Original Article

JHSMR Journal of Health Science and Medical Research

Prognostic Value of the Pretreatment Ratio of Albumin to Alkaline Phosphatase in Patients with Oral Cavity Carcinoma

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Received 2 July 2025 ● Revised 10 August 2025 ● Accepted 19 November 2025 ● Published online 6 July 2026

Abstract:

Objective: This study aimed to assess the prognostic value of the pretreatment albumin-to-alkaline phosphatase ratio (AAPR) regarding survival outcomes in patients with oral squamous cell carcinoma (OSCC) at all stages.

Meterial and Methods: We retrospectively reviewed patients with OSCC who underwent complete treatment between 2008 and 2018. The primary outcome was the ability of pretreatment AAPR to predict the 5-year overall survival (OS) and disease-free survival (DFS) rates, along with other clinical characteristics established for individualized survival prediction.

Results: A total of 327 patients were enrolled in this study. OS and DFS rates were 84.76% and 55.33%, respectively. The optimal cut-off value of pretreatment AAPR to predict OS was 0.52, with no significant difference compared to those with values less than 0.52 (OS: 86.32% vs. 81.03%, p-value=0.275; DFS: 55.18% vs. 55.65%, p-value=0.539, respectively). In both univariate and multivariate analyses using Cox proportional hazard models, advanced age (≥65 years) and the presence of extranodal extension were independent predictors of worse OS (HR: 4.02, 95% CI: 1.87, 8.65, p-value<0.001; HR: 3.83, 95% CI: 1.47, 9.98, p-value=0.014, respectively) and DFS (HR: 3.52, 95% CI: 1.66, 7.46, p-value<0.01; HR: 3.61, 95% CI: 1.42, 9.22, p-value=0.014, respectively).

Conclusion: Pretreatment AAPR was not an independent prognostic factor for OS and DFS in patients with all stages of OSCC. Advanced age and extranodal extension were associated with unfavorable OS and DFS.

Keywords: albumin, alkaline phosphatase, oral cavity squamous cell carcinoma, squamous cell carcinoma

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J Health Sci Med Res
doi: 10.31584/jhsmr.20261383
www.jhsmr.org

Introduction

Oral cavity carcinoma is one of the most prevalent malignancies of the head and neck and represents a significant global health burden. According to epidemiological data, in 2020, 377,713 new cases were reported globally, resulting in 177,757 deaths[1,2]. However, geographic distribution analysis revealed variations across different regions, with Asia bearing the highest burden, accounting for 64.2% of incident cases and a mortality rate reaching 73.3%[3]. Oral squamous cell carcinoma (OSCC) is the most predominant histological subtype, accounting for approximately 90–95% of all oral carcinoma cases[4]. The current standard strategy typically involves a multimodal therapeutic approach, with surgical resection serving as the primary intervention, often followed by adjuvant radiotherapy or chemoradiotherapy, depending on the pathological risk factors and staging parameters. This comprehensive approach aims to improve local control, reduce recurrence rates, and enhance the overall survival (OS) of affected patients. Generally, the TNM staging system remains the primary determinant for treatment decisions and prognostic assessment in OSCC[5]. There are significant variables in treatment outcomes, even among patients with the same TNM stages. As a result, multiple studies have been conducted to identify additional prognostic factors beyond conventional TNM staging, including immunological and nutritional status markers, which may influence disease progression and therapeutic response[6,7]. Understanding these additional prognostic determinants, along with the easily available indicators, is crucial for the early identification of high-risk patients, optimization of treatment strategies, and improvement of patient prognosis.

Serum albumin, produced by the liver, is a crucial protein and key indicator of nutritional status. It plays a vital role in immunological function through its involvement in antioxidant production and cancer-protective mechanisms[8,9]. Serum albumin levels are significant prognostic factors for both survival outcomes and perioperative complications in head and neck cancer[10-12]. Similarly, alkaline phosphatase (ALP), a synthetically produced enzyme, has frequently shown aberrant elevation in various pathological conditions, particularly in malignancies with osseous involvement[13,14]. Notably, patients with OSCC demonstrated elevated ALP levels compared to age-matched individuals in the general population[15]. Thus, the prognostic implications of cancer appear to be closely correlated with these parameters, and the integration of serum albumin and ALP levels may emerge as a potentially important factor for assessing disease progression and patient outcomes. In recent years, the albumin-to-ALP ratio (AAPR) has been identified as a novel prognostic biomarker, initially introduced in hepatocellular carcinoma in 2015[16], and has also demonstrated significant predictive value in several malignancies.

