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Prognostic significance of preoperative Naples prognostic score for disease-free and overall survival in oral cavity squamous cell carcinoma post-surgery

Xue-Lian Xu[1†], Chen-Chen Wu[1†] and Hao Cheng[1,2*]

Abstract

Background Oral cavity squamous cell carcinoma (OCSCC) is a common malignancy with high morbidity and mortality. This research seeks to assess the correlation between Naples Prognostic Score (NPS) and survival outcomes in patients with OCSCC who are receiving surgical treatment, highlighting its potential as a prognostic tool for predicting patient outcomes.

Methods This retrospective study included 589 OCSCC patients from two large regional medical centers in central China, treated between February 2008 and September 2019. Inclusion criteria mandated confirmed OCSCC diagnosis, age ≥ 18 years, and radical surgery, while patients with distant metastasis, multiple tumors, or insufficient data were excluded. Data on 29 clinicopathological variables, including demographic details, tumor characteristics, and nutritional/inflammatory markers, were collected. The statistical approach included both univariate and multivariate Cox regression models to determine factors associated with disease-free survival (DFS) and overall survival (OS). Additionally, Kaplan-Meier survival analysis was employed to evaluate the effect of adjuvant radiotherapy on survival in various NPS subgroups.

Results Surgical margin status, ENE, NPS, age-adjusted Charlson comorbidity index (ACCI), and American Joint Committee on Cancer (AJCC) stage were identified as independent prognostic factors for DFS. Similarly, Eastern Cooperative Oncology Group Performance Status (ECOG PS), surgical margin status, extranodal extension (ENE), NPS, ACCI, and AJCC stage were found to be independent prognostic factors for OS. A higher NPS was associated with a poorer prognosis. In AJCC stage III-IVb patients with NPS 1–2, adjuvant radiotherapy significantly improved both DFS and OS. Likewise, in AJCC stage III-IVb patients with NPS 3–4, adjuvant radiotherapy was associated with better DFS and OS outcomes. However, no significant impact of adjuvant radiotherapy was observed in patients with AJCC stage I-II or in those with NPS 0, regardless of stage. This underscores the importance of NPS in stratifying patients for adjuvant therapy.

[†]Xue-Lian Xu and Chen-Chen Wu contributed equally to this work.

*Correspondence:
Hao Cheng
cheng198861hao@163.com

Full list of author information is available at the end of the article

Conclusion The Naples Prognostic Score is a beneficial prognostic indicator for survival in OCSCC patients. Its integration into clinical practice may assist in risk stratification and treatment decision-making, particularly for those undergoing adjuvant radiotherapy.

Keywords Oral cavity squamous cell carcinoma, Naples prognostic score, Disease-free survival, Overall survival, Adjuvant radiotherapy

Introduction

Head and neck squamous cell carcinoma (HNSCC), the sixth most prevalent malignant tumor globally [1], includes oral squamous cell carcinoma (OCSCC) among its most common subtypes. Oral cavity carcinoma encompasses a spectrum of malignant tumors that manifest in the anterior two-thirds of the tongue, inner lip, gingiva, floor of mouth, and buccal mucosa [2]. Squamous cell carcinoma is the predominant histological subtype, accounting for approximately 90% of all cases [3]. OCSCC tends to have a higher prevalence among individuals from low- and middle-income groups within various nations [2, 4]. Exposure factors causing oral cancer include socioeconomic inequality, poor lifestyle habits (such as alcohol and tobacco intake) [5], poor oral hygiene [6], chronic irritation [7], and viral infections (such as human tumor virus Human papillomavirus (HPV)) [8].

Surgical resection combined with adjuvant radiotherapy is the standard treatment for locally advanced resectable OCSCC [9]. The standard adjuvant therapies for OCSCC after surgical resection typically involve RT with or without concurrent chemotherapy, particularly cisplatin-based regimens, for patients with high-risk pathological features such as positive margins, extranodal extension, or advanced T-stage [9, 10]. The standard adjuvant therapies for OCSCC after surgical resection typically involve RT with or without concurrent chemotherapy, particularly cisplatin-based regimens, for patients with high-risk pathological features such as positive margins, extranodal extension, or advanced T-stage [11]。 Recent clinical trials have also explored intensification of adjuvant therapy, such as combining RT with targeted agents or immunotherapy, to address adverse prognostic factors while managing treatment-related toxicities [11, 12]. Even with the standard application of enhanced surgical techniques and postoperative radiotherapy or chemoradiotherapy, the 5-year survival rate of OCSCC remains less than 50% in recent decades [13–15]. In general, the primary treatment strategies and prognostic tools for OCSCC patients are based on the 8th edition of the American Joint Committee on Cancer (AJCC) staging system [16]. The traditional AJCC 8th TNM staging system underscores that tumor size, lymph node involvement, and the presence of distant metastasis are pivotal in determining the prognosis of patients with OCSCC [17]. However, this system presents several limitations when utilized for prognostic prediction in OCSCC patients. Firstly, the staging system is categorical, which may lead to diverse prognoses among patients classified within the same stage. Secondly, it relies solely on anatomical progression for staging and fails to incorporate numerous potential prognostic factors such as pathological type, surgical safe margin status, nutritional status, inflammation-related factors, patient psychological status, as well as social and economic factors [18–20].

It has been shown that chronic inflammation and metabolic imbalance, key regulators of the tumor microenvironment, have been demonstrated to promote invasion and metastasis of OCSCC through NF-κB and STAT3 pathways [21, 22], while malnutrition can lead to immunosuppressive microenvironment. In recent years, systemic inflammation and nutritional indicators have shown potential in the prognostic evaluation of OCSCC [23, 24],but their isolated use may miss biological synergistic effects. Innovative integration of the Naples Prognostic Score (NPS) consolidates serum albumin, total cholesterol (TC) levels, neutrophil-to-lymphocyte ratio (NLR), and lymphocyte-to-monocyte ratio (LMR). It has shown a prognostic value superior to a single index in colorectal cancer [25] and gastric cancer [26]. Notably, NPS components are highly relevant to OCSCC pathomechanism: low albumin levels reflect IL-6-mediated systemic inflammatory responses [27], high NLR suggest that tumor-associated neutrophils promote angiogenesis through MMP-9 secretion [28], and low LMRs are associated with immune escape resulting from infiltration of M2 tumor-associated macrophages [28].

However, no study has investigated the prognostic value of preoperative NPS in OCSCC, and by prospectively collecting dynamic nutritional/inflammatory data from surgical patients, this study will reveal for the first time the predictive value of preoperative NPS change trajectory for treatment response and provide a basis for individualized adjuvant treatment decisions. To compensate for the lack of cross-sectional studies.

Materials and methods

Data collection

The study enrolled a total of 589 patients with OCSCC from two large regional medical centers in central China, spanning the period from February 2008 to September 2019. Defining the inclusion and exclusion criteria rigorously ensures that only the right candidates are analyzed.

The inclusion criteria were as followed: (1) OCSCC confirmed by pathology and imaging examination; (2) Age ≥ 18 years old; (3) Patients must have completed the entire planned adjuvant radiotherapy or chemotherapy regimen; (4) Patient medical records must be available and traceable. Patients were excluded if they met any of the following criteria: (1) age < 18 years; (2) absence of radical surgery; (3) presence of multiple primary tumors; (4) distant metastasis at the time of initial diagnosis; (5) eastern cooperative oncology group performance status (ECOG PS) score ≥ 3; (6) AJCC staging was unknown; (7) multiple primary tumors; (8) incomplete clinical data; (9) lack of follow-up information; (10) death within 30 days; (11) neoadjuvant radiotherapy; (12) adjuvant chemotherapy alone; or (13) immunotherapy. The flowchart in Fig. 1 provides a comprehensive overview of the sample selection process. We encountered a minor proportion of missing data, approximately 3%. Following the exclusion of samples with missing values, the remaining dataset demonstrated satisfactory representativeness and consistency. We opted for the direct removal of incomplete samples to address this issue. Written informed consent was obtained from all participants before their involvement, and the study's protocol received approval from the institutional review board. Radiotherapy techniques employed included conformal radiotherapy (CRT), intensity-modulated radiotherapy (IMRT), image-guided radiotherapy (IGRT), and volumetric-modulated arc therapy (VMAT). Total radiation doses ranged from 60.0 to 72.0 Gy, delivered in daily fractions of 2.0–2.2 Gy, five days per week. The staging system utilized in this study was based on the 8th edition of AJCC staging system, while postoperative pathological staging was employed. The staging system used in this study was based on the 8th edition of the AJCC staging system, with postoperative pathological staging serving as the reference standard. The follow-up protocol was based on domestic clinical practice guidelines [29].

