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RESEARCH ARTICLE

# Clinical Outcomes in Advanced Oral Cavity Cancer: A Retrospective Analysis

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## Abstract

**Background:** Advanced oral cavity squamous cell carcinoma (stage III–IV) carries a poor prognosis despite aggressive multimodal treatment. We performed a retrospective analysis of patients with advanced oral cancer to evaluate clinical characteristics and survival outcomes.

**Methods:** We identified 148 patients with stage III or IV oral cavity squamous cell carcinoma treated with curative intent. Demographic data, tumor features (TNM stage, subsites), and treatments (surgery, adjuvant radiotherapy, chemotherapy) were collected. Five-year overall survival (OS) and disease-free survival (DFS) were estimated using Kaplan-Meier methodology. Survival differences by stage, nodal status, tumor subsite, adjuvant therapy (chemotherapy or radiotherapy), age, and sex were compared with log-rank tests (significance threshold $p<0.05$).

**Results:** The cohort's mean age was 57 years (range 33–80); 84 patients (56.8%) were male. The majority of tumors were T4 (62.1% T4a/T4b), and 64.9% of patients had no nodal metastases (N0). Stage IV disease constituted 67.6% of cases. Most patients (89.2%) received postoperative radiotherapy, and 24.3% received adjuvant chemotherapy following surgery. The 5-year OS for the entire cohort was 62.2%. By stage group, 5-year OS was 66.7% for stage III versus 60.0% for stage IV (log-rank $p = 0.333$). Nodal status significantly influenced OS: N0 patients had 70.8% 5-year OS vs 46.2% for N+ ($p = 0.001$). Patients who received adjuvant chemotherapy had worse survival than those who did not (44.4% vs 67.9% 5-year OS, $p = 0.012$). All 16 patients who did not receive radiotherapy were alive at 5 years (100% OS), whereas those treated with radiotherapy had 57.6% 5-year OS ($p = 0.001$). Survival also differed by primary tumor subsite (log-rank $p = 0.038$). For example, tongue, hard palate, and maxillary tuberosity tumors had 100% 5-year OS (no deaths), whereas tumors of the upper gingivobuccal sulcus had only ~43% 5-year OS. Patient age was prognostic ($p = 0.007$), with the youngest group (30–39 years) achieving 100% 5-year OS versus ~46% in those aged 50–59. Sex was not significantly associated with OS ($p = 0.055$).

**Conclusion:** In this cohort of advanced oral cavity cancer, cervical nodal metastasis, tumor subsite, and younger age were associated with significantly better or worse survival outcomes, whereas overall stage (III vs IV) and patient sex were less discriminative. Multimodal therapy yielded an overall 5-year survival ~62%, which is favorable compared to historical averages. These findings underscore the need to optimize regional nodal control and tailor adjuvant therapy for high-risk pathological features in order to improve outcomes.

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**Keywords:** Advanced Oral Cavity Cancer, Oral Squamous Cell Carcinoma, Clinical Outcomes, Tumor Staging, Treatment Modalities, Prognostic Factors.

## 1. Introduction

Oral cavity squamous cell carcinoma is a prevalent malignancy worldwide, with especially high incidence in South Asia. Patients often present with locoregionally advanced disease (stage III or IV), which is associated with substantially reduced survival rates. Population-based statistics indicate that only ~35% of patients with stage IV oral cancer survive 5 years, compared to ~55% for stage III.[1–3]The presence of cervical lymph node metastases is one of the strongest adverse prognostic factors in oral cancer, correlating with a markedly increased hazard of death. Standard treatment for stage III–IV oral cavity cancers involves a combination of surgery and adjuvant therapy. Typically, en bloc resection of the primary tumor with neck dissection is performed, followed by postoperative radiotherapy (PORT) or chemoradiotherapy (POCRT) for patients with high-risk pathological features such as multiple positive nodes, extranodal extension, or positive margins. Despite advances in surgical techniques and adjuvant modalities, the 5-year survival in oral cavity cancer has remained in the range of 50–60% over recent decades. In this context, analyzing institutional outcomes can provide insights into prognostic factors and the effectiveness of current treatment approaches. Here we present a retrospective study of 148 patients with advanced (stage III–IV) oral cavity squamous cell carcinoma, focusing on patient characteristics, treatment patterns, and survival outcomes. We specifically examine the impact of stage, nodal status, tumor subsite, and adjuvant therapy on overall and disease-free survival. By identifying which factors most strongly influence prognosis in our cohort, we aim to inform risk stratification and management strategies for advanced oral cavity cancer in similar populations.

## 2. Methods and Materials

This retrospective cohort study included patients with advanced oral cavity cancer treated at a tertiary cancer center. We identified 148 consecutive patients diagnosed with stage III or IV squamous cell carcinoma of the oral cavity were excluded. Clinical data were obtained from medical records. Collected variables included age, sex, primary tumor subsite, TNM stage, and treatment details. Tumor subsites were categorized as buccal mucosa, lower gingivobuccal sulcus (lower GBS), upper gingivobuccal sulcus (upper GBS), retromolar trigone (RMT), maxillary tuberosity (MT), tongue, hard palate, and lip. All patients were staged with thorough physical examination and imaging (CT and/or MRI, with PET as indicated) prior to treatment.

All cases were reviewed in a multidisciplinary tumor board. Surgery was the primary treatment modality whenever feasible, consisting of wide excision of the primary tumor with appropriate margins and ipsilateral ± contralateral neck dissection. Adjuvant therapy was recommended based on pathological risk factors. In general, patients with pT4 disease, perineural invasion, lymphovascular invasion, or a single lymph node metastasis without extranodal extension received postoperative radiotherapy (typically 60–66 Gy to the primary site and neck). Patients with multiple positive nodes, extracapsular spread (ECS) of nodal disease, or positive surgical margins received postoperative concurrent chemoradiotherapy (generally cisplatin-based).

Descriptive statistics were used to summarize patient demographics, tumor characteristics, and treatments. Overall survival (OS) was defined as the time from diagnosis (or from surgery for surgical patients) until death from any cause. Disease-free survival (DFS) was defined as the time from primary treatment until the first tumor recurrence (locoregional or distant) or death, whichever occurred first. Patients alive (for OS) or alive without recurrence (for DFS) at last follow-up were censored. All patients had at least 5 years of potential follow-up or had a failure event within 5 years. Survival curves were estimated by the Kaplan-Meier method. Differences in survival between subgroups (by stage, nodal status, subsite, adjuvant chemotherapy, adjuvant radiotherapy, age group, and sex) were compared using the log-rank test. A two-sided p-value $< 0.05$ was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics (Version 25.0, Armonk, NY). This study was conducted with Institutional Review Board approval and in accordance with the principles of the Helsinki Declaration.