To date, few studies have assessed the utility of AAPR as a prognosticator of survival outcomes in head and neck cancer, especially in patients with OSCC following treatment. To address this knowledge gap, the present study aimed to investigate the potential impact of pretreatment AAPR on the survival outcomes of patients undergoing curative treatment for OSCC.

Material and Methods

Study design/patient selection and evaluation

Following approval from the Institutional Review Board of the Prince of Songkla University, this retrospective study was conducted at the Department of Otolaryngology, Head and Neck Surgery, Songklanagarind Hospital, Prince of Songkla University. The data of all patients diagnosed with oral cavity carcinoma between January 2007 and December 2018 were extracted from the hospital information system database of our center. The study included patients

diagnosed with OSCC, with histopathological confirmation of squamous cell carcinoma, as well as those who received complete treatment. Patients who underwent supportive treatment only, had a history of head and neck cancer, had concomitant secondary primary cancer, had insufficient laboratory parameters, were diagnosed with distant metastasis at the initial diagnosis, had chronic liver disease that may affect AAPR levels, or did not complete treatment were excluded. All data, including demographic, clinical, pathological, and laboratory information, were independently extracted and verified by investigators. A meticulous secondary review was conducted to verify each missing or unusual data point individually against source records, ensuring data consistency and accuracy.

Treatment modalities

Treatment planning was conducted through weekly multidisciplinary tumor board conferences and collaboratively determined by head and neck surgeons, radiation oncologists, and medical oncologists. Thorough physical examinations and pretreatment laboratory parameters were systematically recorded. All patients underwent imaging studies, including computed tomography of the neck and chest with the upper abdomen and whole-body bone scintigraphy, which were interpreted and reviewed by specialized radiologists to determine the clinical staging accurately before treatment initiation. Treatment protocols throughout the study period (2007–2018) were standardized according to the National Comprehensive Cancer Network (NCCN) Head and Neck Cancer Guidelines. To ensure consistency, we retrospectively restaged all cases according to the most current NCCN staging system based on postoperative pathological findings, thereby standardizing the staging criteria across all patients. The primary therapeutic intervention consisted of surgical resection of both the primary tumor and cervical lymph nodes, as clinically indicated. Postoperative adjuvant therapy, either radiation alone or concurrent chemoradiation, was administered to patients with adverse histopathologic features, and post-treatment surveillance protocols were scheduled in accordance with the NCCN guidelines.

Variables and endpoints

Clinical variables, including age, sex, habitual tobacco use, alcohol consumption, and pathological results (surgical margin status, lymphovascular invasion, perineural invasion, and extranodal extension), were collected. Tumor-specific parameters (cancer stage and location) and pretreatment serum biochemical parameters were also documented. The primary outcomes were 5-year OS and 5-year disease-free survival (DFS). OS was defined as the date of operation to the date of death. For AAPR assessment within 2 weeks before or after diagnosis, at our institution, the standardized reference range for serum biochemical parameters was established as 35–52 g/L for albumin and 40–150 IU/L for ALP in adult patients. The AAPR was calculated by dividing the serum albumin level by the ALP level.

Statistical analysis

Statistical analyses were performed using R software version 2023.03.0+386. Continuous variables were reported as mean with standard deviation (S.D.) or median with interquartile range (IQR) and were compared using Student's t-test or Wilcoxon rank-sum test. Categorical variables are presented as frequencies with percentages, and between-group comparisons were analyzed using the chi-square or Fisher's exact test, as appropriate. The optimal AAPR cut-off was determined using the surv_cutpoint function in the "survminer" package in R software, which applies the maximally selected rank statistics method to identify the threshold that best discriminates survival outcomes. This method was used for exploratory purposes to optimize the

internal separation of the survival outcomes, recognizing that such data-driven thresholds may require external validation to avoid overfitting. Patients were subsequently categorized into low and high AAPR groups according to this cut-off value. Survival analyses were conducted using the Kaplan–Meier method, with between-group comparisons performed via the log-rank test or Peto & Peto test, as appropriate, to assess statistical significance. Independent prognostic factors for OS and DFS were identified using Cox proportional hazard regression models. Given the limited number of events, the multivariate model was constructed conservatively, including only clinically relevant variables to mitigate overfitting. Univariate and multivariate analyses were expressed as hazard ratios (HRs) with corresponding 95% confidence intervals (CIs). Statistical significance was defined as a two-tailed p-value<0.05.

