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# Survival rate and prognostic factors of oral squamous cell carcinoma in Indonesia: A single-center retrospective study

**Research Article**

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**Abstract:** **Background:** Oral squamous cell carcinoma (OSCC) is the sixth most common malignancy in Asia. Most patients in Cipto Mangunkusumo Hospital have been diagnosed with an advanced stage. There had not been any survival study for OSCC in Indonesia. This study aimed to investigate the survival rate and prognostic factors of OSCC in Cipto Mangunkusumo Hospital.

**Methods:** A retrospective cohort study was conducted on OSCC patients diagnosed and treated in Cipto Mangunkusumo Hospital from 2014 to 2018. Data regarding age, gender, site of the primary lesion, clinical stage of the disease, tumor differentiation, invasion, and surgical margins were collected. The main outcomes measured were overall survival (OS) and disease-specific survival (DSS). The predictors of survival were then determined.

**Result:** 169 patients were included. The majority of patients were male (51.5%) and above 50 years old (55.6%). The most prevalent tumor site was the tongue (72.8%) followed by buccal mucosa (13%). The majority (82.2%) of patients had advanced (clinical stage IV) disease at diagnosis. A smaller majority of patients had a well-differentiated tumor (60.4%) and a low-grade tumor (53.8%). The worst one-year and two-year overall survival rates were found in the stage IV group (53.5% and 37.5%, respectively). The disease-specific survival rate was 66.9%.

**Conclusion:** The one-year and two-year overall survival rates of OSCC in Cipto Mangunkusumo Hospital were 58.6% and 43.1%. Moreover, clinical stage, tumor size, and lymph node involvement were the most significant prognostic factors for OSCC.

**Keywords:** *oral cancer • squamous cell carcinoma • prognosis • survival • Indonesia*

## 1. Introduction

Oral carcinoma is the sixth most common malignancy in Asia[1]. Based on GLOBOCAN 2018, there are 213,637 new cases, mostly found in South and Middle Asia. It has caused 177,000 deaths in 2018[2]. Oral squamous cell carcinoma (OSCC) is the most frequent histopathological finding (84–97%)[2]. The most common site for OSCC in Asia is buccal mucosa; meanwhile, in Europe and America, OSCC was most frequently found in the tongue[3]. Based on registration data at Cipto Mangunkusumo Hospital (Jakarta, Indonesia), the majority of OSCC was also found in the tongue (68.6%).

Le Campion in Brazil has conducted research and found that the one-, two-, and five-year survival for OSCC was 59.9%, 40.7%, and 27.8%, respectively[4]. Lohia et al. in India noted that the five-year overall survival for OSCC was 88%[5]. There are some factors correlated with OSCC survival. Based on clinical staging, a study from Liang Lo et al. in Taiwan stated that the five-year

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survival of OSCC is 75%, 65.6%, 49%, and 30% (stage I, II, III, and IV, respectively)[6]. A study from Dissayanaka et al. in Sri Lanka stated that the five-year survival based on anatomic location was 65.9% for buccal mucosa and 34.1% for tongue[7]. Meanwhile in India, Thavarool et al. reported that the five-year survival for OSCC based on lymph node involvement was 79% in the negative lymph node group and 59% in the positive lymph node group[8]. Based on research done in Memorial Sloan Kettering Cancer Center; age, comorbid diseases, surgical margin, lymphovascular and perineural involvement, and pathological staging of the tumor and lymph node (pT and pN) were independent prognostic factors of OSCC overall survival ($p < 0.05$)[9]. Tumor location, clinical staging, histologic grade, and tumor invasion pattern were also said to correlate with the five-year survival of OSCC[10]. In Indonesia, there has not been any study regarding the survival of OSCC. Cipto Mangunkusumo Hospital is a national referral hospital in Indonesia. The majority of patients arrived at the hospital in an advanced stage; this condition resulted in high-cost therapy and patients became permanently disabled. Hence, this study aimed to investigate the survival rate of OSCC in Cipto Mangunkusumo Hospital and its prognostic factors in the hope of improving the outcome for the patients.

## 2. Patients and Methods

A retrospective cohort study was conducted on OSCC patients registered in the Surgical Oncology Division, Department of Surgery ot Cipto Mangunkusumo Hospital from January 2014 to December 2018. Primary surgical resection, with or without neck dissection, was carried out for most of the early-stage ancers. Combined radiotherapy or chemotherapy was administered for advanced-stage cancers. OSCC patients who were diagnosed an accurate biopsy and treated accordingly were included in this study. Patients with residual tumors, patients who were diagnosed in 2018 yet didn't have any outcome until December 2019, and loss to follow-up patients were excluded from our study. This study protocol had been approved by the ethics committee on medical research of the Faculty of Medicine, Universitas Indonesia with the following registration number: ND-1035/UN2.F1/ETIK/PPM.00.02/2020.

The main outcome of this study was to calculate the overall survival and disease-specific survival. OS is defined as the duration from the time of diagnosis until death due to the disease. Disease-specific survival is defined as the percentage of patients who are still alive or dead due to a cause other than OSCC.