We collected clinical information from the case systems of two medical centers, examining 29 clinicopathological factors in patients with OCSCC (Table 1). These variables covered a wide range of factors, including demographic details like age at diagnosis and gender, as well as clinical parameters such as primary tumor site, tumor grade, and AJCC Stage. Key pathological features like perineural invasion, vascular invasion (VI), surgical

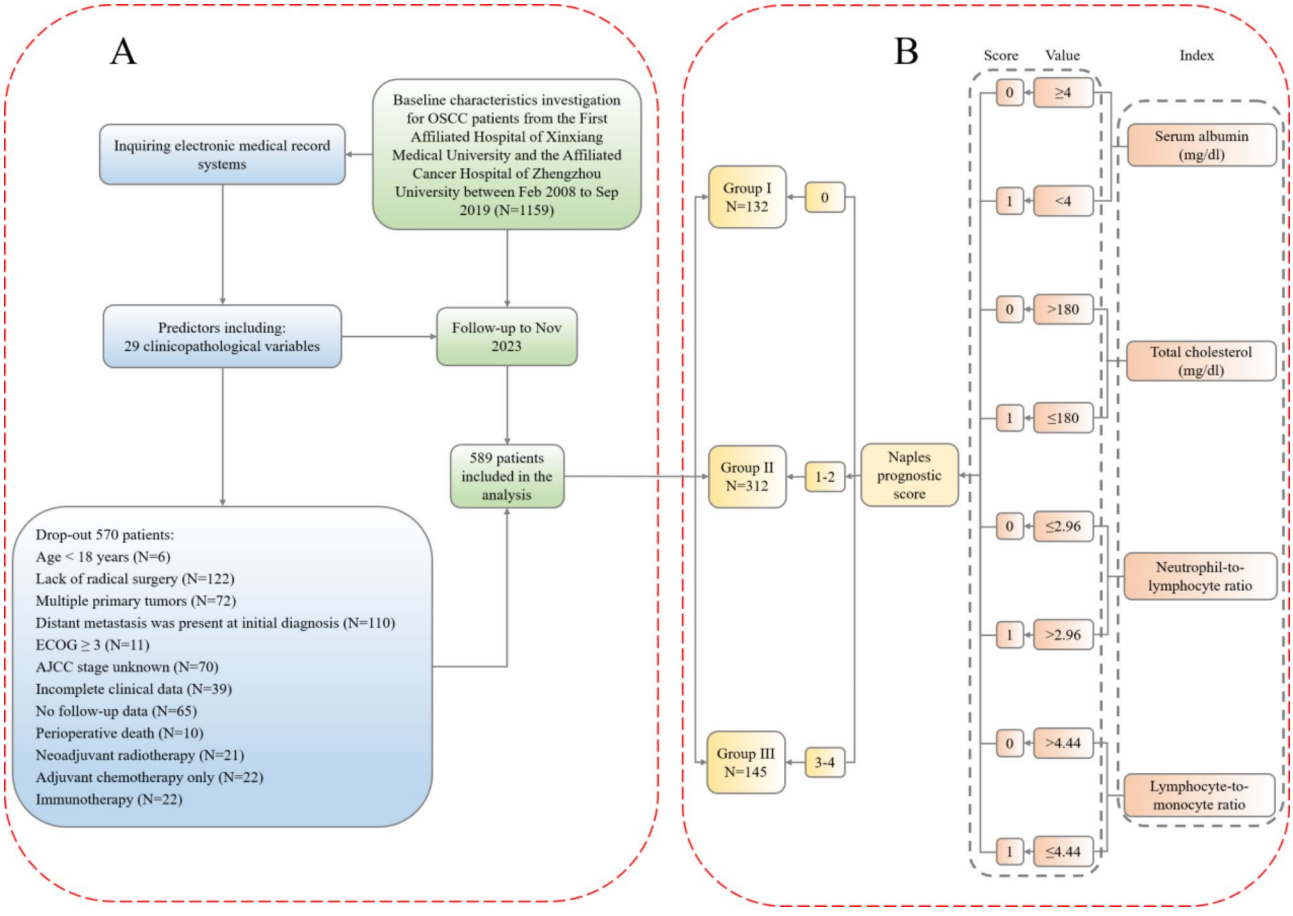

Fig. 1 Sample selection flow chart (**A**) and the calculation method (**B**) of Naples prognostic score

Table 1 Relationship between clinicopathological risk factors and NPS

Characteristics	Group I (NPS 0) *N*%	Group II (NPS 1–2) *N*%	Group III (NPS 3–4) *N*%	*P**
Participants, N	132	312	145	
Age (years)	52.0(40–69)	51.0(38–67)	59.0(43–72)	0.053
Gender				0.568
Male	59 (44.7%)	126(40.4%)	56(38.6%)	
Female	73 (55.3%)	186(59.6%)	89(61.4%)	
Grade				0.004
G1	51 (38.6%)	87(27.9%)	44(30.3%)	
G2	51 (38.6%)	106(34.0%)	39(26.9%)	
G3	30 (22.7%)	119(38.1%)	62(42.8%)	
AJCC Stage				0.013
I	26 (19.7%)	58(18.6%)	25(17.2%)	
II	38 (28.8%)	75(24.0%)	22(15.2%)	
III	44 (33.3%)	127(40.7%)	59(40.7%)	
IVa & IVb	24 (18.2%)	52(16.7%)	39(26.9%)	
Perineural invasion				0.077
No	110 (83.3%)	279(89.4%)	131(90.3%)	
Yes	22 (16.7%)	33(10.6%)	14(9.7%)	
VI				0.652
No	118 (89.4%)	285(91.3%)	132(91.0%)	
Yes	14 (10.6%)	27(8.7%)	13(9.0%)	
Surgical margin				0.634
≥ 5 mm	118 (89.4%)	274(87.8%)	132(91.0%)	
< 5 mm or postive	14 (10.6%)	38(12.2%)	13(9.0%)	
ENE				0.664
Negative	111 (84.1%)	257(82.4%)	119(82.1%)	
Positive	21 (15.9%)	55(17.6%)	26(17.9%)	
DOI				0.003
< 10 mm	121 (91.7%)	260(83.3%)	114(78.6%)	
≥ 10 mm	11 (8.3%)	52(16.7%)	31(21.4%)	
Smoking				0.070
No	118 (89.4%)	273(87.5%)	119(82.1%)	
Yes	14 (10.6%)	39(12.5%)	26(17.9%)	
SIS				0.657
0	86 (65.2%)	231(74.0%)	93(64.1%)	
1	30 (22.7%)	57(18.3%)	30(20.7%)	
2	16 (12.1%)	24(7.7%)	22(15.2%)	
ECOG PS score				0.031
0–1	105(79.5%)	248(79.5%)	100(69.0%)	
2	27(20.5%)	64(20.5%)	45(31.0%)	
SII	1200.5(688-1593.25)	1140.5(620.75–1586.0)	1138.0(614.0-1571.5)	0.787
PNI	72.0(53.0-96.75)	70.0(52.0–90.0)	70.0(46.0–96.0)	0.641
PLR	150.0(99.0-200.75)	149.0(93.0-216.5)	147.0(91.5–217.0)	0.917
NLR	2.43(1.60–3.32)	2.35(1.32–3.37)	2.42(1.42–3.31)	0.790
PAR	7.41(4.10–9.98)	6.46(3.44–9.51)	7.32(3.86–9.86)	0.941
TC	199.11(137.86-262.02)	196.39(130.66-247.55)	197.30(119.34-252.79)	0.359
LMR	5.25(2.53–7.66)	5.34(2.51–7.91)	5.77(2.75–7.75)	0.724
Hemoglobin (g/L)	98.5(92.0-136.7)	98.0(91.0-140.0)	97.0(91.0-142.0)	0.637
BMI (kg/m^2)	22.0(19.6-25.68)	21.2(19.6–25.0)	21.1(19.6–25.0)	0.205
Albumin (g/L)	41.0(36.0-48.75)	42.0(35.0–49.0)	41.0(35.5–48.0)	0.862
ACCI				0.490
2–3	56(42.4%)	135(43.3%)	58(40.0%)	
4–5	42(31.8%)	114(36.5%)	44(30.3%)	