Results

Patient characteristics

The demographic and clinical characteristics of the patients are summarized in Table 1. A total of 327 patients were included in the study, with a median age of 61.8 years (IQR: 52.1–73.3). Approximately 60% of the patients were under the age of 65 years. The majority of the study population was male (57.5%). Lifestyle factors, such as smoking and alcohol consumption, were prevalent among the study population (54.4% and 50.2%, respectively). The median weight of the patients was 55.3 kg (IQR: 49.5–63.3), with a median height of 160 cm (IQR: 154–165), resulting in a median body mass index (BMI) of 21.9 (IQR: 19.4–24.9). Of the total patients, 45% were diagnosed with advanced-stage tumors (T3–T4), while 55% had early-stage tumors (T1–T2). Cervical lymph node involvement was observed in 42.8% of the cases. Regarding TNM cancer staging, the majority of patients (63.3%) were classified as having advanced-stage disease (stage III–IV). The primary tumor site was predominantly the tongue (55.4%), followed by the floor of the mouth (14.4%). In terms of treatment modalities, the majority of patients (42.5%) underwent surgery followed by radiotherapy, whereas 34.4% received a more intensive regimen of surgery followed by chemoradiotherapy. Histopathological analysis indicated that 74.3% of the tumors were well-differentiated squamous cell carcinoma.

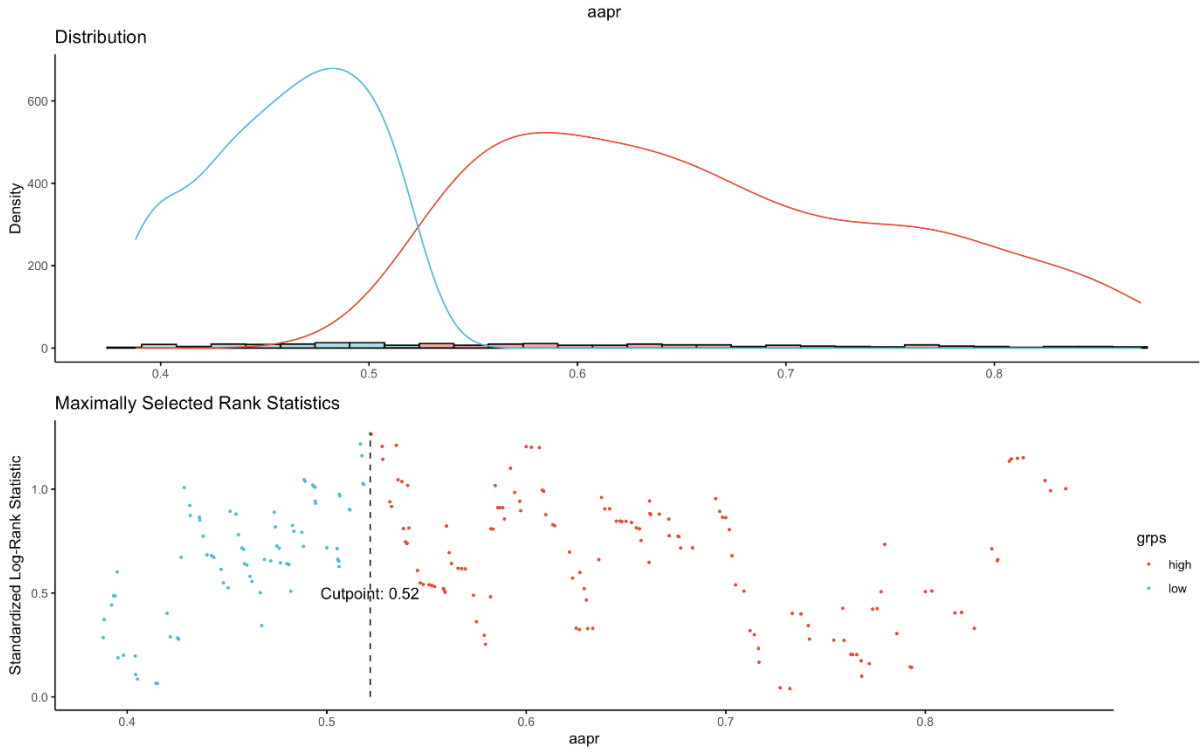
Table 1 Patient characteristics

	Numbers (%)
Number of patients	327
Sex	
Female	139 (42.5)
Male	188 (57.5)
Age (years); median (IQR)	61.8 (52.1–73.3)
Smoking	178 (54.4)
Alcohol use	164 (50.2)
BMI (kg/m^2); median (IQR)	21.9 (19.4–24.9)
Cancer location	
Tongue	181 (55.4)
FOM	47 (14.3)
Others	99 (30.3)
Tumor size	
T1	64 (19.6)
T2	116 (35.5)
T3	56 (17.1)
T4a	88 (26.9)
T4b	3 (0.9)
Nodal status	
Negative	140 (42.8)
Positive	187 (57.2)
Tumor stage	
I	51 (15.6)
II	69 (21.1)
III	68 (20.8)
IVa	124 (37.9)
IVb	15 (4.6)
Categorization of tumor	
Early stage	147 (45)
Advanced stage	180 (55)
Treatment options	
Surgery alone	76 (23.2)
Surgery with radiation	139 (42.5)
Surgery with chemoradiation	112 (34.3)
Recurrence	106 (32.4)

