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Oral Pathology

Preoperative platelet lymphocyte ratio is superior to neutrophil lymphocyte ratio to be used as predictive marker for lymph node metastasis in oral squamous cell carcinoma

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Abstract

Objective: To assess whether the neutophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) before complete surgical staging will provide information on lymph node metastasis (LNM) in oral squamous cell carcinoma (OSCC) patients and to evaluate the relation of NLR and PLR with the various clinicopathologic characteristics.

Methods: The clinicopathological data and the preoperative complete blood investigation details were obtained from 68 OSCC patients who underwent surgical treatment. Receiver operating characteristics (ROC) curve analysis was used to evaluate cut-off, sensitivity, and specificity values for preoperative NLR and PLR in order to predict LNM.

Results: Lymph node involvement was detected in 24 (35%) patients. The best cut-off value for predicting LNM was 128.5 for the PLR, with 75% sensitivity and 70.45% specificity ($P < 0.05$). Fifty-five percent of patients had PLR $\leq$ 128.5 and 45% had PLR > 128.5. The PLR was higher in the lymph-node-positive group than in the negative group (147.63 ± 35.49 vs. 120.51 ± 42.5) ($P < 0.05$). There was an association between PLR cut-off and tumor stage. The best cut-off value for predicting LNM was 1.77 for NLR, with sensitivity of 87.5% and 25% specificity ($P = 0.92$).

Conclusion: Preoperative PLR is directly associated with nodal involvement status of OSCC. Preoperative PLR is superior to NLR for predicting LNM in OSCC.

Introduction

Squamous cell carcinomas (SCC) encompass at least 90% of all oral malignancies. The SCC of the head and neck grows locally and then it spreads to the lymph nodes of the neck.[1] Surgical treatment of these tumors includes local resection and neck dissection.[2] The therapeutic modality currently offered to OSCC patients is based on traditional stage-predicting indices (based mostly on the TNM criteria) and on histological grading. Unfortunately, these predictors are subjective and relatively unreliable, as two tumors with identical staging and grading often behave very differently.[3] Most decisions for cancer patients are now made on the basis of prognostic and predictive factors.[4] Neck metastasis has been considered one of the most significant prognostic factors in head and neck cancers.[5] The presence, number, volume, and extra-nodal spread of cervical lymph nodes reduce local control and overall survival in patients with advanced cancer of the head and neck region. Various tumor markers have been used in this patient group in the past. Despite the high cost of each laboratory investigation, the sensitivity

of the studied markers was low.[6] The assessment of neck metastasis is an unresolved issue as yet. No clinical exploration or imaging techniques are able to show micrometastasis in neck nodes.[2] Most prognostic factors are obtained only by surgical exploration and a subsequent histologic examination. However, before surgery, there is no reliable, critical marker that provides accurate data regarding the likelihood of regional metastasis, postoperative adjuvant therapy, and prognosis.[7]

The use of biomarkers could help to avoid the unnecessary surgical treatment of metastasis free patients. Several proteins and genes are candidates for use as predictors of metastasis due to the heterogeneity of the tumor cells. Some studies have tried to relate the expression of proteins in the primary tumors with occurrence of metastasis; many key proteins have been recognized.[8] Identification of a four-protein signature from the primary tumor that is indicative of lymph node metastasis (LNM) has been described in the literature.[9] Even gene signatures predicting LNM and survival have been identified through microarray analysis. They currently have limited use in the clinical setting because the methods used to identify these cannot, or are difficult, to be performed routinely in the diagnostic setting.[9]

Prognostic stratification in SCC of the head and neck has traditionally relied on the pathological staging of a tumor, but it is increasingly being recognized that host-related factors, particularly the systemic inflammatory response (SIR), have an important role in the assessment of survival and recurrence.[10] Recently, there is increasing evidence that a SIR is of prognostic value in various types of cancers.[11,12]

Inflammation is a critical component in the pathogenesis as well as in the progression of cancer. Leukocyte migration plays a pivotal role in physiological immune responses to the neoplastic process. The inflammatory response involves systemic alterations triggered by circulating cytokines and chemokines, such as an increase in neutrophil counts, a slight increase in platelet counts, and a decline in lymphocyte counts. These hematological changes have been suggested to be cornerstone events in the growth, progression, and spread of tumors.[13] The SIR is deemed to reflect both disease activity as well as the host's innate response towards the tumor. It can be readily and reproducibly quantified in patients using a number of prognostic indices such as the neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR), both derived from inflammation-induced derangements in the full blood count.[14] Elevated NLR and PLR are gaining interest as SIR markers in various clinical circumstances.[13] Recent clinical studies have investigated these ratios as advanced-stage predictors or prognostic factors in different types of human cancer,[13] but study of the predictive value of NLR and/or PLR for LNM in patients with OSCC has been not reported in the English-language literature. There is a paucity of data with regards to the prognostic influence of the SIR in head and neck cancers.[15] Hence, the aim of this study was to investigate whether preoperative NLR and PLR can be used as predictive markers for LNM in patients undergoing complete surgical staging for OSCC.

