patients with esophageal cancer. Ann Surg. 2020;271:693-700.
22. Atasever Akkas E, Erdis E, Yucel B. Prognostic value of the systemic immune-inflammation index, systemic inflammation response index, and prognostic nutritional index in head and neck cancer. Eur Arch Otorhinolaryngol. 2023;280:3821-30.