IQR=interquartile range

Survival outcomes and AAPR

Regarding biochemical markers, statistical analysis was performed using R software to determine the optimal cut-off value for the AAPR. Based on survival analysis, an AAPR of 0.52 was established as the most appropriate cut-off point. Accordingly, the cohort was divided into two groups: patients with an AAPR ≥0.52 were designated as the high AAPR group (N=208; 63.6%), and those with AAPR <0.52 were defined as the low AAPR group (Figure 1). The relationships between AAPR and clinicopathological characteristics are summarized (Table 2). Patients with low AAPR were significantly older than those with high AAPR (p-value=0.031), and bone erosion was more frequent in the low-AAPR group (p-value=0.029). Other clinicopathological variables did not differ significantly between the two groups. Although AAPR was a primary predictive factor in this study, a higher AAPR level (≥0.52) suggested a trend toward improved OS and DFS; however, the results did not reach statistical significance (OS: HR 0.84, 95% CI: 0.4, 1.78, p-value=0.652; DFS: HR 0.93, 95% CI: 0.44, 1.97, p-value=0.858). The 5-year OS and DFS rates were 84.6% and 55.33%, respectively. When stratified by AAPR, the 5-year OS rates in the AAPR <0.52 group and ≥0.52 group were 81.03% and 86.32%, respectively (Figure 2), while the 5-year DFS rates were 55.65% for the AAPR <0.52 group and 55.18% for the AAPR ≥0.52 group (Figure 3).



AAPR=albumin/alkaline phosphatase ratio

Figure 1 The optimal cut-off value for AAPR was obtained using R software, and an AAPR of 0.52 was established as the most appropriate cut-off point. Patients with an AAPR ≥0.52 were designated as the high AAPR group, and those with AAPR <0.52 were defined as the low AAPR group

Table 2 Association of AAPR with patient characteristics

Variables	AAPR <0.52 (N=119)	AAPR ≥0.52 (N=208)	p-value
Sex			0.498
Female	54 (45.4)	85 (40.9)	
Male	65 (54.6)	123 (59.1)	
Age (years)			0.031
<65	62 (52.1)	135 (64.9)	
≥65	57 (47.9)	73 (35.1)	
Cancer location			0.088
Tongue	58 (48.7)	123 (59.1)	
FOM	15 (12.6)	32 (15.4)	
Others	46 (38.7)	53 (25.5)	
Tumor stage			0.106
T1–T2	61 (51.3)	86 (41.3)	
T3–T4	58 (48.7)	122 (58.7)	
Nodal status			0.57
Positive	48 (40.3)	92 (44.2)	
Negative	71 (59.7)	116 (55.8)	
Categorization of tumor			1
Advanced stage	75 (63)	132 (63.5)	
Early stage	44 (37)	76 (36.5)	
Pathological result			0.986
SCCA Poor diff	30 (25.2)	54 (26)	
SCCA Well diff	89 (74.8)	154 (74)	
Extranodal extension			0.481
Negative	109 (91.6)	184 (88.5)	
Positive	10 (8.4)	24 (11.5)	
Lymphovascular invasion			0.992
Negative	101 (84.9)	178 (85.6)	
Positive	18 (15.1)	30 (14.4)	
Perineural invasion			0.894
Negative	101 (84.9)	174 (83.7)	
Positive	18 (15.1)	34 (16.3)	
Bony erosion			0.029
Negative	99 (83.2)	191 (91.8)	
Positive	20 (16.8)	17 (8.2)	
Tumor margin			0.673
<5 mm	43 (36.1)	69 (33.2)	
≥5 mm	76 (63.9)	139 (66.8)	