Methods

The databases of the Department of Oral Pathology, Oral Surgery and Craniofacial Unit (CFU) of our institution were reviewed to identify patients with pathologically proven OSCC who underwent complete surgical staging between 2011 and 2014. The study was carried out in accordance with the ethical standards of the Helsinki Declaration, and was approved by the ethics and Institutional Review Board (IRB) committee of this institution (IRB No. 2015/S/OP/32).

Retrospective clinicopathological data, including age, gender, tumor location, extension, type of lesion, tumor size, and tumor–node–metastasis (TNM) staging was recorded in case notes according to the American Joint Committee on Cancer (AJCC) classification 2002 edition. Histopathological grade, number of excised and positive lymph nodes, surgical margins, recurrence, and preoperative complete blood cell counts (CBCs) were retrieved from the original medical records. All the baseline blood parameters were tested within 1 week preoperatively using Sysmex, automated hematology analyzer, pocH-100i (Sysmex Corporation, Kobe, Japan) at the clinical hematology laboratory at the CFU. The NLR was defined as the absolute neutrophil count divided by the absolute lymphocyte count, and the PLR was defined as the absolute platelet count divided by the absolute lymphocyte count.[13] Results recorded were subjected to statistical analysis.

The exclusion criteria were cases of oral malignancy other than OSCC; patients who underwent preoperative chemoradiotherapy or those with clinical evidence of infection or inflammation that would acutely or chronically evoke a systemic inflammatory response; patients with any hematological disease, or other malignancy that could affect the CBC results; those who used corticosteroids or β-agonists; and patients with missing preoperative data on markers of systemic inflammation. The diagnosis of SCC was made by an incision biopsy of the oral lesion. All patients were treated with surgical excision of the lesion and radical neck dissection; the histopathology details were obtained from the departmental data base.

MedCalc Version 9.3 (MedCalc Software, Ostend, Belgium) was used for statistical analyses. Data are presented

as means ± standard deviations and percentages. The normality of continuous variable distributions was assessed using the Kolmogorov–Smirnov test. The chi-squared test was used to analyze categorical variables, Student's *t*-test was used for normally distributed variables, and the Mann–Whitney *U*-test was used for variables that were not normally distributed. Receiver operating characteristics (ROC) curve analysis was used to evaluate the cut-off, sensitivity, and specificity values. The ROCs were used to determine the best NLR and PLR values that yielded the optimal predictive values for determining lymph node status. A *P*-value of <0.05 was considered to indicate statistical significance.

Results

One hundred six patients with OSCC who underwent complete staging surgery between 2011 and 2014 were identified. Thirty-eight patients did not meet the study inclusion criteria and were excluded. Thus, the analysis included a total of 68 patients treated in the CFU of our institution. Patients' mean age was 48.75 ± 14.07 years, with an age range from 25 to 75 years. Tumors of 2 cm or less in greatest dimension were noted in 12 cases, tumors more than 2 cm but <4 cm in greatest dimension were noted in 37 cases, that is, 72% (49/68) were <4 cm. Tumors more than 4 cm in greatest dimension were noted in 19 cases (28%).

Thirty-three (49%) patients had early stage disease and 35 (51%) were in the advanced stage. Lymph node involvement was detected in 24 (35%) patients. A total of 459 lymph nodes were analysed in 68 OSCC cases treated with surgical excision and neck dissection. One hundred and seventy-six lymph nodes were removed and assessed in 24 OSCC cases with nodal metastasis and 283 nodes were screened in 44 OSCC cases without nodal metastasis. Table 1 shows the clinical characteristics of the patients. Eighty two percent of the patients were males. Fifty-nine percent of patients were >45 years. Buccal mucosa was the most commonly involved site at about 76%. Sixty-six percent of patients had the lesion involving a single site, whereas 34% had the lesion extending to involve multiple sites. Seventy-five percent of tumors were exophytic and 76% were well differentiated. Only 3% (2/68) of cases showed local recurrence. One was a stage IV lesion, involving multiple sites with the nodal metastasis and another retromolar, stage II lesion without LNM.