Table 1 (continued)

Characteristics	Group I (NPS 0) *N*%	Group II (NPS 1–2) *N*%	Group III (NPS 3–4) *N*%	*P**
≥ 6	34(25.8%)	63(20.2%)	43(29.7%)	
Adjuvant radiotherapy				0.076
No	81(61.4%)	210(67.3%)	75(51.7%)	
Yes	51(38.6%)	102(32.7%)	70(48.3%)	
Adjuvant chemotherapy				0.010
No	93(70.5%)	247(79.2%)	121(83.4%)	
Yes	39(29.5%)	65(20.8%)	24(16.6%)	

*Normally distributed continuous variables are described as means ± SEs, and continuous variables without a normal distribution are presented as medians [interquartile ranges]. Categorical variables are presented as numbers (percentages)

Abbreviations ACCI, age-adjusted Charlson comorbidity index; AJCC, American Joint Committee on Cancer; BMI, body mass index; DFS, disease-free survival; DOI, depth of invasion; ECOG PS, eastern cooperative oncology group performance status; ENE, extranodal extension; IQR, interquartile range; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio; NPS, Naples prognostic score; OS, overall survival; OCSCC, oral squamous cell carcinoma; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutrition index; SII, systemic immune-inflammation index; SIS, systemic inflammation score; TC, total cholesterol; VI, vascular invasion

margins, extranodal extension (ENE), and depth of invasion (DOI) were also included. Nutritional and inflammatory markers, such as the NPS, systemic inflammation score (SIS), systemic immune-inflammation index (SII), prognostic nutrition index (PNI), platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-albumin ratio (PAR), TC, lymphocyte-to-monocyte ratio (LMR), hemoglobin, albumin, and body mass index (BMI), were also included. In addition, smoking history, age-adjusted Charlson comorbidity index (ACCI), and ECOG PS were also included. Treatment details, including adjuvant chemotherapy and adjuvant radiotherapy, were recorded. Positive margins were defined as resection margins within 1 mm of the tumor. The study's primary endpoints were OS and DFS. The Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 were employed to assess the therapeutic efficacy [30]. DFS in this study was defined as the interval from the initiation of surgery until disease recurrence or death due to any cause.

Calculations

The SIS, SII, PNI, PLR, NLR, PAR, LMR, and BMI are all markers associated with inflammation and nutritional status, with their respective calculation formulas presented in Table S1. Similarity, the calculation method for ACCI is detailed in Table S2. In accordance with the definition and classification criteria established by Galizia et al. [31], we detail the calculation process of NPS in Fig. 1B and Table S1.

Statistical analysis

All statistical analyses were conducted using SPSS 20.0 and R 4.2.2 software. Our study employed a backward stepwise Cox regression method. A univariate Cox regression analysis was performed to identify potential predictors of DFS and OS. These potential predictors were then included in a multivariate Cox regression analysis to determine the independent predictors of DFS and OS. Then, adjusted p-values were calculated using the Benjamini-Hochberg procedure, which is employed to control the false discovery rate in multiple hypothesis testing, thereby minimizing the occurrence of false positives due to multiple comparisons. Furthermore, the Kaplan-Meier method was employed to assess disparities in DFS and OS among patients with varying NPS. Lastly, all OCSCC patients were divided into six subgroups based on their AJCC stage and NPS scores to elucidate the specific benefits of adjuvant radiotherapy (Table 2). The advantages of adjuvant radiotherapy across these distinct subgroups were depicted using Log-Rank method and Kaplan-Meier curves, with statistical significance set

Table 2 Effect of adjuvant radiotherapy on DFS and OS across different subgroups of postoperative OCSCC patients

Subgroups	Adjuvant radiotherapy	DFS		OS	
		Chi-Square	P	Chi-Square	P
AJCC Stage I-II, NPS 0 (*n* = 64)	No (*n* = 43) Yes (*n* = 21)	0.193	0.664	1.42	0.233
AJCC Stage III-IVb, NPS 0 (*n* = 68)	No (*n* = 38) Yes (*n* = 30)	0.970	0.325	1.22	0.296
AJCC Stage I-II, NPS 1–2 (*n* = 133)	No (*n* = 88) Yes (*n* = 45)	0.628	0.235	1.38	0.240
AJCC Stage III-IVb, NPS 1–2 (*n* = 179)	No (*n* = 122) Yes (*n* = 57)	6.82	**0.009**	7.58	**0.006**
AJCC Stage I-II, NPS 3–4 (*n* = 47)	No (*n* = 31) Yes (*n* = 16)	0.975	0.323	0.654	0.420
AJCC Stage III-IVb, NPS 3–4 (*n* = 98)	No (*n* = 44) Yes (*n* = 54)	4.55	**0.033**	7.53	**0.006**

Abbreviation ACCI, age-adjusted Charlson comorbidity index, DFS: disease-free survival; OS: overall survival, OCSCC, oral squamous cell carcinoma

at a p-value of less than 0.05. The Schoenfeld residuals test was conducted using R software to evaluate whether the prognostic effect remained relatively stable throughout the entire follow-up period. The final date for data analysis is set for October 2024.

Results

Baseline characteristics

A total of 589 OCSCC patients who underwent surgical treatment were included in this study. The median age at diagnosis was 52 years (IQR, 40–69). Among the cohort, 241 patients (40.90%) were male and 348 (59.10%) were female. Regarding tumor differentiation, 184 patients (31.20%) had well-differentiated tumors (G1), 197 (33.40%) moderately differentiated (G2), and 208 (35.30%) poorly differentiated (G3). According to AJCC staging, 109 patients (18.50%) were in Stage I, 135 (22.90%) in stage II, 230 (39.00%) in Stage III, and 115 (19.50%) in stages IVa and IVb. This suggests an increase in the proportion of patients presenting with locally advanced disease (stages III-IVB). Among the patients, 453 (76.90%) had an ECOG PS score of 0–1, while 136 (23.10%) had an ECOG PS score of 2. Perineural invasion was noted in 69 patients (11.70%), while 520 (88.30%) showed no signs of perineural invasion. The presence of VI was observed in 54 patients, accounting for 9.20%. The surgical margins were deemed adequate in 524 patients (89.0%), with margins measuring ≥ 5 mm, while 65 patients (11.00%) exhibited margins < 5 mm or positive. In terms of treatment, 223 patients (37.90%) received adjuvant radiotherapy, and 128 patients (21.70%) received adjuvant chemotherapy. ENE was positive in 102 patients (17.3%). The ACCI indicated that 249 patients (42.30%) had a score of 2–3, 200 (34.00%) had a score of 4–5, and 140 (23.80%) had a score of ≥ 6. The NPS distribution revealed 132 patients (22.40%) in Group I (NPS 0), 312 (53.00%) in Group II (NPS 1–2), and 145 (24.60%) in Group III (NPS 3–4). The median DFS was 29 months, and the median OS was 39 months. Relationship between clinicopathological risk factors and NPS are presented in Table 1. Furthermore, following the multicollinearity test, the variance inflation factor (VIF) for all independent variables was found to be below 5 (see Table S3).

Identification process of independent predictors

Univariate and multivariate Cox regression analyses identified independent prognostic factors for disease-free survival (DFS) and overall survival (OS) in patients with oral squamous cell carcinoma (OSCC). In the DFS analysis (Table 3), univariate results showed that higher ECOG PS (HR = 1.513, $P = 0.001$), poorly differentiated (G3) tumors (HR = 1.565, $P = 0.001$), DOI ≥ 10 mm (HR = 1.475, $P = 0.012$), surgical margin < 5 mm or positive margin (HR = 1.674, $P = 0.001$), vascular invasion (VI) (HR = 1.551, $P = 0.012$), perineural invasion (HR = 1.577, $P = 0.004$), ENE (HR = 1.942, $P < 0.001$), AJCC stage III (HR = 2.020, $P < 0.001$) or IVa and IVb stages (HR = 2.642, $P < 0.001$), NPS 1–2 (HR = 1.382, $P = 0.030$) or 3–4 (HR = 1.863, $P < 0.001$), ACCI ≥ 6 (HR = 1.880, $P < 0.001$), age (HR = 1.008, $P = 0.017$), and PNI (HR = 0.993, $P = 0.006$) were all significantly associated with DFS deterioration. The multivariate analysis confirmed that ECOG PS = 2 (HR = 1.323, $P = 0.033$), DOI ≥ 10 mm (HR = 1.373, $P = 0.047$), insufficient/positive margins (HR = 1.846, $P < 0.001$), ENE (HR = 1.678, $P = 0.001$), NPS 3–4 (HR = 1.527, $P = 0.014$), ACCI ≥ 6 (HR = 1.991, $P < 0.001$), and AJCC stage III (HR = 1.654, $P = 0.004$), IVa/IVb stages (HR = 2.419, $P < 0.001$) were independent risk factors for DFS. After applying the Benjamini-Hochberg procedure to adjust the P-values, we found that the P-values for ECOG PS = 2 and DOI ≥ 10 mm were no longer significant (> 0.05). Therefore, the final independent prognostic factors for DFS were surgical margin status, ENE, NPS, ACCI, and AJCC stage.