## 3. Results

A total of 148 patients met the inclusion criteria. The median age was 56 years (mean 56.95 ± 10.05), with a range of 33 to 80 years. Sixteen patients (10.8%) were under 40 years old, while the largest age bracket was 60–69 years (56 patients, 37.8%), followed by 50–59 years (52 patients, 35.1%). There was a male

predominance: 84 patients (56.8%) were male and 64 (43.2%) female.

By definition, all cases were locally advanced (stage III or IV). The primary tumor (T) stage distribution was: T2 in 16 patients (10.8%), T3 in 40 patients (27.0%), T4a in 68 patients (45.9%), and T4b in 24 patients (16.2%). Thus, nearly two-thirds of tumors (92/148) were T4 lesions (indicative of extensive tumor size and/or bone invasion). Cervical nodal involvement was present in 52 patients (35.1%); specifically, 96 patients (64.9%) were node-negative (N0), 44 (29.7%) had N1 disease, and 8 (5.4%) had N2 disease. By AJCC stage group, 48 patients (32.4%) had stage III disease and 100 patients (67.6%) had stage IV disease. (Stage IV cases included stage IVA and a few stage IVB; none had distant metastasis at diagnosis to be stage IVC.)

Regarding the primary tumor subsite, the buccal mucosa was the most common location (52 cases, 35.1%). Tumors of the gingivobuccal sulcus were also frequent, with 24 tumors (16.2%) in the lower gingivobuccal sulcus and 28 (18.9%) in the upper gingivobuccal sulcus. The retromolar trigone accounted for 20 cases (13.5%). Less common subsites included the anterior tongue (4 cases, 2.7%), hard palate (4 cases, 2.7%), maxillary tuberosity (4 cases, 2.7%), and lip (12 cases, 8.1%). The smaller subsite groups (tongue, palate, maxillary tuberosity) tended to present with advanced stage primarily due to nodal metastases rather than extremely large primaries, given the limited size of those anatomical sites.

All 148 patients underwent surgery as the primary treatment. Among them, 132 received postoperative radiotherapy, while the remaining 16 did not receive adjuvant radiotherapy due to personal financial constraints, despite our tumor board recommending it for all patients.Adjuvant systemic chemotherapy was administered to 36 patients, typically concurrently with radiation, for cases with indications such as extranodal extension, multiple positive lymph nodes, and/or positive margins according to the RTOG trial [4]. The remaining 112 patients (75.7%) did not require chemotherapy (they received postoperative radiotherapy alone or no radiotherapy). In summary, the treatment breakdown was: surgery + PORT in 96 patients (64.9%), surgery + POCRT in 36 (24.3%), and surgery alone in 14 patients (9.5%).

At a median follow-up of 60 months, 92 of the 148 patients were alive, yielding an estimated 5-year overall survival of 62.2% for the entire cohort. A total of 56 patients (37.8%) died within the 5-year follow-up period.

Survival outcomes differed by disease stage and nodal status. Patients with stage IV disease had slightly worse OS compared to those with stage III, although this difference was not statistically significant in our sample. The 5-year OS was 66.7% for stage III vs 60.0% for stage IV (log-rank $p = 0.333$). In contrast, nodal status had a pronounced impact on survival. Node-negative (N0) patients had a 5-year OS of 70.8%, whereas node-positive (N+) patients (combining N1–N2) had only 46.2% 5-year OS.This 24% absolute survival difference was statistically significant (log-rank $p = 0.001$). In other words, the presence of nodal metastases was associated with a markedly worse prognosis in our cohort.

Adjuvant therapy status was also associated with survival outcomes. Patients who received adjuvant chemotherapy (typically due to high-risk pathological features) had inferior survival compared to those who did not receive chemotherapy. Five-year OS was 44.4% for patients who received chemotherapy vs 67.9% for those who did not. This difference was statistically significant (log-rank $p = 0.012$). Similarly, patients who received adjuvant radiotherapy had a lower unadjusted 5-year OS (57.6%) compared to the small subset of patients who did not receive radiotherapy (100% 5-year OS). All 16 patients who omitted radiotherapy were alive at 5 years, whereas 56 of 132 patients (42.4%) who received radiation died within 5 years. This disparity reflects a selection bias, as the no-radiotherapy group consisted entirely of low-risk cases. Statistically, the radiotherapy vs no-radiotherapy groups showed a significant difference in OS (log-rank $p = 0.001$). It should be emphasized that this does not imply radiotherapy was detrimental; rather, those who required no radiation had intrinsically better prognosis.

We observed no significant difference in 5-year OS by primary tumor subsite in univariate analysis ($p > 0.05$ for overall comparison), although there were notable trends. Tumors of the gingivobuccal sulcus (particularly upper GBS) tended to have poorer survival rates than other subsites. For instance, among upper gum sulcus tumors, only about 42.9% of patients were alive at 5 years. In contrast, several subsites had 100% 5-year OS in our series (no deaths observed), including tumors of the tongue, hard palate, and maxillary tuberosity. Overall, the log-rank test for differences across all subsites suggested a statistically significant variation ($p = 0.038$); however, given

some subsite categories had very small samples, these results should be interpreted with caution. Conversely, the DFS analysis showed no significant differences across subsites ($p = 0.64$), suggesting that the OS finding may reflect competing risks or non-cancer mortality rather than subsite-specific tumor biology.

When stratified by age, younger patients fared better than older patients. Notably, all 8 patients in the youngest age group (30–39 years) were alive at 5 years (100% OS). In contrast, survival was roughly 50–60% in middle-aged groups. For example, patients aged 50–59 had a 5-year OS of ~46% (24 of 52 alive at 5 years). The differences among age groups were significant (log-rank p = 0.007)[20], indicating that younger age was associated with better survival. Patient sex did not significantly influence OS in this cohort: the 5-year OS was approximately 64% in males vs 59% in females (log-rank p = 0.055), a difference that did not reach statistical significance.

Disease-Free Survival (DFS) was analyzed to account for tumor recurrences in addition to mortality. The 5-year DFS for the entire cohort was 70.3%, meaning 104 of 148 patients remained free of disease at 5 years. A total of 44 patients (29.7%) experienced a DFS event (recurrence or cancer-related death) within 5 years. Because fewer events occurred for DFS than for OS, the Kaplan-Meier curve for DFS stayed above 50% throughout the 60-month follow-up; in fact, the median DFS was not reached at 5 years (more than half the patients had no recurrence by that time). The estimated mean DFS was 53.2 ± 1.3 months (95% confidence interval 50.7–55.8 months). By contrast, among patients who did have a recurrence or cancer death, the median time to event was around 24 months, indicating that most failures happened early.

Indeed, the timing of recurrences showed that the majority of failures occurred in the first 2–3 years after treatment. Approximately 80% of all recurrences in our cohort took place within the first 24 months post-surgery. After 3 years, the recurrence rate dropped substantially and the survival curves plateaued, suggesting late relapses were relatively uncommon. Figure 1B illustrates the DFS curve for all patients, which has an initial steep decline in the first 2 years and then flattens out, reflecting this pattern.