Patient characteristics according to lymph node involvement are depicted in Tables 2 and 3. The mean age was similar. There was an association between lymph node status and tumor extension. In the single site tumors, 20 cases (83%) exhibited LNM, whereas 25 cases (57%) did not. However, in the multiple site tumors, only four cases (17%) showed LNM and 19 cases (43%) did not ($P < 0.05$). Other parameters like age, gender, tumor location, type, size, stage, and grading did not show an association with lymph node status. Mean PLR was higher in the lymph node positive group than in the negative group. There was significant difference between means in the case of PLR between the lymph node positive and negative groups only (<0.05).

The ROC findings indicating the utility of the NLR and PLR as predictive markers for LNM in OSCC are shown in Figure 1 and Table 4. The NLR range was 1.3–5.21 in the present study. The patients were divided into two groups according to the NLR cut-off values (Table 5). Fourteen (21%) patients with OSCC had NLR ≤1.77 and 54 (79%) had NLR > 1.77. None of the clinicopathologic features have shown an association with NLR cut-off.

Patient characteristics according to the PLR are listed in Table 6. The PLR range was 68.2–229.5 in the present study. Thirty-seven (54%) patients with OSCC had PLR ≤ 128.5 and 31 (46%) had PLR > 128.5. There was an association between PLR cut-off values and lymph node status ($P < 0.05$). The rate of lymph node involvement was higher in the PLR > 128.5 group than

Table 1. Clinical characteristics of the study population

Parameters	Category	No of cases	% of cases
Gender	Male	56	82
	Female	12	18
Age	≤45 years	28	41
	>45 years	40	59
Tumor location	Buccal mucosa	52	76
	Tongue	14	21
	Gingiva	2	3
Tumor extension	Single site†	45	66
	Multiple multiple‡	23	34
Tumor type	Exophytic	51	75
	Endophytic	17	25
Tumor size	1 + 2 (<4 cm)	49	72
	3 + 4 (>4 cm)	19	28
Tumor stage	Early	33	49
	Advanced	35	51
Broder's grading	Well differentiated	52	76
	Moderate differentiated	16	24
Lymph node metastasis	Positive	24	35
	Negative	44	65
Lymph node with ECS	Positive	17	25
	Negative	51	75
Surgical margins	Positive	6	9
	Negative	62	91
Recurrence	Yes	2	3
	No	66	97

†Tumor involving only single intraoral site.
‡Tumor extending and involving adjacent intraoral sites.

Table 2. Comparative analyses of clinicopathologic characteristics in oral squamous cell carcinoma patients with and without lymph node metastasis

Parameters	Category	OSCC patients (%) LN Positive *n* = 24	LN Negative *n* = 44	*P*-value
Gender†	Male	6 (25)	6 (14)	0.240
	Female	18 (75)	38 (86)	
Age‡	Mean ± SD	50.12 ± 12.06	48.00 ± 13.3	0.519
Tumor location†	Buccal mucosa	15 (63)	37 (84)	0.131
	Tongue	8 (33)	6 (14)	
	Gingiva	1 (4)	1 (2)	
Tumor extension†	Single site	20 (83)	25 (57)	**0.027**
	Multiple site	4 (17)	19 (43)	
Tumor type †	Exophytic	18 (75)	33 (75)	1.000
	Endophytic	6 (25)	11 (25)	
Tumor size†	1 + 2 (<4 cm)	18 (75)	31 (70)	0.690
	3 + 4 (>4 cm)	6 (25)	13 (30)	
Tumor stage†	Early stage	8 (33)	25 (57)	0.064
	Advanced stage	16 (67)	19 (43)	
Broder's grading†	Well differentiated	21 (88)	31 (70)	0.113
	Moderate differentiated	3 (12)	13 (30)	

†Chi-square test.
‡*t*-test.