Similarity, for OS analysis (Table 4), univariate results showed that ECOG PS high (HR = 1.552, $P = 0.001$), poorly differentiated (G3) tumors (HR = 1.555, $P = 0.003$), surgical margins < 5 mm or positive (HR = 1.823, $P < 0.001$), ENE (HR = 2.180, $P < 0.001$), perineural invasion (HR = 1.620, $P = 0.003$), AJCC stage III (HR = 2.287, $P < 0.001$), IVa/IVb (HR = 2.870, $P < 0.001$), NPS 1–2 (HR = 1.412, $P = 0.029$) and 3–4 (HR = 1.937, $P < 0.001$), ACCI ≥ 6 (HR = 1.894, $P < 0.001$), and SII (HR = 1.024, $P = 0.015$) were associated with decreased OS. Multivariate analysis finally identified ECOG PS = 2 (HR = 1.390, $P = 0.020$), poorly differentiated (G3) tumors (HR = 1.414, $P = 0.028$), surgical margins < 5 mm or positive (HR = 2.038, $P < 0.001$), ENE (HR = 1.876, $P < 0.001$), NPS 1–2 (HR = 1.410, $P = 0.033$) and 3–4 (HR = 1.742, $P = 0.002$), ACCI ≥ 6 (HR = 1.979, $P < 0.001$), AJCC stage III (HR = 1.764, $P = 0.003$), and IVa/IVb (HR = 2.506, $P < 0.001$) as independent risk factors for OS, ACCI ≥ 6 (HR = 1.979, $P < 0.001$) as an independent factor for OS suggests that comorbidities may be associated with disease progression. After applying the Benjamini-Hochberg correction for multiple comparisons, the adjusted P value for poorly differentiated (G3) tumors was 0.060, which no longer reached statistical significance. Finally, it was found that the independent prognostic factors affecting OS included ECOG PS, surgical margins, ENE, NPS, ACCI, and AJCC stage.

Impact of the Naples prognostic score on survival

The results depicted in Fig. 2 demonstrate statistically significant differences in both DFS and OS among patients with varying NPS statuses. The C-index values of NPS for predicting 3-year and 5-year DFS were 0.632 and 0.610, respectively, while those for predicting 3-year

Table 3 Univariate and multivariate analyses of clinicopathological data in postoperative OCSCC patients for assessing DFS

Characteristics	Univariate analysis	*P*	Adjusted *P*	Multivariate analysis	*P*	Adjusted *P*
	HR (95% CI)			HR (95% CI)		
Age at diagnosis (years)	1.008 (1.001–1.014)	**0.017**	**0.042**	0.997 (0.989–1.005)	0.470	0.497
Gender						
Male	Reference					
Female	1.116 (0.888–1.403)	0.346	0.395			
Smoking						
No	Reference					
Yes	1.252 (0.915–1.714)	0.160	0.223			
ECOG PS score						
0–1	Reference			Reference		
2	1.513 (1.177–1.946)	**0.001**	**0.005**	1.323 (1.022–1.712)	**0.033**	0.074
Grade						
Well differentiate (G1)	Reference			Reference		
Moderate differentiate (G2)	1.232 (0.930–1.632)	0.146	0.212	1.165 (0.866–1.565)	0.313	0.376
Poor differentiate (G3)	1.565 (1.188–2.063)	**0.001**	**0.005**	1.325 (0.985–1.782)	0.063	0.103
DOI						
< 10 mm	Reference			Reference		
≥ 10 mm	1.475 (1.089–1.998)	**0.012**	**0.035**	1.373 (1.004–1.879)	**0.047**	0.094
Surgical margin						
≥ 5 mm	Reference			Reference		
< 5 mm or Positive	1.674 (1.226–2.287)	**0.001**	**0.004**	1.846 (1.339–2.547)	**< 0.001**	**< 0.001**
VI						
No	Reference			Reference		
Yes	1.551 (1.100–2.188)	**0.012**	**0.032**	0.958 (0.625–1.468)	0.842	0.842
Perineural invasion						
No	Reference			Reference		
Yes	1.577 (1.158–2.148)	**0.004**	**0.014**	1.213 (0.797–1.847)	0.368	0.414
ENE						
Negative	Reference			Reference		
Positive	1.942 (1.465–2.574)	**< 0.001**	**< 0.001**	1.678 (1.253–2.248)	**0.001**	**0.006**
PNI	0.993 (0.989–0.998)	**0.006**	**0.019**	0.995 (0.990–1.000)	0.063	0.095
PAR	0.985 (0.953–1.017)	0.345	0.409			
PLR	1.015 (0.996–1.025)	0.233	0.311			
NLR	1.079 (0.975–1.194)	0.140	0.213			
LMR	0.995 (0.959–1.033)	0.797	0.823			
TC	0.999 (0.997–1.000)	0.075	0.133			
Hemoglobin (g/L)	1.000 (0.995–1.005)	0.917	0.917			
Albumin (g/L)	0.992 (0.979–1.005)	0.244	0.312			
BMI (kg/m^2)	0.996 (0.968–1.025)	0.777	0.829			
NPS						
0 (Group I)	Reference			Reference		
1–2 (Group II)	1.382 (1.032–1.850)	**0.030**	0.060	1.336 (0.996–1.793)	0.053	0.095
3–4 (Group III)	1.863 (1.342–2.585)	**< 0.001**	**< 0.001**	1.527 (1.088–2.143)	**0.014**	**0.036**
SIS						
0	Reference					
1	1.384 (0.998–1.640)	0.103	0.165			
2	1.412 (1.149–1.799)	0.057	0.107			
SII	1.003 (1.000–1.007)	**0.028**	0.060			
ACCI						
2–3	Reference			Reference		
4–5	1.361 (1.048–1.767)	**0.021**	**0.048**	1.250 (0.955– 1.635)	0.105	0.145
≥ 6	1.880 (1.404–2.516)	**< 0.001**	**< 0.001**	1.991 (1.478–2.682)	**< 0.001**	**< 0.001**
AJCC stage						

Table 3 (continued)

Characteristics	Univariate analysis	*P*	Adjusted *P*	Multivariate analysis	*P*	Adjusted *P*
	HR (95% CI)			HR (95% CI)		
I	Reference			Reference		
II	1.219 (0.840–1.761)	0.299	0.368	1.258 (0.860–1.840)	0.237	0.305
III	2.020 (1.461–2.792)	**< 0.001**	**< 0.001**	1.654 (1.174–2.330)	**0.004**	**0.009**
IVa&b	2.642 (1.827–3.820)	**< 0.001**	**< 0.001**	2.419 (1.653–3.540)	**< 0.001**	**< 0.001**
Adjuvant chemotherapy						
No	Reference					
Chemotherapy	0.783 (0.597–1.026)	0.076	0.128			
Adjuvant radiotherapy						
No	Reference					
Yes	0.899 (0.713–1.133)	0.366	0.404			

Abbreviations ACCI, age-adjusted Charlson comorbidity index; AJCC, American Joint Committee on Cancer; BMI, body mass index; CI, confidence interval; DFS, disease-free survival; DOI, depth of invasion; ECOG PS, eastern cooperative oncology group performance status; ENE, extranodal extension; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio; NPS, naples prognostic score; OCSCC, oral squamous cell carcinoma; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutrition index; SII, systemic immune-inflammation index; SIS, systemic inflammation score; TC, total cholesterol; VI, vascular invasion

and 5-year OS were 0.624 and 0.615, respectively. These validation results suggest that the NPS possesses a moderate predictive capability. The Kaplan-Meier analysis highlighted the influence of adjuvant radiotherapy on DFS and OS among different subgroups of postoperative OCSCC patients (Table 5; Figs. 3 and 4). In AJCC stage III-IVb patients with NPS 1–2, adjuvant radiotherapy significantly improved both DFS (Chi-Square = 6.82, $P = 0.009$) and OS (Chi-Square = 7.58, $P = 0.006$). Similarly, in AJCC stage III-IVb patients with NPS 3–4, adjuvant radiotherapy was associated with better DFS (Chi-Square = 4.55, $P = 0.033$) and OS (Chi-Square = 7.53, $P = 0.006$). However, no significant impact of adjuvant radiotherapy was observed in patients with AJCC stage I-II or in those with NPS 0, regardless of stage. These findings suggest that adjuvant radiotherapy may provide a survival benefit in more advanced stages (III-IVb) and higher NPS (1–4) subgroups.