Data regarding age, gender, site of the primary lesion, clinical stage of the disease, tumor differentiation, tumor invasion, and surgical margins were also obtained. The clinical stage of OSCC in this study was based on the TNM staging system of the 8th edition of AJCC. Tumor differentiation was based on Broder's and WHO classifications evaluated by pathologists from the Department of Anatomic Pathology. Tumor invasion was evaluated as a parameter of invasive front grading based on Bryne's classification.

All data were analyzed using SPSS version 20. OS and DSS outcomes were calculated using the Kaplan-Meier method followed by log-rank (Mantel-Cox) analysis. Firstly, we determined the time-to-event, which is the duration from the time of diagnosis until the death of the patient. The data was then arranged on the basis of the duration of observation, ranging from the shortest to the longest duration. The prognostic variables were identified with multivariate analysis using the Cox regression method.

## 3. Results

One hundred sixty-nine OSCC patients were included in this study. The majority (55.6%) of patients were >50 years old, 51.5% of them were male (Table 1). The most prevalent tumor site was the tongue (72.8%) followed by buccal mucosa (13%). The majority (82.2%) of patients presented with the most advanced disease (stage IV) at diagnosis. The majority of patients had a well-differentiated tumor (60.4%) and a low-grade tumor (53.8%). There were 42 subjects who underwent surgery, of which 54.8% were female; 54.8% were >50 years old; 73.8% had a tumor on the tongue; and 61.9% were in stage IV. There were 61.9% who had a well-differentiated tumor, and 54.8% who had a low-grade tumor. Clear surgical margins were achieved in 92.9% of subjects. Of 24 subjects that didn't survive, 3 subjects had positive surgical margins, 18 subjects were in stage IV, and 4 subjects were in the N2 stage.

The one-year and two-year overall survival of OSCC patients in Cipto Mangunkusumo Hospital were 58.6% and 43.1%. The average survival was 9.4 months (95% CI: 8.88–10.09).

The one-year survival rates for stage I, II, III, and IV were 66.7%, 90%, 76.4%, and 53.5%, respectively (Figure 1), with $p = 0.161$. The two-year survival rates were 66.7%, 66.5%, 76.4%, and 36.1% for stage I, II, III, and IV, respectively (Figure 2), with $p = 0.148$.

The disease-specific survival rate of OSCC patients in Cipto Mangunkusumo Hospital was 66.9%. Based on clinical staging, the disease-specific survival rate for

Table 1: Baseline characteristics of OSCC patients in Surgical Oncology Division, Department of Surgery from 2014 to 2018.

| Characteristic | N | % |
|---|---|---|
| **Age** | | |
| - **≤50 years old** | 75 | 44.4 |
| - **>50 years old** | 94 | 55.6 |
| **Gender** | | |
| - **Male** | 87 | 51.5 |
| - **Female** | 82 | 48.5 |
| **Tumor location** | | |
| - **Tongue** | 123 | 72.8 |
| - **Buccal mucosa** | 22 | 13.0 |
| - **Mandible-maxilla** | 16 | 9.4 |
| - **Palate** | 5 | 3.0 |
| - **Gingiva** | 3 | 1.8 |
| **T stage** | | |
| - **T1** | 3 | 1.8 |
| - **T2** | 14 | 8.3 |
| - **T3** | 13 | 7.7 |
| - **T4** | 139 | 82.2 |
| **N stage** | | |
| - **N0** | 57 | 33.7 |
| - **N1** | 48 | 28.4 |
| - **N2** | 61 | 36.1 |
| - **N3** | 3 | 1.8 |
| **Distant metastasis (M)** | | |
| - **0** | 158 | 93.5 |
| - **1** | 11 | 6.5 |
| **Clinical stage** | | |
| - **I** | 3 | 1.8 |
| - **II** | 14 | 8.3 |
| - **III** | 13 | 7.7 |
| - **IV** | 139 | 82.2 |
| **Keratinization** | | |
| - **Keratin** | 140 | 82.8 |
| - **Non keratin** | 29 | 17.2 |
| **Tumor differentiation** | | |
| - **Well differentiated** | 102 | 60.4 |
| - **Moderately differentiated** | 42 | 24.9 |
| - **Poorly differentiated** | 25 | 14.8 |
| **Tumor invasion (Bryne 1992)** | | |
| - **Low grade (Bryne score ≤8)** | 91 | 53.8 |
| - **High grade (Bryne score >8)** | 78 | 46.2 |
| **Surgical margin** | 39 | 92.9 |
| - **Clear** | 3 | 7.1 |
| - **Involved** | | |

stage I, II, III, and IV were 66.7%, 73.8%, 83.3%, and 37.5% (Figure 3), with $p = 0.051$. Of 169 subjects, 113 of them were either still alive or dead due to causes other than OSCC. Five subjects died from septic shock ($n = 2$), STEMI ($n = 1$), cerebral hemorrhage ($n = 1$), and cardiac failure ($n = 1$).