Table 3. Patient characteristics according to lymph node involvement

Characteristics	LN Positive (*n* = 24)	LN Negative (*n* = 44)	*P*-value
Hemoglobin†	12.80 ± 1.6	13.65 ± 1.7	0.052
Total WBC count‡	7879.16 ± 2180.94	8660.22 ± 3022.02	0.453
Absolute neutrophil‡	5184.95 ± 1483.73	5829.36 ± 2479.10	0.500
Neutrophil§·¶ <6000/≥6000	17/7	29/15	0.678
Absolute Lymphocyte‡	2197.5 ± 633.45	2481.56 ± 866.53	0.110
Lymphocyte count§·¶ <2100/≥2100	13/11	19/25	0.386
NLR‡	2.28 ± 0.47	2.37 ± 0.76	0.928
Absolute Eosinophil‡	285.16 ± 168.51	303.75 ± 256.25	0.898
Eosinophil count§·¶ <200/≥200	10/14	17/27	0.807
Platelets‡	3.11 ± 0.74	2.80 ± 0.74	0.061
PLR†	147.63 ± 35.49	120.51 ± 42.5	**0.010**

†*t*-test.
‡Chi-square test.
§Mann–Whitney *U* test.
¶Cells/mm^3.

in the PLR ≤ 128.5 (58% vs. 16%; $P = 0.000$). Of the lymph node positive cases, 18 out of 24 were had a PLR > 128.5. In the lymph node negative group, 31 out of 44 cases were had a PLR ≤ 128.5. There was an association between PLR cut-off and tumor stage. Advanced stage patients were more likely to be in the PLR > 128.5 group than in PLR ≤ 128.5 group (65% vs. 41%). Early stage patients were more likely to be in the PLR ≤ 128.5 group than in PLR > 128.5 (59% vs. 35%) ($P < 0.05$).

Discussion

Systemic inflammatory responses are associated with alterations in circulating white blood cell counts, with neutrophilia and relative lymphopenia.[15] The NLR, a biomarker of the host systemic inflammatory response, has been shown to be highly promising in stratifying outcome in large cohorts of patients with cancers arising from unselected sites, with a higher pretreatment ratio associated with a poorer prognosis. Despite the heterogeneous nature

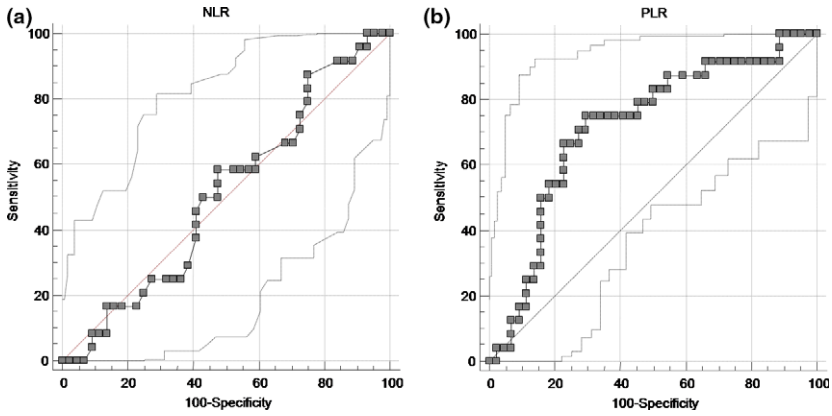

Figure 1. Receiver operating characteristic (ROC) for (a) the neutrophil: lymphocyte ratio (NLR) and (b) platelet: lymphocyte ratio (PLR) used to make the clinical decision regarding lymph node metastasis. The areas under curves were 0.51 and 0.72, respectively.

Table 4. Area under the curve and cut –off values obtained in receiver operating characteristic curve analysis

Variable	Cut –off value	Sensitivity	Specificity	AUC	*P*-value
NLR	1.77	87.5%	25%	0.51	0.9270
PLR	128.5	75%	70.45%	0.72	**0.0010**

of the studies performed, the NLR has a consistent prognostic impact, suggesting an association with more aggressive tumor biology. Other components of the SIR, including platelet counts, albumin, and C-reactive protein (CRP) levels, are prognostically important in some studies.[16] The PLR is prognostically important in some tumor sites.[17] The NLR and PLR are potentially interesting and effective markers of SIR that can be readily calculated from data obtained using a basic CBC test. The importance of these as prognostic indicators is increasing with evidence reported from cancer studies. Several human studies have demonstrated that preoperatively increased NLR and/or PLR are significantly associated with advanced stage disease and are significant prognostic predictors in cancers such as breast, lung, pancreas, colorectal, renal cell, and in gynecologic cancers including ovarian, cervix, and endometrium.[13,18] A raised PLR has shown a significant association with advanced stage disease in the present study. Rassouli *et al.*, in a study on systemic inflammatory

Table 5. Patient characteristics according to neutrophil: lymphocyte ratio (NLR)