Subgroup analyses for DFS largely paralleled the OS findings. Stage IV disease was associated with significantly worse DFS compared to stage III. The 5-year DFS was 83.3% for stage III vs 64.0% for stage IV, and this difference was statistically significant (log-rank p = 0.027). Similarly, nodal status strongly influenced DFS: N0 patients had 79.2% 5-year DFS, whereas N+ patients had only 53.8%. This 25% absolute difference was highly significant (log-rank p < 0.001). The DFS curves by nodal status show a wide separation; for example, by 3 years post-treatment, roughly 25% of node-positive patients had relapsed (DFS ~75%), compared to <10% of node-negative patients relapsed by 3 years..

Adjuvant therapy effects on DFS were similar to those on OS. Patients who received chemotherapy had worse DFS than those who did not: 5-year DFS was 55.6% with adjuvant chemotherapy vs 75.0% without. This difference was significant (log-rank p = 0.012), reinforcing that the chemotherapy group represented a higher-risk subset. The DFS curves (Figure 1C) show more early failures in the chemo group; by 1 year, DFS was ~85% with chemo vs ~95% without, and by 3 years this gap widened (~60% vs ~80%). Adjuvant radiotherapy did not show a statistically significant impact on DFS, although the no-radiotherapy group again had a numerically higher 5-year DFS (~94% vs ~68%). In our data, 15 of 16 patients (93.8%) who did not receive radiation remained disease-free at 5 years, compared to ~68% (about 90 of 132) of those who received radiation. This difference did not reach significance (log-rank p = 0.055 for DFS by radiotherapy status), likely might be due to the small size of the no-RT group and its favorable composition. Notably, all 44 DFS events (recurrences) occurred in the radiotherapy group, since those were the higher-risk patients. The Kaplan-Meier curves illustrate that early on, the no-RT patients have a higher DFS, but given their low numbers, the confidence intervals were wide.

Overall, the incorporation of DFS analysis provides a more nuanced understanding of outcomes. While OS captures overall mortality, DFS specifically captures the burden of cancer recurrence. In this study, the 5-year DFS (70%) was higher than the 5-year OS (62%), suggesting that a proportion of patients died of causes unrelated to cancer or beyond the 5-year period, and/or that some recurrences were successfully salvaged without impacting 5-year OS. The patterns in DFS (worse with advanced stage and nodal metastasis) mirrored the OS patterns, underscoring the prognostic significance of these factors. Furthermore, the DFS data pinpoint that recurrences predominantly occur early (within 2 years), highlighting the importance of vigilant surveillance during the initial post-treatment years.

**Table 1.** *Demographic Characteristics of the Study Population (N = 148)*

| Characteristic | No. (%) |
|---|---|
| Age Group (y) | |
| 30–39 | 8 (5.4) |
| 40–49 | 16 (10.8) |
| 50–59 | 52 (35.1) |
| 60–69 | 56 (37.8) |
| 70–79 | 16 (10.8) |
| Sex | |
| Male | 84 (56.8) |
| Female | 64 (43.2) |

**Table 2.** *Clinical Characteristics of the Study Population (N = 148)*

| Characteristic | No. (%) |
|---|---|
| Tumor Size (T category, TNM) | |
| T2 | 16 (10.8) |
| T3 | 40 (27.0) |
| T4a | 68 (45.9) |
| T4b | 24 (16.2) |
| Nodal Status (N category, TNM) | |
| N0 | 96 (64.9) |
| N1 | 44 (29.7) |
| N2 | 8 (5.4) |
| Primary Tumor Site | |
| Buccal mucosa | 52 (35.1) |
| Lower gingivobuccal sulcus | 24 (16.2) |
| Upper gingivobuccal sulcus | 28 (18.9) |
| Retromolar trigone | 20 (13.5) |
| Maxillary tuberosity | 4 (2.7) |
| Tongue | 4 (2.7) |
| Palate | 4 (2.7) |
| Lip | 12 (8.1) |
| Binary Node Group | |
| N0 | 96 (64.9) |
| N+ | 52 (35.1) |
| Stage Group | |
| Stage III | 48 (32.4) |
| Stage IV | 100 (67.6) |
| Adjuvant Radiotherapy | |
| Yes | 132 (89.2) |
| No | 16 (10.8) |
| Adjuvant Chemotherapy | |
| Yes | 36 (24.3) |
| No | 112 (75.7) |