Fig S1 & S2 demonstrate that the p-values of the Schoenfeld residual test for all independent prognostic variables in predicting DFS and OS were greater than 0.05. This outcome did not reject the null hypothesis, thereby confirming that these variables adhered to the proportional hazards (PH) assumption. Additionally, the global test p-value exceeded 0.05, which further validated that the Cox regression model as a whole satisfied the PH assumption and was appropriate for conducting survival analysis. Furthermore, Schoenfeld residual tests were conducted across six distinct subgroups. The results indicated that all global Schoenfeld residual tests yielded p-values greater than 0.05, reinforcing the conclusion that there was no substantial violation of the proportional hazards assumption. Finally, Fig S3 showed the Time-dependent ROC curves. The AUC values obtained from Cox regression analysis for predicting 1-year, 3-year, and 5-year DFS were 0.578, 0.606, and 0.608, respectively. Additionally, the AUC values for predicting 1-year, 3-year, and 5-year OS were 0.625, 0.603, and 0.600, respectively.

Discussion

Most oral cancers are of the histopathological type squamous cell carcinoma, and it is also one of the most common malignancies of the head and neck region [32]. In recent years, the mortality rate of OCSCC has continued to rise worldwide [33]. The overall 5-year survival rate for oral cancer has consistently remained low, at approximately 50%, positioning it among the malignancies with the highest mortality rates over the past few decades [34]. The AJCC staging system is widely recognized as the best prognostic factor for malignancy. However, it is possible to find significant survival heterogeneity in patients with the same stage of OCSCC in clinical practice. The AJCC staging system, on its own, does not adequately pinpoint the optimal treatment approach or accurately categorize patients' mortality risk or prognosis. Therefore, it is particularly important to find more variables that affect prognosis. Some current studies have revealed that systemic inflammatory response and nutritional status of the host are critical factors in predicting the prognosis of OCSCC [35–37]. As a novel indicator among numerous inflammatory and nutritional markers, the NPS score incorporates albumin, total cholesterol, LMR, and NLR to provide strong prognostic predictive power [31]. In the present study, we conducted a multivariate analysis of a series of variables that impact prognosis and discovered that NPS significantly influences the survival of post- surgery OCSCC patients.

Research in the last decade has clarified the critical role of inflammation in tumor formation, and the inflammatory microenvironment has emerged as a universal and important component of tumors [38]. Bacterial and viral

Table 4 Univariate and multivariate analyses of clinicopathological data in postoperative OCSCC patients for assessing OS

Characteristics	Univariate analysis	*P*	Adjusted *P*	Multivariate analysis	*P*	Adjusted *P*
	HR (95% CI)			HR (95% CI)		
Age at diagnosis (years)	1.007 (1.002–1.014)	0.049	0.121			
Gender						
Male	Reference					
Female	1.051 (0.824–1.340)	0.686	0.732			
Smoking						
No	Reference					
Yes	1.339 (0.969–1.850)	0.076	0.128			
ECOG PS score						
0–1	Reference			Reference		
2	1.552 (1.189–2.026)	**0.001**	**0.005**	1.390 (1.053–1.834)	**0.020**	**0.049**
Grade						
Well differentiate (G1)	Reference			Reference		
Moderate differentiate (G2)	1.109 (0.820–1.498)	0.502	0.574	1.112 (0.776–1.606)	0.510	0.542
Poor differentiate (G3)	1.555 (1.165–2.077)	**0.003**	**0.012**	1.414 (1.037–1.927)	**0.028**	0.060
DOI						
< 10 mm	Reference					
≥ 10 mm	1.235 (0.885–1.722)	0.213	0.284			
Surgical margin						
≥ 5 mm	Reference			Reference		
< 5 mm or Positive	1.823 (1.322–2.513)	**< 0.001**	**< 0.001**	2.038 (1.461–2.843)	**< 0.001**	**< 0.001**
VI						
No	Reference					
Yes	1.437 (0.993–2.082)	0.055	0.117			
Perineural invasion						
No	Reference			Reference		
Yes	1.620 (1.172–2.238)	**0.003**	**0.011**	1.191 (0.763–1.859)	0.441	0.500
ENE						
Negative	Reference			Reference		
Positive	2.180 (1.619–2.936)	**< 0.001**	**< 0.001**	1.876 (1.378–2.555)	**< 0.001**	**< 0.001**
PNI	0.993 (0.988–0.998)	**0.008**	**0.026**	0.995 (0.990–1.000)	0.076	0.123
PAR	0.989 (0.955–1.024)	0.530	0.585			
PLR	1.011 (0.956–1.075)	0.225	0.288			
NLR	1.081 (0.971–1.204)	0.153	0.233			
LMR	1.002 (0.963–1.042)	0.927	0.927			
TC	0.998 (0.997–1.000)	0.072	0.128			
Hemoglobin (g/L)	0.996 (0.991–1.002)	0.203	0.282			
Albumin (g/L)	0.982 (0.978–1.006)	0.268	0.330			
BMI (kg/m^2)	0.996 (0.967–1.027)	0.815	0.841			
NPS						
0 (Group I)	Reference			Reference		
1–2 (Group II)	1.412 (1.035–1.925)	**0.029**	0.077	1.410 (1.029–1.933)	**0.033**	0.062
3–4 (Group III)	1.937 (1.369–2.740)	**< 0.001**	**< 0.001**	1.742 (1.218–2.491)	**0.002**	**0.007**
SIS						
0	Reference			Reference		
1	1.337 (1.000–1.786)	0.063	0.119	1.264 (0.934–1.710)	0.129	0.199
2	1.441 (0.961–2.161)	0.050	0.114	1.355 (0.884–2.078)	0.163	0.213
SII	1.024 (1.009–1.050)	**0.015**	**0.044**	1.000 (1.000–1.000)	0.314	0.381
ACCI						
2–3	Reference			Reference		
4–5	1.146 (0.868–1.513)	0.335	0.397	1.009 (0.755–1.348)	0.952	0.952
≥ 6	1.894 (1.396–2.570)	**< 0.001**	**< 0.001**	1.979 (1.446–2.710)	**< 0.001**	**< 0.001**
AJCC stage						

Table 4 (continued)

Characteristics	Univariate analysis HR (95% CI)	*P*	Adjusted *P*	Multivariate analysis HR (95% CI)	*P*	Adjusted *P*
I	Reference			Reference		
II	1.394 (0.934–2.080)	0.104	0.166	1.352 (0.896–2.042)	0.151	0.214
III	2.287 (1.614–3.240)	**< 0.001**	**< 0.001**	1.764 (1.208–2.576)	**0.003**	**0.009**
IVa&b	2.870 (1.933–4.263)	**< 0.001**	**< 0.001**	2.506 (1.644–3.821)	**< 0.001**	**< 0.001**
Adjuvant chemotherapy						
No	Reference					
Chemotherapy	0.820 (0.617–1.090)	0.172	0.250			
Adjuvant radiotherapy						
No	Reference					
Yes	0.787 (0.613–1.011)	0.060	0.120			

Abbreviations ACCI, age-adjusted Charlson comorbidity index; AJCC, American Joint Committee on Cancer; BMI, body mass index; CI, confidence interval; DOI, depth of invasion; ECOG PS, eastern cooperative oncology group performance status; ENE, extranodal extension; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio; NPS, naples prognostic score; OS, overall survival; OCSCC, oral squamous cell carcinoma; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutrition index; SII, systemic immune-inflammation index; SIS, systemic inflammation score; TC, total cholesterol; VI, vascular invasion