Characteristics	Category	NLR ≤ 1.77 *n* = 14 (%)	NLR > 1.77 *n* = 54 (%)	*P*-value
Gender†	Male	13 (93)	43 (80)	0.247
	Female	1 (7)	11 (20)	
Age‡	Mean ± SD	53.00 ± 12.82	47.64 ± 12.77	0.167
Tumor location†	Buccal mucosa	12 (86)	40 (74)	0.590
	Tongue	2 (14)	12 (22)	
	Gingiva	0 (0)	2 (4)	
Tumor extension†	Single	9 (64)	36 (67)	0.902
	Multiple	5 (36)	18 (33)	
Tumor type†	Endophytic	3 (21)	14 (26)	0.729
	Exophytic	11 (79)	40 (74)	
Tumor size†	1 + 2 (<4 cm)	11 (79)	38 (70)	0.542
	3 + 4 (>4 cm)	3 (21)	16 (30)	
Tumor stage†	Early stage	7 (50)	26 (48)	1.000
	Advanced stage	7 (50)	28 (52)	
Broder's grading†	Well differentiated	11 (79)	41 (76)	0.835
	Moderate Differentiated	3 (21)	13 (24)	
Lymph node metastasis†	Positive	3 (21)	21 (39)	0.223
	Negative	11 (79)	33 (61)	
No. of nodes analysed§	*n*	95	364	0.637

†Chi-square test.
‡*t*-test.
§Mann–Whitney *U* test.

Table 6. Patient characteristics according to platelet: lymphocyte ratio (PLR)

Characteristics	Category	PLR ≤ 128.5 *n* = 37 (%)	PLR > 128.5 *n* = 31 (%)	*P*-value
Gender†	Male	31 (84)	25 (81)	0.735
	Female	6 (16)	6 (19)	
Age‡	Mean ± SD	48.48 ± 13.65	49.06 ± 12.08	0.661
Tumor location†	Buccal mucosa	31 (84)	21 (68)	0.157
	Tongue	6 (16)	8 (26)	
	Gingiva	0 (0)	2 (6)	
Tumor extension†	Single	24 (65)	21 (68)	0.803
	Multiple	13 (35)	10 (32)	
Tumor type†	Endophytic	7 (19)	10 (32)	0.206
	Exophytic	30 (81)	21 (68)	
Tumor size†	1 + 2 (<4 cm)	28 (76)	21 (68)	0.468
	3 + 4 (>4 cm)	9 (24)	10 (32)	
Tumor stage†	Early stage	22 (59)	11 (35)	**0.049**
	Advanced stage	15 (41)	20 (66)	
Broder's grading†	Well differentiated	28 (76)	24 (77)	0.866
	Moderate differentiated	9 (24)	7 (23)	
Lymph node metastasis†	Positive	6 (16)	18 (58)	**0.000**
	Negative	31 (84)	13 (42)	
No. of nodes analysed§	*n*	230	229	0.097

†Chi-square test.
‡*t*-test.
§Mann–Whitney *U* test.

markers in head and neck SCC, concluded that PLR is an independent predictor of mortality; with NLR as an independent predictor of recurrence in head and neck SCC. These parameters might be used to identify advanced stages rapidly and economically.[17]

Disease progression in cancer is dependent on complex interactions between the tumor and host inflammatory response. In a review on the role of SIR in predicting survival in patients with primary operable cancer, approximately 80 studies have evaluated the role of the SIR using biochemical and hematologic markers such as elevated CRP, hypoalbuminemia, increased white cell, neutrophil, and platelet counts. Combinations of such factors have been used to derive simple inflammation based prognostic scores, such as the Glasgow prognostic score, the NLR, and PLR. A review demonstrated that there is good evidence that preoperative measures of SIR predict cancer survival, independent of tumor stage, in primary operable cancer. The authors of this review concluded that measurement of SIR is simple, reliable, and can be incorporated into current staging algorithms.[19]