**Abbreviation:** *TNM, tumor-node-metastasis classification system.*

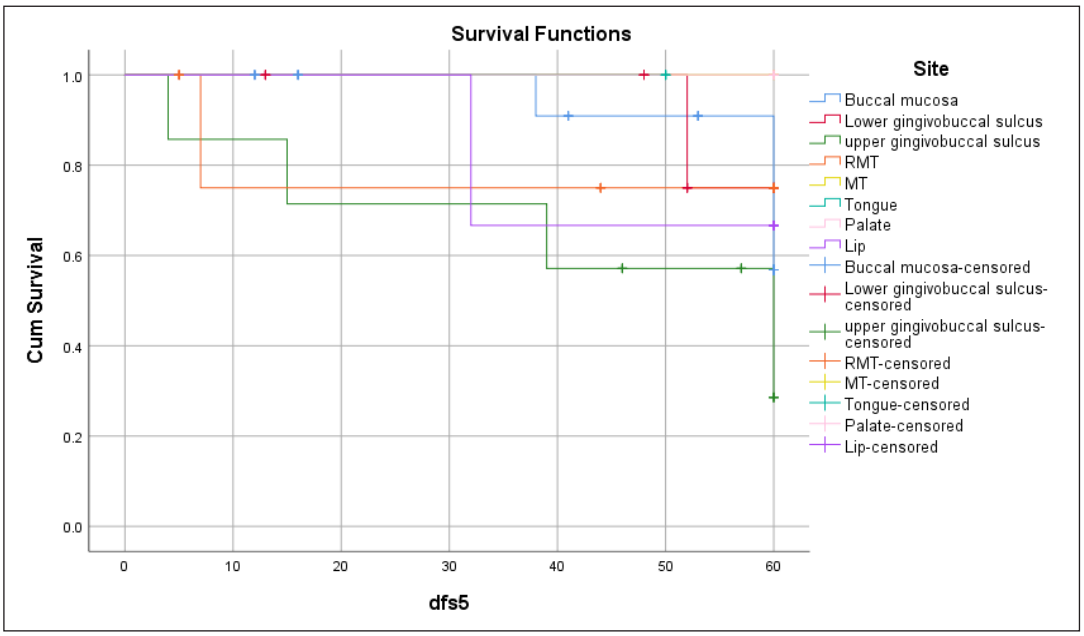


**Figure 1.** *Kaplan–Meier curve showing 5-year overall survival according to primary tumor site of oral cancer.*

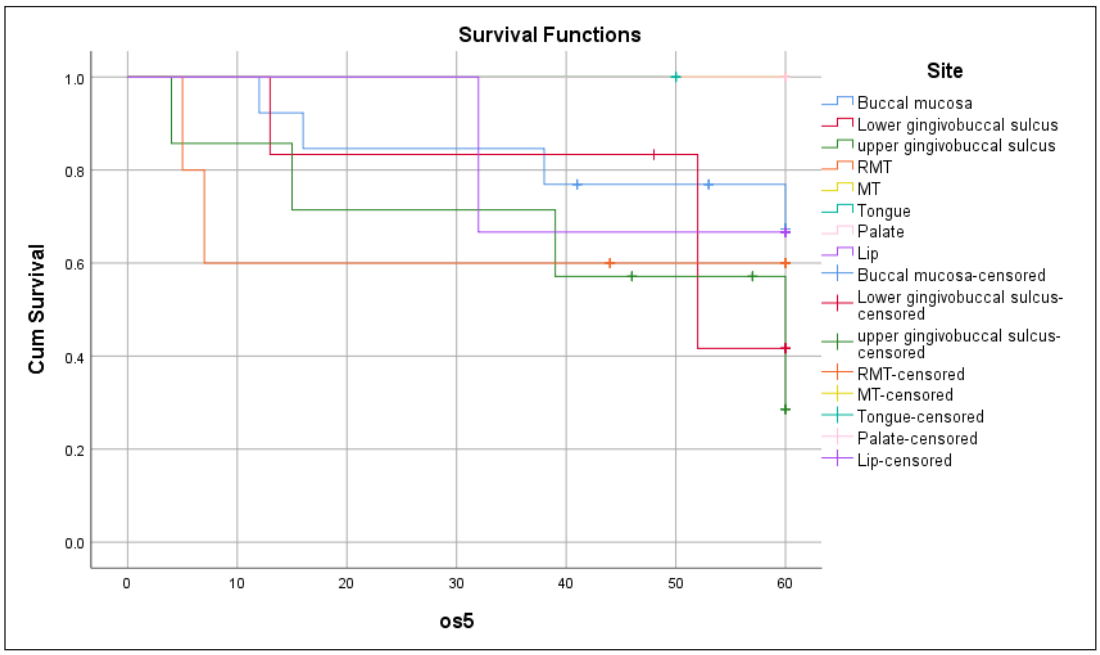


**Figure 2.** *Kaplan–Meier curve showing 5-year disease-free survival according to primary tumor site of oral cancer.*

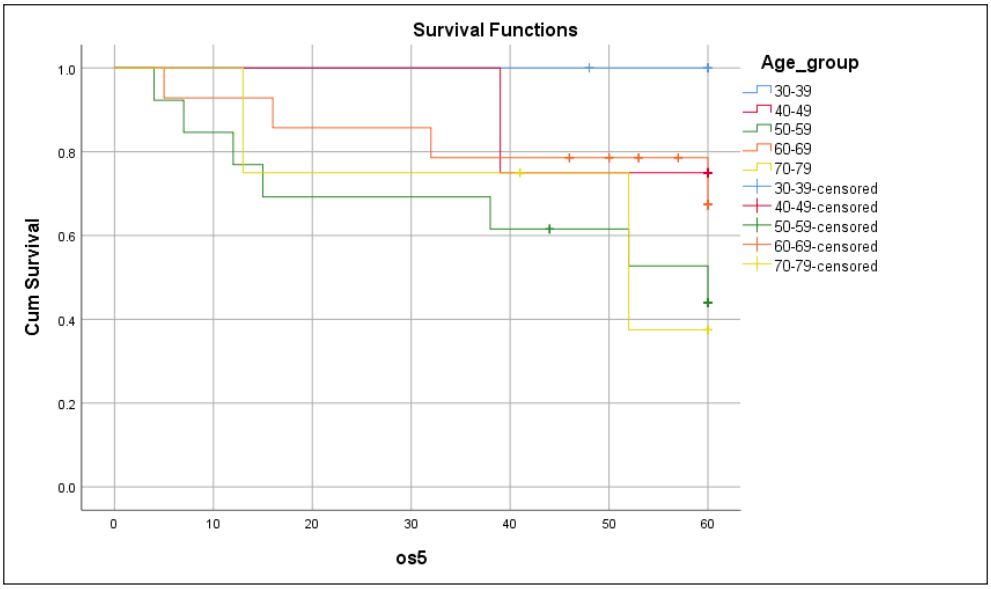


**Figure 3.** *Kaplan–Meier curve showing 5-year overall survival stratified by age group.*

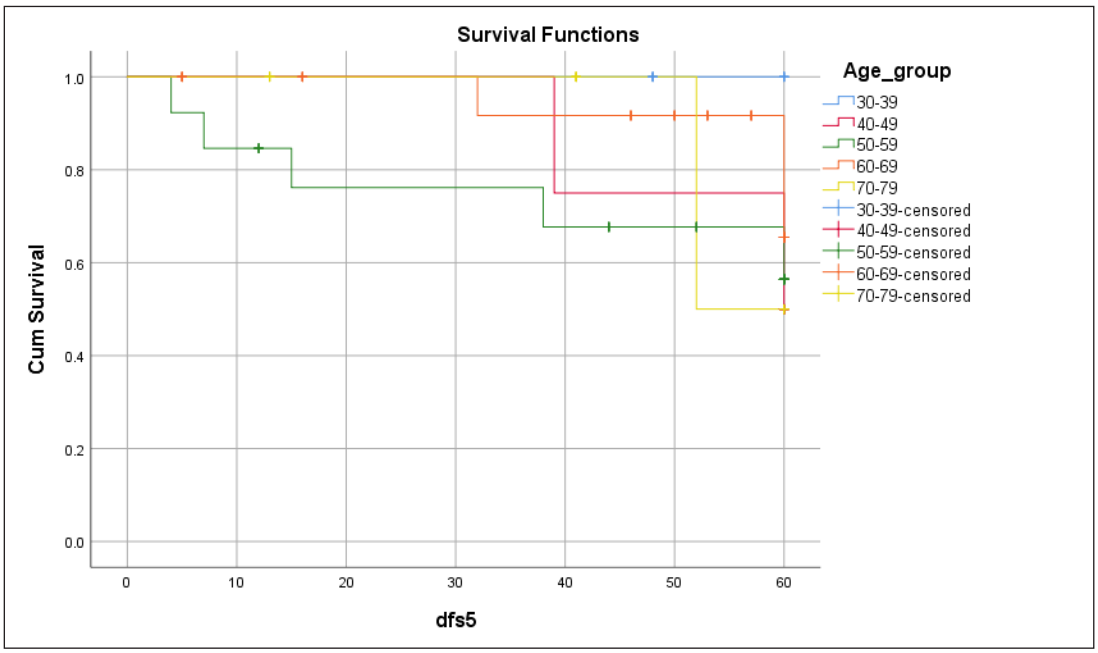