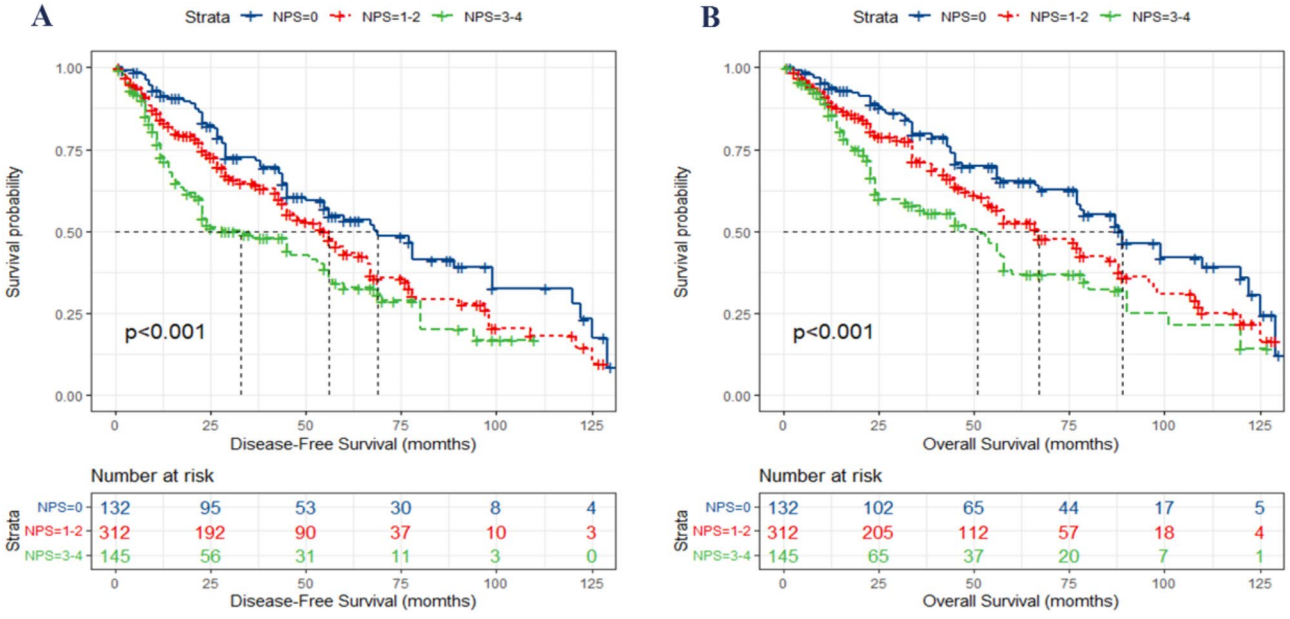

Fig. 2 The Assessment of DFS and OS in patients classified into various NPS subgroups. *Abbreviations* OS, overall survival; DFS, disease-free survival; NPS, Naples prognostic score

infections, tobacco smoke, and obesity all increase cancer risk by triggering chronic inflammation [39]. Inflammation not only fosters tumor development but also influences the host's immune reactions to cancer, playing a pivotal role in responses to both immunotherapy and chemotherapy [40, 41]. Inflammation not only directly promotes tumor proliferation and metastasis by releasing factors such as IL-6 and TNF-α, but also weakens host immune surveillance of tumors by recruiting MDSCs, TAMs, and Tregs to form an immunosuppressive microenvironment [31, 42]. For example, IL-6 upregulates PD-L1 expression via the STAT3 pathway, resulting in a decreased rate of response to PD-1 inhibitor therapy [43, 44]. In addition, nutrition is another important indicator affecting the prognosis of cancer patients, and tumor cells promote immunosuppression and interaction between immune cells and tumors by metabolizing and consuming surrounding nutrients, which in turn creates favorable conditions for tumor growth [45, 46]. The optimization of nutritional status can bolster immune function, attenuate inflammatory response, and impede tumor progression [47]. Increasing evidence suggests that some inflammatory and nutrition-related indicators, such as NLR, PLR, LMR, SIS, and PNI, are associated with tumor survival prognosis [48–50]. Furthermore, decreased preoperative albumin levels are linked to an unfavorable prognosis in patients with OCSCC [51, 52]. Recently, some studies have reported the relationship

Table 5 Univariate and multivariate Cox regression analyses of clinicopathological factors in postoperative OCSCC patients for OS assessment

Characteristics	Univariate analysis	*P*	Multivariate analysis	*P*
	HR (95% CI)		**HR (95% CI)**	
Age at diagnosis (years)	1.007 (1.002–1.014)	0.049		
Gender				
Male	Reference			
Female	1.051 (0.824–1.340)	0.686		
Smoking				
No	Reference			
Yes	1.339 (0.969–1.850)	0.076		
ECOG PS score				
0–1	Reference		Reference	
2	1.552 (1.189–2.026)	**0.001**	1.390 (1.053–1.834)	**0.020**
Grade				
Well differentiate (G1)	Reference		Reference	
Moderate differentiate (G2)	1.109 (0.820–1.498)	0.502	1.112 (0.776–1.606)	0.510
Poor differentiate (G3)	1.555 (1.165–2.077)	**0.003**	1.414 (1.037–1.927)	**0.028**
DOI				
< 10 mm	Reference			
≥ 10 mm	1.235 (0.885–1.722)	0.213		
Surgical margin				
≥ 5 mm	Reference		Reference	
< 5 mm or Positive	1.823 (1.322–2.513)	**< 0.001**	2.038 (1.461–2.843)	**< 0.001**
VI				
No	Reference			
Yes	1.437 (0.993–2.082)	0.055		
Perineural invasion				
No	Reference		Reference	
Yes	1.620 (1.172–2.238)	**0.003**	1.191 (0.763–1.859)	0.441
ENE				
Negative	Reference		Reference	
Positive	2.180 (1.619–2.936)	**< 0.001**	1.876 (1.378–2.555)	**< 0.001**
PNI	0.993 (0.988–0.998)	**0.008**	0.995 (0.990–1.000)	0.076
PAR	0.989 (0.955–1.024)	0.530		
PLR	1.011 (0.956–1.075)	0.225		
NLR	1.081 (0.971–1.204)	0.153		
LMR	1.002 (0.963–1.042)	0.927		
TC	0.998 (0.997–1.000)	0.072		
Hemoglobin (g/L)	0.996 (0.991–1.002)	0.203		
Albumin (g/L)	0.982 (0.978–1.006)	0.268		
BMI (kg/m^2)	0.996 (0.967–1.027)	0.815		
NPS				
0 (Group I)	Reference		Reference	
1–2 (Group II)	1.412 (1.035–1.925)	**0.029**	1.410 (1.029–1.933)	**0.033**
3–4 (Group III)	1.937 (1.369–2.740)	**< 0.001**	1.742 (1.218–2.491)	**0.002**
SIS				
0	Reference		Reference	
1	1.337 (1.000–1.786)	0.063	1.264 (0.934–1.710)	0.129
2	1.441 (0.961–2.161)	0.050	1.355 (0.884–2.078)	0.163
SII	1.024 (1.009–1.050)	**0.015**	1.000 (1.000–1.000)	0.314
ACCI				
2–3	Reference		Reference	
4–5	1.146 (0.868–1.513)	0.335	1.009 (0.755–1.348)	0.952
≥ 6	1.894 (1.396–2.570)	**< 0.001**	1.979 (1.446–2.710)	**< 0.001**

Table 5 (continued)

Characteristics	Univariate analysis	*P*	Multivariate analysis	*P*
	HR (95% CI)		HR (95% CI)	
AJCC stage				
I	Reference		Reference	
II	1.394 (0.934–2.080)	0.104	1.352 (0.896–2.042)	0.151
III	2.287 (1.614–3.240)	**< 0.001**	1.764 (1.208–2.576)	**0.003**
IVa&b	2.870 (1.933–4.263)	**< 0.001**	2.506 (1.644–3.821)	**< 0.001**
Adjuvant chemotherapy				
No	Reference			
Chemotherapy	0.820 (0.617–1.090)	0.172		
Adjuvant radiotherapy				
No	Reference			
Yes	0.787 (0.613–1.011)	0.060		