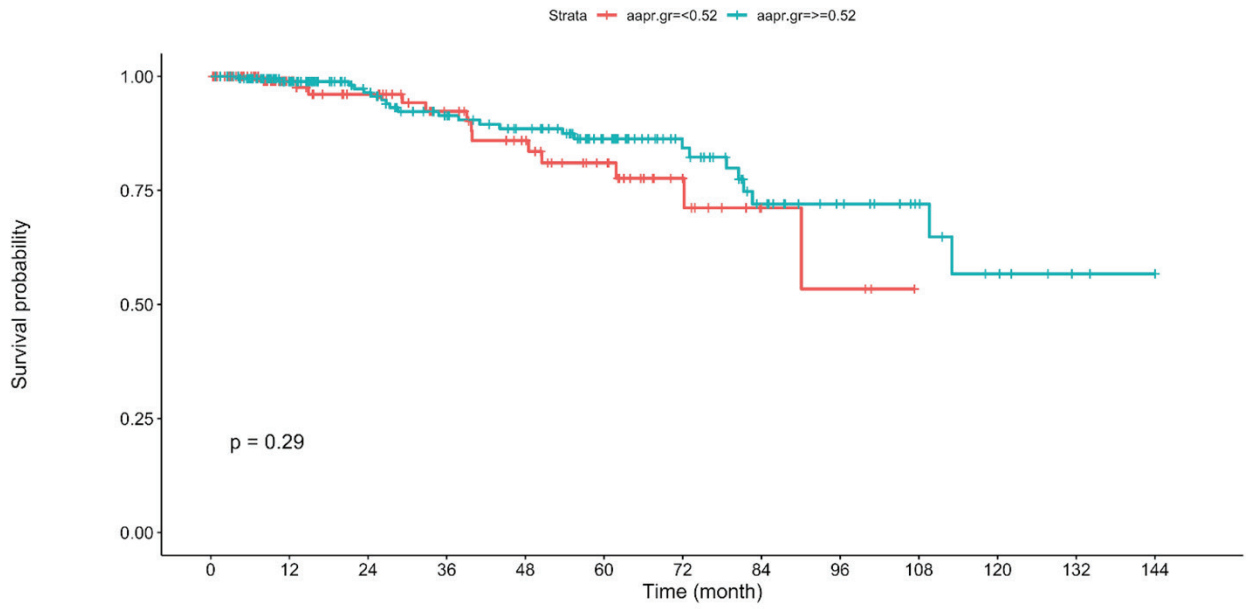
SCC=squamous cell carcinoma, AAPR=albumin/alkaline phosphatase ratio, IQR=interquartile range, diff=differentiated, FOM=floor of mouth

The median follow-up duration for the entire cohort was 21.45 months (IQR: 5.93–57.06). During the follow-up period, a total of 37 patients died due to the disease, with a median time to death of 35.51 months (IQR: 18.10–58.34), while 106 patients experienced treatment failure, including both locoregional recurrence and distant metastasis, with a median time to treatment failure of 4.86 months (IQR: 2.80–11.71). Univariate analysis, as shown in Table 3, revealed several significant prognostic factors for OS and DFS. Advanced age (≥65 years) emerged as

a significant unfavorable predictor (OS: HR 4.09, 95% CI: 2.01, 8.30, p-value<0.001; DFS: HR 3.74, 95% CI: 1.84, 7.63, p-value<0.001). Similarly, extranodal extension was an independent, significant adverse factor for both OS (HR: 4.16, 95% CI: 1.67, 10.35, p-value=0.008) and DFS (HR: 3.49, 95% CI: 1.42, 8.59, p-value=0.017). Other clinicopathological factors, such as tumor stage, depth of tumor invasion, nodal status, presence of perineural invasion, lymphovascular invasion, surgical margin, and pathological bony involvement, showed no significant association with survival outcomes. Multivariate analysis using Cox proportional hazards models was conducted to identify independent prognostic factors after adjusting for potential confounders. The analysis demonstrated that advanced age and extranodal extension maintained their prognostic significance as independent predictors of OS and DFS (Table 3).

Discussion

Patients with OSCC often develop cachexia, which is characterized by progressive weight loss, skeletal muscle deterioration, and malnutrition. Even in the early stages, patients with OSCC may experience inadequate nutritional intake due to functional impairments in mastication, deglutition, or oral consumption. This may lead to treatment interruptions and delays, ultimately affecting patient prognosis. Serum albumin is a popular biomarker for predicting survival in various malignancies, including hepatocellular carcinoma, prostate cancer, renal cell carcinoma, and colorectal cancer[17-20]. However, albumin may not serve as a definitive prognostic factor in isolation. Patients can improve their nutritional status prior to treatment once they receive guidance from physicians, whether through feeding tube insertion or