**Figure 4.** *Kaplan–Meier curve showing 5-year disease-free survival stratified by age group;*

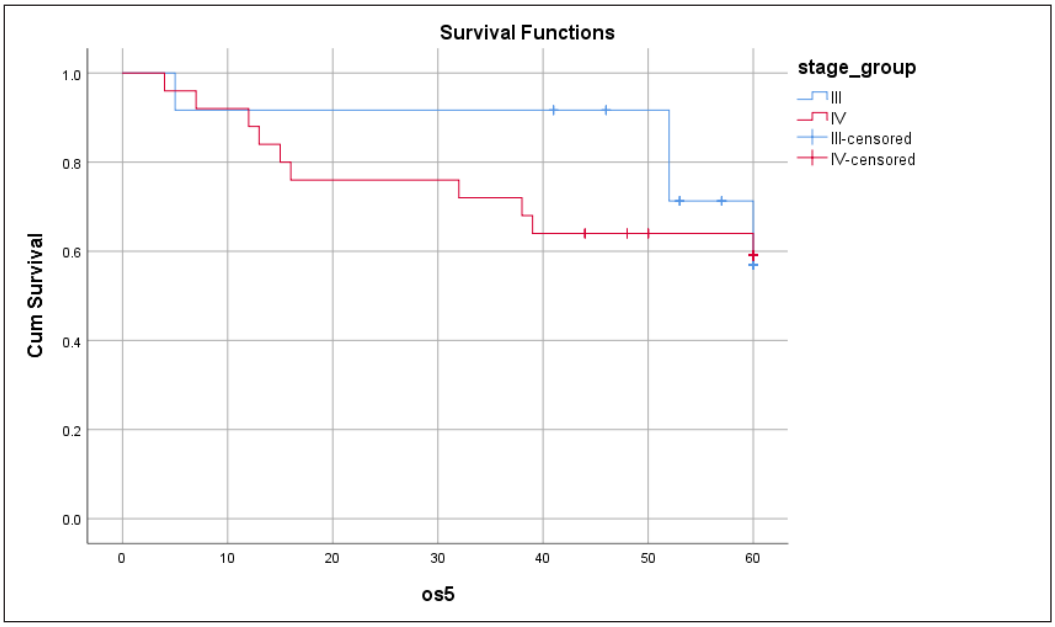


**Figure 5.** *Kaplan–Meier curve showing 5-year overall survival stratified by stage group (Stage III vs Stage IV).*

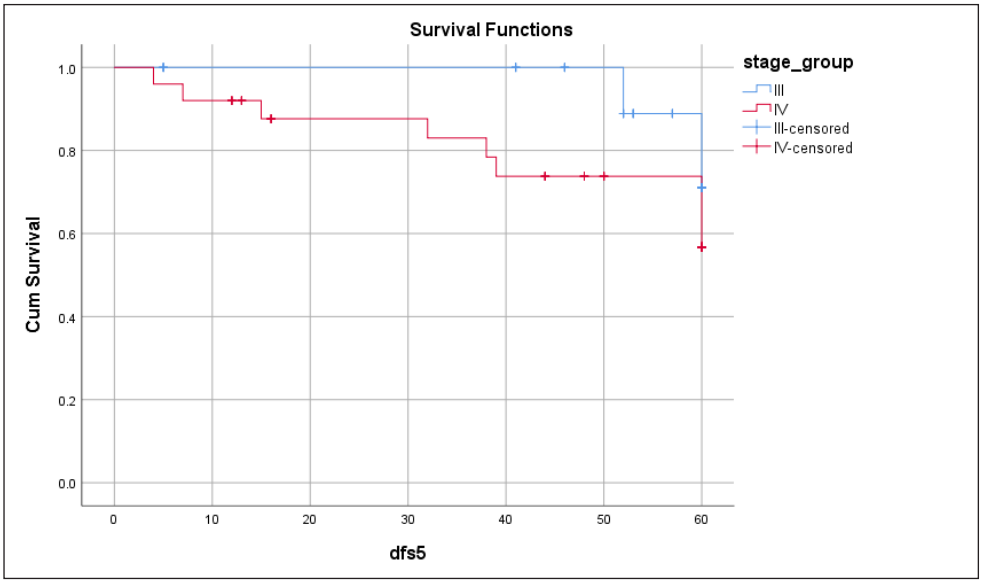


**Figure 6.** *Kaplan–Meier curve showing 5-year disease-free survival stratified by stage group.*

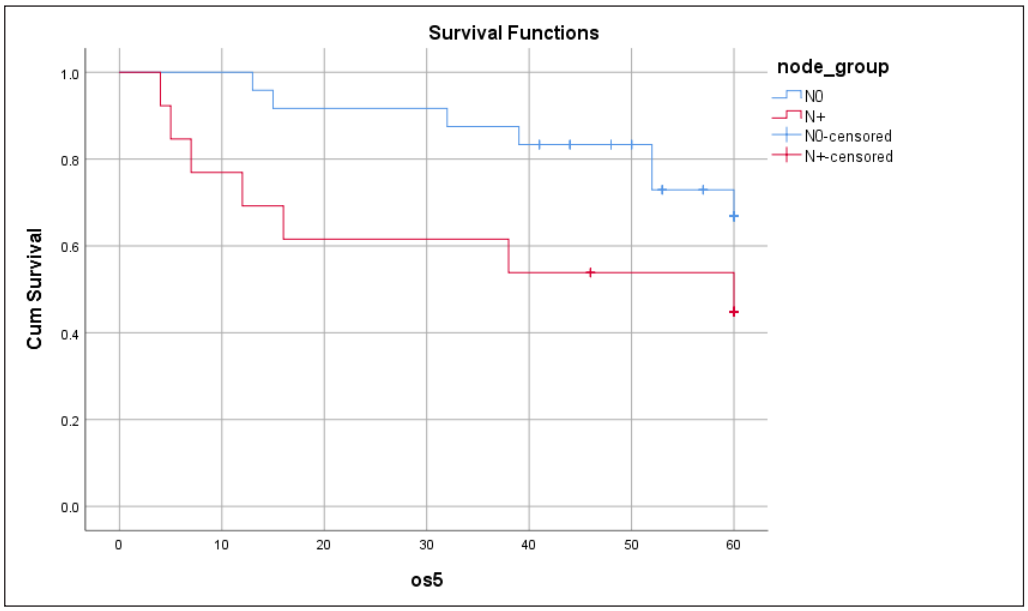


**Figure 7.** *Kaplan–Meier curve showing 5-year overall survival according to nodal status (N0 vs N+).*

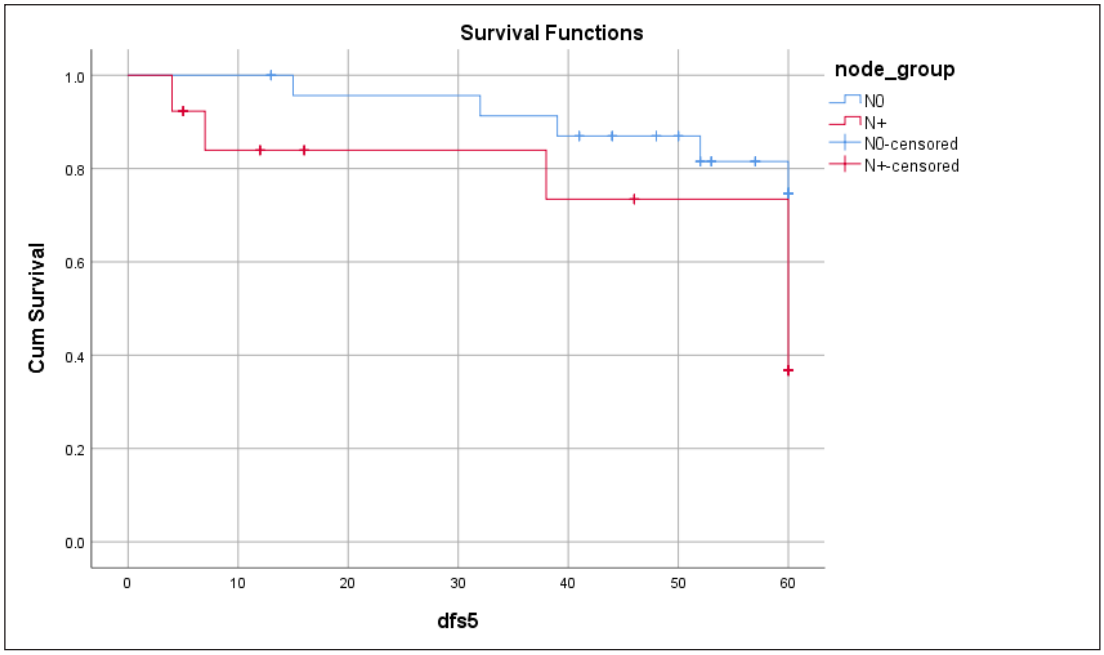