Abbreviations ACCI, age-adjusted Charlson comorbidity index; AJCC, American Joint Committee on Cancer; BMI, body mass index; CI, confidence interval; DOI, depth of invasion; ECOG PS, eastern cooperative oncology group performance status; ENE, extranodal extension; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio; NPS, naples prognostic score; OS, overall survival; OCSCC, oral squamous cell carcinoma; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutrition index; SII, systemic immune-inflammation index; SIS, systemic inflammation score; TC, total cholesterol; VI, vascular invasion

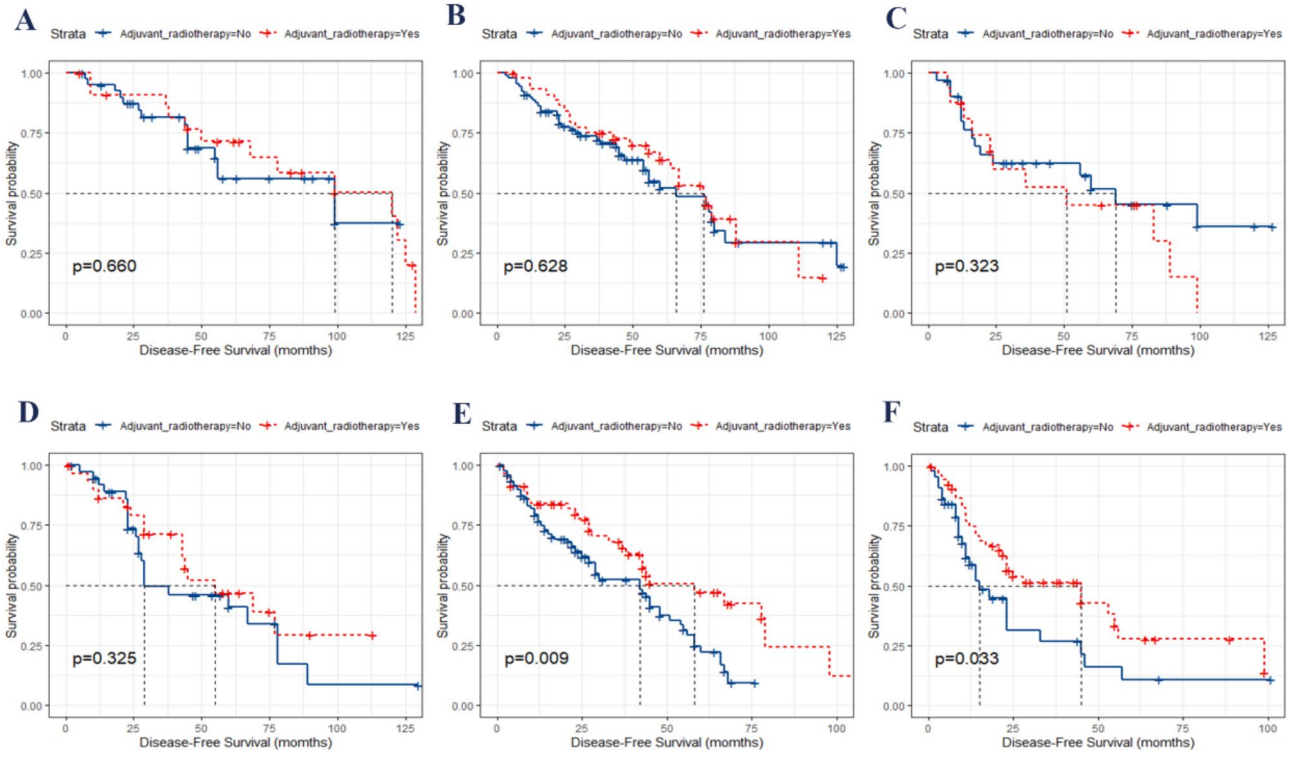

Fig. 3 The impact of adjuvant radiotherapy on DFS across different subgroups, as assessed by Log-Rank test with Kaplan-Meier curves. (**A**) AJCC Stage I-II and NPS 0, (**B**) AJCC Stage I-II and NPS 1–2, (**C**) AJCC Stage I-II and NPS 3–4, (**D**) AJCC Stage III-IVb and NPS 0, (**E**) AJCC Stage III-IVb and NPS 1–2, (**F**) AJCC Stage III-IVb and NPS 3–4. *Abbreviations* AJCC, American Joint Committee on Cancer; DFS, disease-free survival; NPS, Naples prognostic score

between serum cholesterol and tumors. For example, it has been reported that cholesterol accumulation may be associated with immune suppression in the tumor microenvironment. Liver X receptor (LXR) binds to ligands to release cholesterol metabolites, which prevent dendritic cells (DCs) from migrating to lymphoid organs to exert antitumor activity by inhibiting chemokine receptor 7 (CCR7) expression on mature DCs, ultimately leading to tumor escape immune surveillance [53]. The findings of another relevant study demonstrated that, high cholesterol levels have been reported to promote angiogenesis and accelerate breast cancer development in vivo [54]. In this study, the NPS score is a more comprehensive inflammatory and nutritional score, and components of NPS (TC, ALB, NLR, LMR) are commonly used blood tests in clinical practice. NPS has been shown to be a

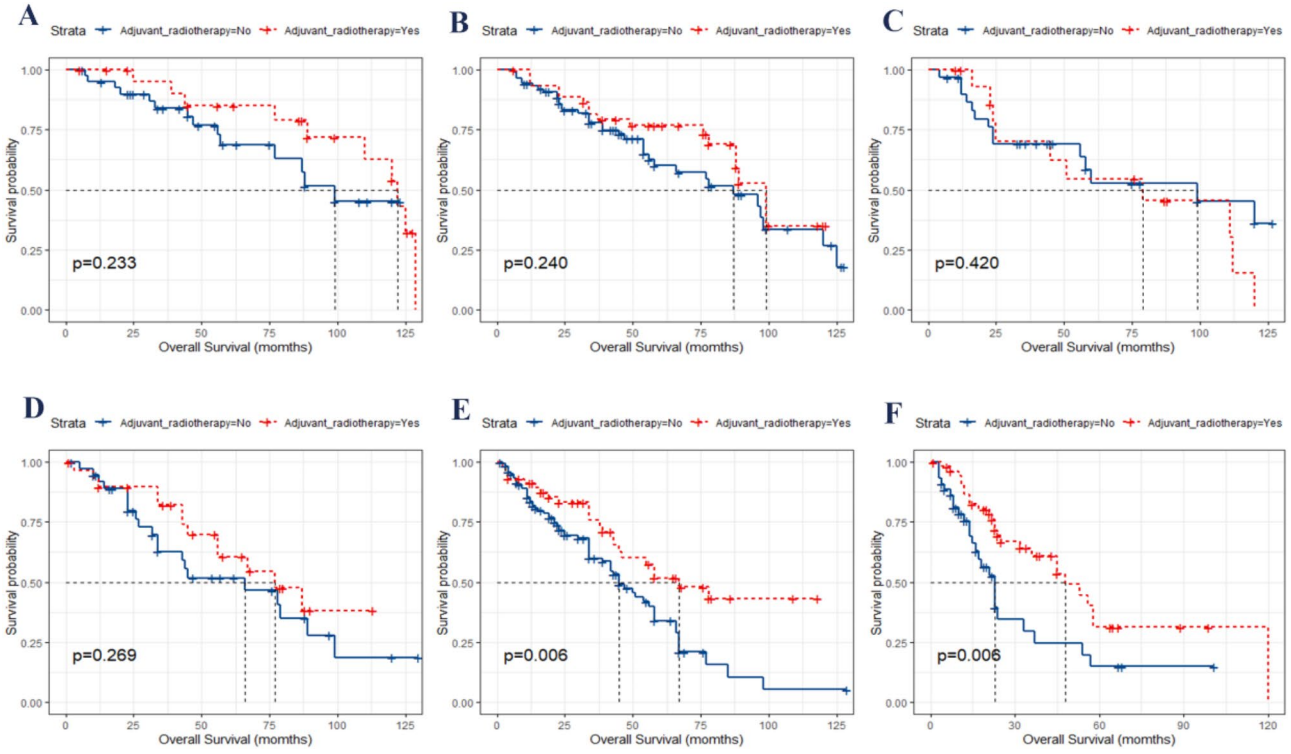

Fig. 4 The effect of adjuvant radiotherapy on OS across different subgroups, as evaluated using the Log-Rank test with Kaplan-Meier curves. (**A**) AJCC Stage I-II and NPS 0, (**B**) AJCC Stage I-II and NPS 1–2, (**C**) AJCC Stage I-II and NPS 3–4, (**D**) AJCC Stage III-IVb and NPS 0, (**E**) AJCC Stage III-IVb and NPS 1–2, (**F**) AJCC Stage III-IVb and NPS 3–4. *Abbreviations* AJCC, American Joint Committee on Cancer; NPS, Naples prognostic score; OS, overall survival

reliable prognostic indicator in various tumors such as triple-negative breast cancer [55], cholangiocarcinoma [56], esophageal cancer [57], lung cancer [58], and gastric cancer [59]. However, the relationship between OCSCC and NPS remains unclear, which constitutes the primary focus of this study. In this regard, this study provides an important addition to previous research. The higher the NPS score, the more unfavorable are the DFS and OS outcomes for patients with OCSCC after surgical treatment, thereby establishing it as an independent prognostic factor for OCSCC patients.