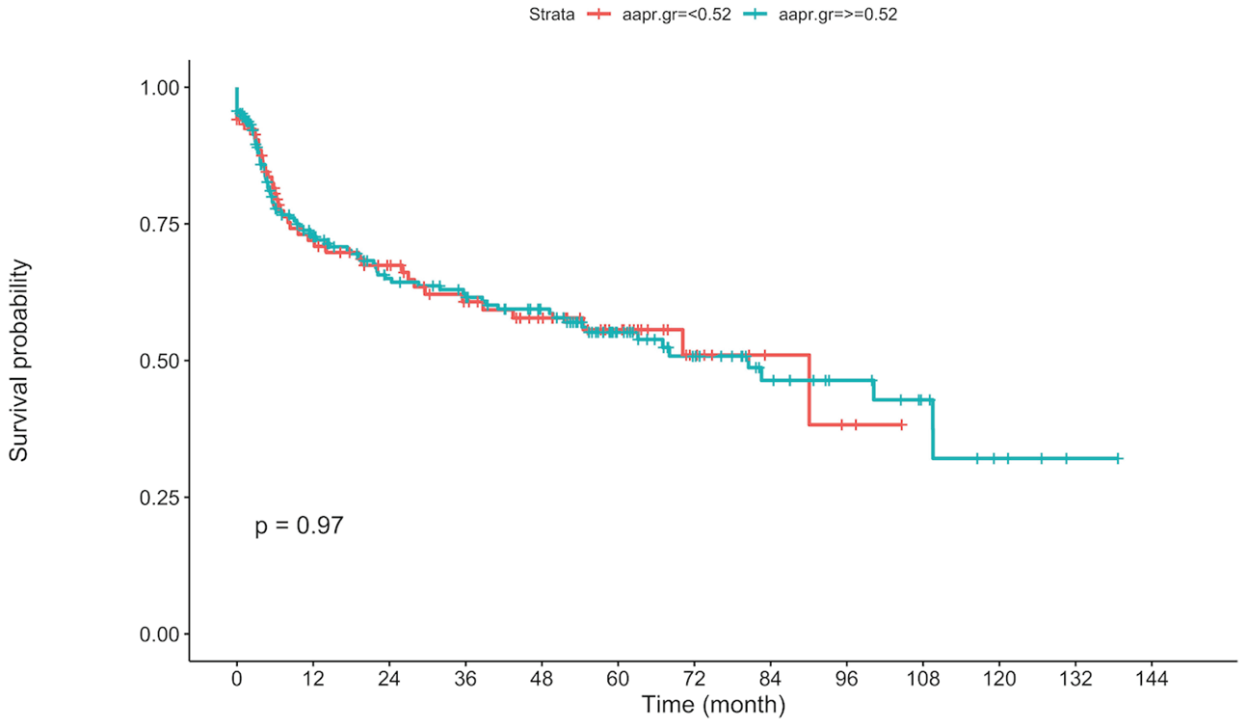


OSCC=oral squamous cell carcinoma, AAPR=albumin/alkaline phosphatase ratio

Figure 2 Overall survival curves based on the AAPR cut-off value of 0.52 in patients with OSCC (OSCC: oral squamous cell carcinoma; AAPR: albumin/alkaline phosphatase ratio)

nutritional supplementation. Therefore, rather than being a standalone predictive prognostic factor, nutritional deficits or poor nutritional status should be considered indicators for targeted nutritional interventions to optimize patient outcomes. ALP, a critical hydrolase enzyme expressed throughout the body with particularly high activity in the liver, bile ducts, bones, and kidneys, has also been demonstrated as a prognostic biomarker across various malignancies[21,22]. In head and neck cancer, the elevation of serum ALP predicts worse survival outcomes in patients with skeletal and/or liver metastasis of nasopharyngeal carcinoma[23,24]. In OSCC, increased ALP levels may reflect tumor burden and disease severity, although the precise prognostic value remains controversial.

AAPR has been proposed as a novel independent prognostic factor, as albumin serves as an indicator of nutritional and immunological status, whereas ALP correlates with tumor burden, liver function, and bone disorders. Earlier studies in nasopharyngeal carcinoma showed that a lower AAPR has been associated with inferior outcomes, potentially attributable to nutritional deficiency and immune response compromise or increased tumor-related metabolic activity[25–27]. Tsai et al.[28] conducted a study focusing on locally advanced OSCC and found a positive association between higher AAPR levels and survival outcomes, suggesting its potential role as a supplementary prognostic parameter in survival prediction models. While Tsai et al. focused primarily on locally advanced disease, our



OSCC=oral squamous cell carcinoma, AAPR=albumin/alkaline phosphatase ratio

Figure 3 Disease-free survival curves based on the AAPR cut-off value of 0.52 in patients with OSCC

Table 3 Univariate and multivariate analysis of the factors associated with OS and DFS