**Figure 8.** *Kaplan–Meier curve showing 5-year disease-free survival according to nodal status (N0 vs N+)*

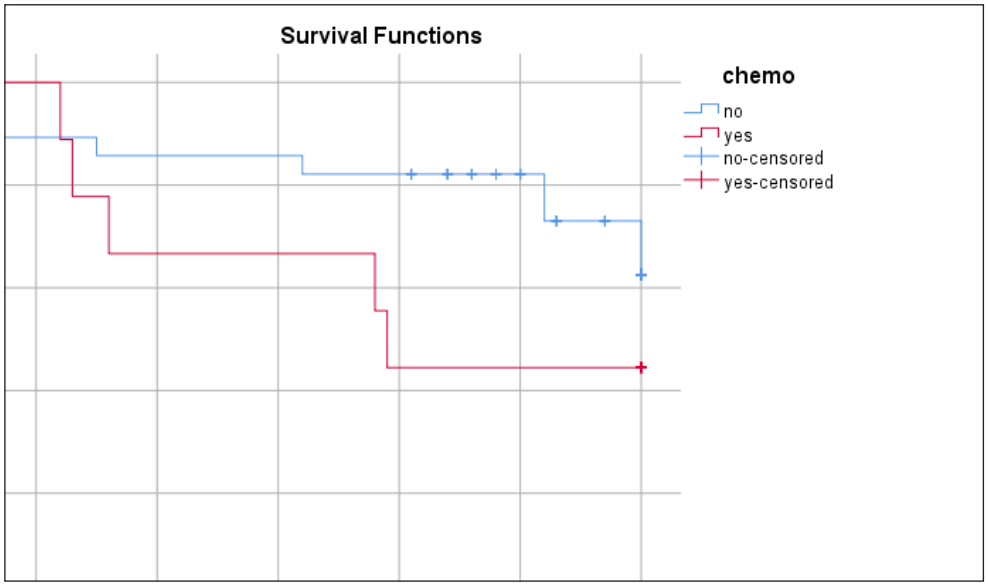


**Figure 9.** *Kaplan–Meier curve showing 5-year overall survival in patients treated with adjuvant chemotherapy compared with those who did not receive adjuvant chemotherapy.*

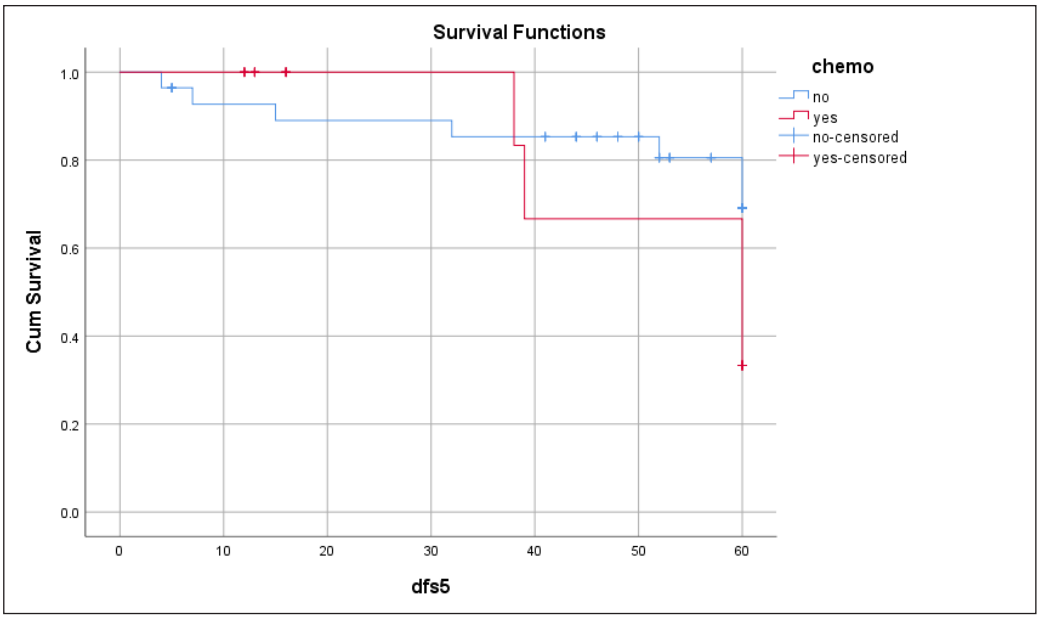


**Figure 10.** *Kaplan–Meier curve showing 5-year disease-free survival in patients treated with adjuvant chemotherapy compared with those who did not receive adjuvant chemotherapy*