In some clinical practice guidelines, postoperative radiation therapy is recommended for patients with locally advanced (stage III, IVa-IVb) OCSCC [29, 60]. This study showed that there was significant heterogeneity in the survival benefit of adjuvant radiotherapy: adjuvant radiotherapy significantly improved DFS and OS for patients with locally advanced (AJCC Stage III-IV) and high NPS score (Score 1–4); however, no survival benefit was observed in patients with early (AJCC Stage I-II) or low NPS score (Score 0). Therefore, it is recommended to screen the potential benefit population of adjuvant radiotherapy in combination with AJCC stage and NPS score to avoid overtreatment for low-risk patients.

Our study suggests that both surgical safety margin and ENE status may serve as independent prognostic factors in OCSCC. Yamada S et al. demonstrated that surgical margins exceeding 5 mm correlated with a heightened risk of local recurrence [61]. Mannelli G et al.'s study underscores the importance of obtaining negative surgical margins as a key predictor of disease-free survival and locoregional control [62]. ENE refers to tumors that metastasize to cervical lymph nodes break through the lymph node capsule and invade the surrounding soft tissues. The latest 8th edition of the AJCC staging system for oral cancer has undergone significant modifications, including the incorporation of ENE presence or absence as a determinant in N staging [63, 64]. ENE significantly affects the prognosis of OCSCC patients, being linked to an increased rate of local recurrence and reduced overall survival [65, 66]. Our study's results align with prior research, affirming that ENE and surgical margins are independent prognostic factors for DFS and OS in postoperative OCSCC patients.

The Charlson comorbidity index has been widely used in clinical practice to assess comorbidities [67]. Further, the age-adjusted Charlson comorbidity index (ACCI) incorporates age as a contributing factor. A higher ACCI score indicates a greater number of comorbidities, which can impact treatment efficacy and patient survival. This enhancement has been established as a crucial prognostic indicator in gastric, pancreatic, ovarian, and prostate

cancers [68–72]. Furthermore, a separate study corroborated that the ACCI is an independent prognostic factor for patients with OCSCC following surgery [73]. The findings of our study further support the previous results, demonstrating a robust association between ACCI > 6 and unfavorable survival outcomes in patients with OCSCC, thus establishing it as a significant prognostic factor.

The ECOG PS is a widely utilized scoring system for evaluating the functional status of cancer patients. The more severe the patient's physical condition, the greater the likelihood of accompanying clinical symptoms and dysfunction, resulting in decreased treatment tolerance, increased risk of complications, and compromised treatment efficacy. Patients with such a poor performance status often exhibit impaired immune function and struggle to cope with the stress of tumor treatment, ultimately leading to an unfavorable prognosis and shortened survival. Previous research has indicated a link between substantial alterations in ECOG performance status and weakened immune responses among cancer patients [74]. Furthermore, the PS score has been found to be significantly and independently correlated with overall survival among advanced cancer patients [75]. A study focusing on OCSCC revealed that a PS ≥ 2 was linked to a poorer prognosis for OCSCC patients [76]. Similarly, this study demonstrated that a ECOG PS of 2 was also associated with worse OS outcomes in OCSCC patients.

Our study represents the first retrospective analysis of NPS in a distinct population of patients with OCSCC following surgical treatment. Given the significant association between this crucial indicator and prognosis across various tumor types, our findings make a valuable contribution to existing research. Furthermore, the novel subgroup analysis provides useful insights based on NPS and AJCC stage criteria for selecting appropriate populations for postoperative adjuvant radiotherapy, thereby facilitating individualized treatment. The NPS score provides biological information not covered by the AJCC stage by integrating systemic inflammation and nutritional status, and in particular shows significant advantages in refining prognostic stratification, dynamic monitoring, and individualized treatment decisions. Although AJCC version 8 improves staging accuracy by incorporating DOI and ENE, its combination with NPS may be a critical direction for optimizing prognostic assessment and treatment strategies for OCSCC in the future.

However, this study has some limitations. Firstly, all included studies were retrospective in nature. Secondly, the sample data came from central China, which may have affected the generalisability of the results to some extent. Specifically, environmental exposures, dietary habits, and medical accessibility (e.g., compliance with postoperative follow-up) are potentially different from other geographic populations and therefore need to be validated in future large-scale multicenter studies. Thirdly, NPS, as an independent variable, demonstrates only moderate discriminative ability with its C-index, indicating its limited predictive power for DFS and OS. If combined with additional clinicopathological features, the predictive performance could be improved. Therefore, in future studies, we may consider developing a prognostic model that incorporates NPS along with other prognostic variables. Lastly, several potential prognostic factors such as economic and social factors, pain scores, psychological factors of patients and life were not incorporated into the analysis.

Conclusion

As a relatively easily accessible novel biomarker, NPS integrates factors such as inflammation and nutrition. This research revealed that elevated preoperative NPS scores were markedly linked to diminished DFS and OS outcomes in OCSCC patients post-surgery. Preoperative assessment of NPS can be used to guide personalized treatment to prolong survival in patients with OCSCC.

Abbreviations

ACCI	Age-adjusted Charlson comorbidity index
AJCC	American Joint Committee on Cancer
AUC	Area under the curve
BMI	Body mass index
CCR7	Chemokine receptor 7
CRT	Conformal radiotherapy
DCs	Dendritic cells
DFS	Disease-free survival
DOI	Depth of invasion
ECOG PS	eastern cooperative oncology group performance status
ENE	Extranodal extension
HNSCC	Head and neck squamous cell carcinoma
HPV	Human papillomavirus
IGRT	Image-guided radiotherapy
IMRT	Intensity-modulated radiotherapy
LMR	lymphocyte-to-monocyte ratio
LXR	Liver X receptor
NLR	Neutrophil-to-lymphocyte ratio
NPS	Naples prognostic score
OS	Overall survival
OCSCC	Oral cavity squamous cell carcinoma
PAR	Platelet-to-albumin ratio
PH	Proportional hazards
PLR	Platelet-to-lymphocyte ratio
PNI	Prognostic nutrition index
ROC	Receiver operating characteristic
SII	Systemic immune-inflammation index
SIS	Systemic inflammation score
TC	Total cholesterol
VI	Vascular invasion
VIF	Variance inflation factor
VMAT	Volumetric-modulated arc therapy

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-025-14146-4.

Supplementary Material 1

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Author contributions
Conception and design: Hao Cheng. Collection and assembly of data: Xue-Lian Xu. Data analysis and interpretation: Xue-Lian Xu, Hao Cheng. Manuscript writing: Xue-Lian Xu, Chen-Chen Wu, Hao Cheng. Funding: Xue-Lian Xu. Final approval of manuscript: All authors.

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Data availability
Detailed data are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study is conducted in accordance with the declaration of Helsinki, and has been approved by the ethics committee of the First Affiliated Hospital of Xinxiang Medical University and the Affiliated Cancer Hospital of Zhengzhou University. The study is retrospective and only clinical information of patients will be collected without containing personal identifiers, interfering with patients' treatment plans, or posing physiological risks to patients. All research procedures complied with the relevant guidelines and regulations. Informed consent was obtained from all patients before being included.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Radiotherapy Oncology, the First Affiliated Hospital of Xinxiang Medical University, Xinxiang, Henan 453100, China
[2]Department of Radiotherapy Oncology, Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, Henan 450000, China

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