	5-year OS				5-year DFS			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
AAPR: ≥0.52 <0.52	0.68 (0.34, 1.35)	0.275	0.84 (0.4, 1.78)	0.652	0.8 (0.40,1.60)	0.539	0.93 (0.44,1.97)	0.858
Age (years): ≥65 <65	4.09 (2.01, 8.30)	<0.001	4.02 (1.87, 8.65)	<0.001	3.74 (1.84,7.63)	<0.001	3.52 (1.66, 7.46)	<0.001
Sex: Male Female	1.65 (0.83, 3.29)	0.144			1.67 (0.84,3.34)	0.135		
Stage: Early Advanced	0.63 (0.31, 1.25)	0.174			0.74 (0.37,1.47)	0.381		
Extranodal extension	4.16 (1.67, 10.35)	0.008	3.83 (1.47, 9.98)	0.014	3.49 (1.42,8.59)	0.017	3.61 (1.42, 9.22)	0.014
Bone erosion	2.06 (0.90, 4.70)	0.112			1.79 (0.78,4.09)	0.194		
Margin: ≥5 mm <5 mm	0.55 (0.29, 1.05)	0.077			0.55 (0.29,1.06)	0.079		
Subsite: Tongue Others	0.62 (0.32, 1.19)	0.144			0.62 (0.32,1.20)	0.155		

OS=overall survival, DFS=disease free survival, AAPR=albumin/alkaline phosphatase ratio, HR=hazard ratio, CI=confidence interval

cohort contained a substantial number of early-stage cases, allowing us to evaluate whether the prognostic significance of AAPR extends across the full clinical spectrum of OSCC. Despite these findings, comprehensive data across all disease stages remain limited in the current literature. We therefore aimed to bridge this gap by including patients from all stages who underwent a similar treatment paradigm to ensure clinical comparability with prior studies. Based on our comprehensive literature review and current understanding, we conducted the first retrospective study encompassing all stages of OSCC with curative intent to evaluate the potential prognostic significance of preoperative AAPR. Although AAPR is a simple and easy-to-use tool for initial risk stratification, our primary analysis did not demonstrate a statistically significant association between AAPR and OS or DFS. Clinically, this finding suggests that AAPR alone may not serve as a reliable prognostic biomarker across all OSCC stages. However, it may retain prognostic value in selected subgroups—particularly patients with advanced disease—where nutritional depletion, systemic inflammation, and tumor burden more profoundly influence outcomes. The determination of optimal AAPR cut-off values after merging albumin and ALP levels demonstrates that this new prognostic indicator varies across different malignancies and studies. For head and neck cancer, the optimal cut-off values also differ across studies. Nasopharyngeal carcinoma shows remarkable consistency in cut-off values across independent studies, varying from 0.44 to 0.48[25–27]. Additionally, 0.49 was established as the cut-off for locally advanced laryngeal and hypopharyngeal carcinoma[29].

These variations highlight the influence of tumor type, disease stage, and treatment modalities on the prognostic significance of AAPR. Interestingly, the optimal AAPR cut-off value in our study (0.52) was nearly identical to that reported by Tsai et al. (0.51)[28], suggesting the reproducibility of this threshold across independent cohorts. Regarding the cut-off selection method, we acknowledge that using the "surv_cutpoint" function in R software may raise concerns about potential data-driven bias. However, this approach, based on maximally selected rank statistics, is widely used in exploratory prognostic studies to identify clinically meaningful thresholds. To mitigate overfitting, we cross-validated our findings against the previously established cut-off of 0.51 from Tsai et al., demonstrating consistency in both value and prognostic trend. This concordance suggests that the derived cut-off is not arbitrary but reflects a reproducible biological relationship between AAPR and clinical outcome. Several plausible factors may explain our observed results. Despite our efforts to include all the stages of OSCC and achieve a larger sample size to represent the entire disease spectrum, the inherent heterogeneity of OSCC remains a challenge. Tumor characteristics and behavior vary considerably across different disease stages and anatomical subsites within the oral cavity, potentially influencing our findings. Moreover, as a single-center study, our patient population likely reflects the referral patterns, treatment protocols, and demographic composition unique to our institution. This may limit the external generalizability of the findings, particularly across centers with different patient profiles, surgical philosophies, or adjuvant therapy strategies. Future studies with larger, stage-stratified cohorts are warranted to confirm whether distinct AAPR thresholds should be applied for early versus advanced OSCC. Specifically, the relatively limited number of death and recurrence events in our study may have restricted the statistical power of multivariate models, resulting in wider confidence intervals and nonsignificant trends. AAPR possibly interacts with other prognostic factors or potential confounding variables, although our current analysis may have been underpowered to detect these complex interactions. A lower pretreatment AAPR is associated with worse clinical outcomes in locally advanced OSCC. In OSCC, a higher stage is related to lower albumin levels due to insufficient nutritional intake, while ALP is an important index for assessing liver and bone function, which may be affected by metastasis or neighboring bony erosion. In contrast, early-stage OSCC is less aggressive and may not severely affect nutritional status, which allows for better preservation of albumin and no distant metastasis that would impact ALP metabolism. Thus, the negative result does not diminish the clinical importance of AAPR but rather helps clarify its scope of application. Our findings indicate that AAPR may have limited prognostic utility when applied universally across all stages of OSCC, yet it could remain useful as part of an integrated prognostic framework combining other nutritional and inflammatory markers to refine risk stratification in advanced disease. Moreover, the optimal cut-off value of AAPR as a predictive factor may differ among various cancer stages and tumor subsites; this should be further explored. From a clinical standpoint, this finding is relevant for patient management. For early-stage OSCC, clinicians may place less emphasis on AAPR during risk assessment, focusing instead on established prognostic factors such as tumor stage, extranodal extension, and surgical margin status. Conversely, in advanced disease, a lower pretreatment AAPR may still serve as an indicator of impaired nutritional or metabolic reserve, supporting early nutritional intervention and closer postoperative monitoring.