## 4. Discussion

This study provides a comprehensive analysis of clinical outcomes in advanced-stage oral cavity cancer, with an emphasis on identifying prognostic factors affecting survival. We evaluated both overall survival and disease-free survival, which offers insight not only into mortality but also into patterns of recurrence after definitive treatment. Consistent with the broader literature, our findings confirm that cervical nodal metastasis and advanced tumor extent are key determinants of prognosis in oral cavity squamous cell carcinoma. Patients with nodal involvement had dramatically poorer outcomes than those without, which aligns with the well-established observation that the presence of cervical lymph node metastases can reduce 5-year survival by roughly half.[4,5,6] In our cohort, N0 patients had an approximately 25% higher absolute 5-year OS than N+ patients (70.8% vs 46.2%). This highlights the critical importance of early detection and effective management of neck disease. Aggressive control of regional lymph nodes – through comprehensive neck dissection and appropriate adjuvant therapy – is crucial for improving survival in advanced oral cancer.[7] Interestingly, overall AJCC stage (III vs IV) was not as strong a discriminator of survival in our series. The 5-year OS for stage IV patients was only modestly lower than for stage III (60% vs 66.7%, not significant). The modest survival difference between stages III and IV likely stems from the composition of our stage IV cohort. A considerable proportion of stage IV cases were T4N0 (stage IVA) – patients with very locally advanced primaries but no nodal spread – whose outcomes were closer to those of stage III patients. In other words, consistent with the literature emphasizing cervical nodal metastasis as the dominant prognostic factor—reducing 5-year survival by roughly half [5,6] a T4N0 tumor may have prognosis approaching that of a smaller tumor with nodal involvement (e.g., T1-2N1 stage III cases), resulting in overlapping survival curves for stages III and IV. This underscores that within "advanced stage," nodal status may be more prognostically significant than the T category or the numeric stage group per se. Primary tumor subsite emerged as a significant factor on univariate analysis of OS ($p = 0.038$), largely due to the especially poor outcomes in tumors of the upper gingivobuccal sulcus compared to other sites. However, in multivariate context and when accounting for stage and nodal status, we did not find an independent effect of subsite on survival. This suggests that the observed subsite differences were driven by the distribution of high-risk features (for example, many sulcus tumors were stage IV with nodal metastases). Our results are in line with other large studies reporting no significant survival difference by oral cavity subsite after adjustment for stage and other factors. In practical terms, this means that where in the oral cavity the tumor arises is less important than how advanced it is. An exception in the literature is tongue cancer in early stages, which some studies have noted can behave aggressively; but in advanced stages, subsite per is usually outweighed by stage and biological features.

Patient age was a notable prognostic factor in our cohort, with younger patients (30s) having excellent survival and older patients faring worse. Younger individuals may tolerate treatments better and have

fewer comorbid conditions, potentially contributing to their improved outcomes. Additionally, tumors in younger patients might have different biology or risk-factor profiles (for example, less association with chronic tobacco/alcohol use) that could influence survival favorably. Our finding that patients under 40 had 100% 5-year OS, versus around 50% in the 50–59 age group, underscores the impact of age on prognosis. However, age is of course a non-modifiable factor; its main implication is to ensure that older patients receive attentive supportive care to get them through aggressive therapy, and that comorbidities are optimally managed.

We found sex was not significantly associated with survival, although males had a slight survival advantage that did not reach statistical significance. Some population data have suggested marginal survival differences by sex in oral cancer (with females sometimes reported to do slightly better), but our sample did not demonstrate a meaningful sex-based disparity in outcomes. Therefore, sex does not appear to be a major prognostic factor in advanced oral cavity cancer, and both male and female patients should be treated with equally aggressive standard approaches.

Our analysis of adjuvant therapy effects needs to be interpreted in the context of indication bias. Patients who received postoperative radiation and/or chemotherapy did so because they had high-risk pathological features – features that inherently predict worse outcomes. Thus, it is not surprising that the crude survival of the adjuvant therapy groups was lower. Importantly, the subgroup of patients who did *not* receive radiotherapy (just 16 patients) had an excellent outcome (100% 5-year OS and ~94% 5-year DFS), but these were uniformly low-risk cases (mostly stage III, margin-negative, no ECS, etc.). This creates a stark contrast with the radiotherapy group, where 42% died by 5 years, yielding a significant difference on Kaplan-Meier analysis. One might misinterpret this to mean "radiotherapy caused worse survival," but in reality it reflects selection – those needing radiation had aggressive disease and higher likelihood of failure. In fact, it is likely that PORT improved the outcomes of those high-risk patients, even though their survival was still worse than that of low-risk patients.[7,8] The same reasoning applies to chemotherapy: patients requiring chemoradiation (due to ECS or multiple nodes) had significantly poorer survival than those who did not require chemotherapy. Adjuvant chemotherapy itself did not seem to "rescue" their outcomes, which remained poor (only 46% 5-year OS). This suggests that current standard chemotherapy (e.g. cisplatin) is not sufficient to overcome the adverse prognosis conferred by features like extranodal extension. New systemic therapies (such as immune checkpoint inhibitors or targeted agents in the adjuvant setting) may be needed to improve outcomes in this very high-risk subgroup[9,10]. Our data reinforce that the necessity for adjuvant chemotherapy is essentially a marker of aggressive disease – these patients should be considered for clinical trials or novel adjunctive treatments to try to improve survival.

One noteworthy observation is that all 16 patients who did not receive radiotherapy were alive and disease-free at 5 years. These patients could not receive radiotherapy due to personal financial constraints, despite our tumor board unanimously advising adjuvant radiotherapy for all of them. But this group's outcomes demonstrate that surgery alone was curative for appropriately selected early-stage III cases. It also underscores that omission of adjuvant therapy was confined to just 16 patients—a tiny fraction of the cohort, all with low-risk features who faced insurmountable financial barriers despite unanimous tumor board recommendation—and thus cannot be generalized to broader populations or routine clinical practice. The excellent survival of the no-RT group should *not* be interpreted as evidence that radiotherapy is unnecessary; rather, it indicates that we correctly identified which patients could safely be observed. Conversely, despite PORT, the majority of advanced cases still did well (nearly 58% 5-year OS and 68% 5-year DFS in radiated patients). Failures in the radiotherapy group included locoregional recurrences and distant metastases. It is possible that without radiotherapy, many of those locoregional failures would have occurred even earlier or in greater numbers. Thus, the data mainly reflect that underlying risk factors drive outcomes: patients with adverse features have worse survival despite appropriate therapy, and those without such features do very well with less treatment.