There is only limited data exploring the role of SIR in head and neck cancer. Markers of SIR in patients with head and neck cancers have not been compared to the normal population or to patients with nonmalignant inflammatory conditions.[15] Markers of SIR seem to be particularly robust prognostic indicators in operable colorectal, gastro-oesophageal, and renal cancers. They also have value in other common solid tumors, of which one of the least studied in detail is oral cancer.[10] Very few studies have investigated the relationship between markers of SIR and prognosis in OSCC.[10,18] The foremost attempt of the present study was to analyse the importance of preoperative NLR and PLR as predictive markers of LNM in OSCC. The ROC analysis determined preoperative cut-off values of 1.77 and 128.5 for NLR and PLR respectively. The area under the curve (AUC) was 0.51 ($P = 0.92$) for NLR and 0.72 ($P = 0.00$) for PLR, indicating that PLR was superior to NLR as a predictive factor for LNM in OSCC: 37 (54%) patients with OSCC had PLR ≤ 128.5 and 31 (46%) had PLR 128.5. There was an association between PLR cut-off value and lymph node status ($P < 0.05$). The rate of lymph node involvement was higher in the PLR > 128.5 group than in the PLR ≤ 128.5 (58% vs. 16%; $P = 0.000$), thus suggesting PLR to be useful in predicting LNM and can be included in the surgical workup of patients with OSCC. An increased PLR has been significantly associated with nodal involvement status and advanced stage disease. Similar finding have been mentioned in the literature by Ertas *et al.*,[13] in a study on NLR and PLR in SCC of the vulva. In a study to determine the prognostic value of NLR and PLR in patients with esophageal SCC, Feng *et al.* stated that preoperative NLR and PLR were significant predictors of overall survival in patients with oesophageal SCC,

however, PLR was superior to NLR as a predictive factor in patients with esophageal SCC.[11,12]

A raised NLR has been associated with a poorer prognosis in patients with nasopharyngeal carcinoma.[20] Similarly, markers of blood leukocyte activation have been linked to survival in head and neck cancer.[21] In multiple tumor types, the NLR appears to be related to more advanced disease stage and possibly a more aggressive tumor behavior. A literature review suggests that a raised NLR reflects an upregulated innate immune response.[22] Studies have demonstrated that elevation of NLR in cancer patients indicates a decrease of antitumor activity, thus implying that tumor development may be related to NLR imbalance in cancer patients. Elevated NLR was demonstrated to be associated with tumor progression and metastasis.[18] In a systematic review, correlative studies (15 studies, >8500 patients) have shown that NLR is elevated in patients with more advanced or aggressive disease evidenced by increased tumour stage, nodal stage, and number of metastatic lesions, and as such these patients may represent a particularly high-risk patient population.[22] In the present study there was no significant association between NLR cut-off and clinicopathologic features. There was no significant difference between the means in the case of NLR between the lymph node positive and negative groups (2.28 ± 0.47 vs. 2.37 ± 0.76) ($P = 0.928$). Analysing a larger cohort of OSCC patients is required to validate the above finding.

One limitation of the analysis in our study is that we could not obtain complete data on patient survival. Hence correlation between the markers of SIR and survival was unworkable. Another limitation is that this is a cohort study based at a single medical center. Therefore, a multicenter study with longer follow up duration and a larger sample is required in the future for more clarity in this area of research.

More recently, markers like modified Glasgow Prognostic Score (mGPS), NLR and PLR have been combined to form inflammation-based prognostic scores which have been validated. Farhan-Alanie has suggested mGPS of activated systemic inflammation to be a seemingly powerful adverse prognostic indicator in resectable OSCC, which suggest that acute-phase protein based systemic inflammatory markers (C-reactive protein and albumin) are superior to those based on cellular components of the white cells in blood (neutrophils, lymphocytes and platelets). The hepatic system has a more important role than the haemopoietic system in SIR to oral cancer.[10] Further prospective studies with large sample size are required to determine the potential role of modified Glasgow prognostic score, NLR, and PLR before complete surgical staging, on lymph node involvement status in OSCC.

Conclusions

Evidence for the use of hematologic markers of inflammation as predictors of clinical outcome in head and neck cancer patients is limited. The prognostic relevance of NLR and PLR as biomarkers in a cohort of OSCC subjects in relation to LNM has been barely reported. We retrospectively analysed the clinicopathologic features and haematological investigations of 68 OSCC patients treated in our institution. Results suggest that preoperative PLR is directly associated with nodal involvement status of OSCC. Preoperative PLR is superior to NLR to predict LNM in OSCC. A raised PLR has been associated with nodal involvement status and advanced stage disease. The addition of preoperative PLR calculation can be useful for the prediction of LNM in the clinical setting of OSCC. Prospective validated studies with larger samples evaluating preoperative cut-off values for the NLR and PLR are required to confirm the present findings. The incorporation of hematologic markers of inflammation into clinical palpation and imaging procedures might improve ability to predict LNM. These indicators are effortless, easily accessible and computed, and can be amalgamated into surgical work-up of patients with OSCC at no additional expense.

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Conflict of interest

The authors declare no conflict of interests.

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