Additionally, extranodal extension was a prognostic factor for OS and DFS, indicating inferior oncologic outcomes. Kang et al. also reported that extranodal extension is an independent prognosticator of survival endpoint[30]. Moreover, the present study showed that

advanced age is associated with unfavorable predictions for OS and DFS. Older patients often have comorbidities and frailty syndrome, which may contraindicate the use of cisplatin or lead to intolerance to the standard treatment protocol, necessitating treatment adaptations or changes to alternative strategies[31]. The most critical factor to consider is the potential influence of confounding variables, particularly the socioeconomic status (SES) of patients with OSCC, which may affect both albumin and ALP levels. Patients with head and neck cancer predominantly come from lower SES backgrounds and often experience significant delays in diagnosis and treatment initiation due to financial constraints, inadequate health insurance coverage, and limited access to specialized healthcare. However, in this retrospective study, detailed SES indicators such as income level, education, and insurance type were not uniformly available in the medical records and thus could not be incorporated into the statistical analysis. This represents a crucial gap for further research, as longitudinal tracking of this biomarker could provide more insights into disease progression and treatment response. These limitations should not be viewed as setbacks but rather as opportunities for more targeted and comprehensive investigations, highlighting the complex interplay of nutritional and inflammatory markers in patients with OSCC. Overall, while our findings confirm that AAPR alone may have limited prognostic significance across all stages, they help delineate the clinical context in which this biomarker remains useful—particularly in advanced disease—and underscore the need for integrated prognostic models combining AAPR with other inflammatory and nutritional indices. AAPR remains a simple and cost-effective biomarker with potential clinical utility when used in conjunction with other prognostic markers or within specific patient subgroups.

This study had some limitations. First, as a retrospective study, although we attempted to include all the stages of OSCC and achieve a larger sample size, its findings may be subject to selection bias and limited generalizability. Furthermore, the limited number of death and recurrence events in our cohort may have reduced the statistical power to detect weaker associations in multivariate models. Additionally, the inclusion of all disease stages without separate stratified analyses may have obscured potential stage-specific associations, which should be explored in future multicenter and prospective studies. Future prospective clinical trials and multicenter collaborations are needed to enhance the accuracy and applicability of these findings. Second, the presence of undetected chronic diseases, incomplete patient histories, including current medications from nearby hospitals, and substance use in some patients, as well as unmeasured confounding factors, such as SES and psychosocial stress, may have influenced the results. Third, the dynamic change in AAPR during the treatment course was unexplored, and its values might change throughout treatment. Moreover, whether fluctuations in AAPR over time can serve as a prognostic indicator is yet to be determined.

Conclusion

Pretreatment AAPR was not an independent prognostic factor for OS and DFS in patients with OSSC at all stages. The clinical application and optimal cut-off value of AAPR as a predictive factor in OSCC may vary across different tumor stages, which should be investigated. Advanced age and extranodal extension are associated with unfavorable OS and DFS, and these factors have prognostic value in patients with OSCC. They can also serve as initial risk stratification tools for these patients, estimating individual survival outcomes while considering personalized therapeutic modalities.

Ethics statement

The Ethics Committee at the Faculty of Medicine, Prince of Songkla University, approved the study protocol.

The reference number of the study approval was REC. 65-462-13-1. All participants were recruited and studied in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Acknowledgement

The authors thank Editage (www.editage.com) for editing the draft of this manuscript.

Conflict of interest

The authors declare no conflicting interests.

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