The inclusion of disease-free survival in our analysis provides additional perspective. We observed that DFS was about 8% higher than OS at 5 years (70% vs 62%), indicating that some patients died of non-cancer causes or beyond the 5-year window. Additionally, examining DFS allowed us to determine that most recurrences happen early, within 2 years post-treatment. This finding underscores the importance of intensive surveillance in the first couple of years after therapy[11]. Patients should be closely monitored during this period – with frequent clinical examinations and

perhaps imaging – to detect recurrences when they are potentially salvageable. After about 3 years, the risk of relapse drops considerably, which could inform follow-up scheduling (though lifelong follow-up is still advisable given the risk of second primary tumors in head-neck cancer patients).

In summary, this study highlights the critical prognostic impact of nodal metastases and other high-risk tumor features in advanced oral cavity cancer. It also demonstrates that with modern multimodal treatment, long-term survival around 60% can be achieved even in stage III–IV disease, which is somewhat higher than historical survival rates of advanced oral cancer (on the order of 35–50%)[3,12]. This improvement may reflect advances in surgical techniques, reconstruction, and adjuvant therapy delivery over time, as well as aggressive management of the neck. Nonetheless, a significant subset of patients still relapse early and succumb to disease, indicating room for improvement. Future efforts should focus on personalized therapy – for instance, using molecular or genomic markers to identify patients at highest risk of failure who might benefit from novel adjuvant treatments. Additionally, prevention and early detection remain paramount: improving public awareness and screening could shift more presentations to an earlier stage, where 5-year survival is substantially better. Our results, showing stark contrasts between outcomes in early vs advanced presentations, reinforce the survival advantage of catching oral cancer before extensive spread.

## 5. Conclusion

In advanced oral cavity cancer, the presence of nodal metastases, the tumor's anatomical site, and patient age significantly affect survival outcomes, whereas overall stage group (III vs IV) and sex are less predictive in this cohort. With combined modality therapy (surgery and appropriate adjuvant treatment), we achieved a 5-year overall survival of ~62%, exceeding some historical benchmarks for advanced oral cancer. However, patients with high-risk pathological features (e.g. extranodal extension, multiple nodes, positive margins) continue to have high rates of early recurrence and mortality despite standard chemotherapy and radiotherapy – indicating that current adjuvant treatments are insufficient for this subgroup. Innovative strategies (such as immunotherapy or targeted therapies in the adjuvant setting) are needed to improve disease-free survival for these high-risk patients. Meanwhile, emphasis on early-stage detection will improve overall outcomes, as evidenced by the much better survival in patients with lower tumor burden. In conclusion, our study underlines the importance of both OS and DFS as complementary endpoints: OS captures ultimate patient survival, while DFS reflects success in preventing recurrence. Both measures together provide a comprehensive view of prognosis and can guide future improvements in therapy and post-treatment surveillance for advanced oral cavity cancer.

## 6. References


1. Bobdey S, Sathwara J, Jain A, al. et. Squamous cell carcinoma of buccal mucosa: an analysis of prognostic factors. South Asian Journal of Cancer [Internet]. 2018;7:49. Available from: https://doi.org/10.4103/sajc.sajc_317_16.
2. Ansarin M, De Berardinis R, Corso F, al. et. Survival outcomes in oral tongue cancer: a mono-institutional experience focusing on age. Frontiers in Oncology [Internet]. 2021;11:616653. Available from: https://doi.org/10.3389/fonc.2021.616653.
3. Listl S, Jansen L, Stenzinger A, Fröhling S, Hoffmeister M, Herpel E, et al. Survival of patients with oral cavity cancer in Germany. PLOS ONE [Internet]. 2013;8. Available from: https://doi.org/10.1371/journal.pone.0053415.
4. Bernier J, Cooper JS, Pajak TF, van Glabbeke M, Bourhis J, Forastiere A, et al. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. New England Journal of Medicine [Internet]. 2004;350:1945. Available from: https://doi.org/10.1056/nejmoa032641.
5. Arduino PG, Carrozzo M, Chiecchio A, Broccoletti R, Tirone F, Borra E, et al. Clinical and Histopathologic Independent Prognostic Factors in Oral Squamous Cell Carcinoma: A Retrospective Study of 334 Cases. Journal of Oral and Maxillofacial Surgery [Internet]. 2008 [cited 2025 Sep];66:1570. Available from: https://doi.org/10.1016/j.joms.2007.12.024.
6. Struckmeier A,Buchbender M, Lutz R, Kesting M. Improved recurrence rates and progression-free survival in primarily surgically treated oral squamous cell carcinoma – results from a German tertiary medical center. Clinical Oral Investigations [Internet]. 2024 [cited 2025 Oct];28. Available from: https://doi.org/10.1007/s00784-024-05644-z.
7. Wichmann G, Pavlychenko M, Willner M, Halama D, Kuhnt T, Kluge R, et al. Standardized Diagnostic Workup and Patient-Centered Decision Making for Surgery and Neck Dissection Followed by Risk-Factor Adapted Adjuvant Therapy Improve Loco-Regional Control in Local Advanced Oral Squamous Cell Carcinoma. Frontiers in Oncology [Internet]. 2021 [cited 2025 Aug];11. Available from: https://doi.org/10.3389/fonc.2021.737080.

8. Harley RJ, Iheagwara UK, Faraji F, Sridharan S, Kubik MW. Postoperative radiotherapy and survival in oral cavity squamous cell carcinoma with mandibulectomy. JAMA Otolaryngology–Head & Neck Surgery [Internet]. 2024;150:233. Available from: https://doi.org/10.1001/jamaoto.2023.4444.

9. Uppaluri R, Haddad RI, Tao Y. Neoadjuvant and adjuvant pembrolizumab in locally advanced head and neck cancer. New England Journal of Medicine [Internet]. 2025;393:37. Available from: https://doi.org/10.1056/nejmoa2415434.

10. Yaniv D, Seiwert TY, Margalit DN. Neoadjuvant chemotherapy for advanced oral cavity cancer. CA: A Cancer Journal for Clinicians [Internet]. 2024;74:213. Available from: https://doi.org/10.3322/caac.21829.

11. Justesen MM, Stampe H, Jakobsen KK, Andersen AO, Jensen JM, Nielsen KJ, et al. Impact of tumor subsite on survival outcomes in oral squamous cell carcinoma: A retrospective cohort study from 2000 to 2019. Oral Oncology [Internet]. 2024;149:106684. Available from: https://doi.org/10.1016/j.oraloncology.2024.106684.

12. Kowalski LP, de Oliveira MM, López RVM, al. et. Survival trends of patients with oral and oropharyngeal cancer treated at a cancer center in São Paulo, Brazil. Clinics (São Paulo) [Internet]. 2020;75. Available from: https://doi.org/10.6061/clinics/2020/e1507.