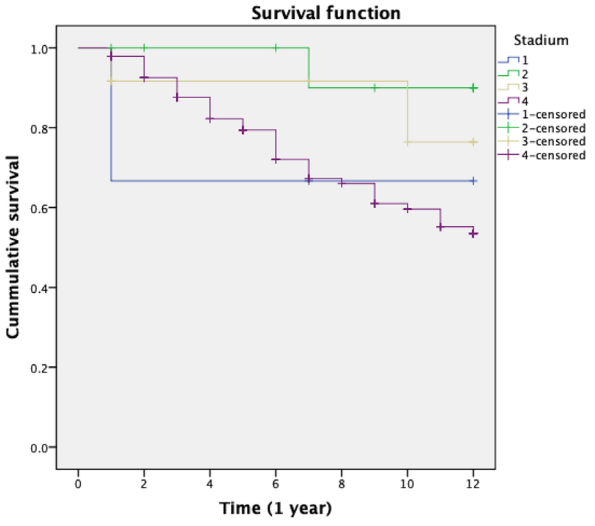



Figure 1: One-year survival based on clinical staging.

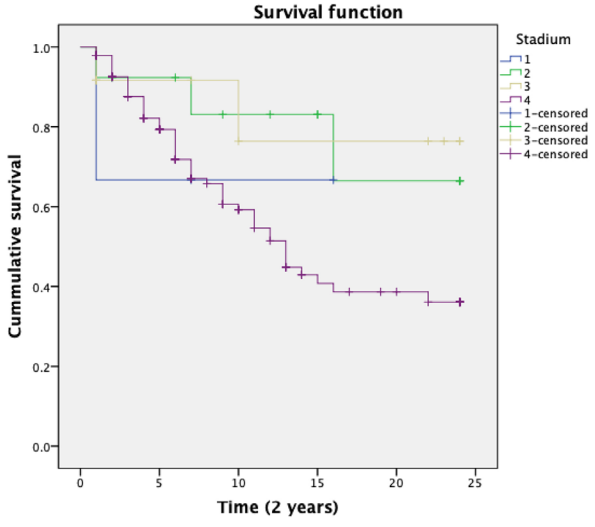



Figure 2: Two-year survival based on clinical staging.

Bivariate analysis of one-year (Table 2) and two-year survival (Table 3) prognostic factors showed that tumor size (T), nodal status (N), clinical stage, and marginal status significantly affected the overall survival ($p < 0.05$). Based on the multivariate analysis for one-year survival (Table 4), tumor size (T) and clinical stage were the only factors significantly correlated with the one-year survival ($p < 0.05$). However, tumor size (T), nodal status (N), and clinical stage were significantly correlated with two-year survival ($p < 0.05$) (Table 5). Tumor size (hazard ratio [HR]: 1.749; 95% CI: 1.261–2.425; $p < 0.05$), nodal status (HR: 1.212; 95% CI: 0.997–1.474; $p < 0.05$) and

Table 2: Bivariate analysis of prognostic factors for one-year survival.

| Prognostic factor | Event (+) | OS | *p* value |
|---|---|---|---|
| **Age** | | | |
| - **≤50 years old** | 50 (66.6) | 25 (33.4) | 0.448 |
| - **>50 years old** | 64 (68) | 30 (32) | |
| **Gender** | | | |
| - **Male** | 61 (70.1) | 26 (29.9) | |
| - **Female** | 53 (64.6) | 29 (35.4) | 0.396 |
| **Tumor location** | | | |
| - **Tongue** | 81 (65.8) | 42 (34.2) | |
| - **Buccal mucosa** | 16 (72.8) | 6 (27.2) | |
| - **Mandible-maxilla** | 13 (81.2) | 3 (18.8) | 0.121 |
| - **Palate** | 4 (80) | 1 (20) | |
| - **Gingiva** | 0 (0) | 3 (100) | |
| **T stage** | | | |
| - **T1** | 1 (33.3) | 2 (66.7) | |
| - **T2** | 4 (28.5) | 10 (71.5) | 0.006 |
| - **T3** | 6 (46.1) | 7 (53.9) | |
| - **T4** | 103 (74.2) | 36 (25.8) | |
| **N stage** | | | |
| - **N0** | 35 (61.5) | 22 (38.5) | |
| - **N1** | 29 (60.4) | 19 (39.6) | 0.034 |
| - **N2** | 48 (78.7) | 13 (21.3) | |
| - **N3** | 2 (66.7) | 1 (33.3) | |
| **Distant metastasis** | | | |
| - **M0** | 106 (67) | 52 (33) | 0.490 |
| - **M1** | 8 (72.7) | 3 (27.3) | |
| **Clinical stage** | | | |
| - **I** | 1 (33.3) | 2 (66.7) | |
| - **II** | 4 (28.5) | 10 (71.5) | 0.006 |
| - **III** | 6 (46.1) | 7 (53.9) | |
| - **IV** | 103 (74.2) | 36 (25.8) | |
| **Tumor differentiation** | | | |
| - **Well differentiated** | 66 (64.7) | 36 (35.3) | |
| - **Moderately differentiated** | 30 (71.4) | 12 (28.6) | 0.810 |
| - **Poorly differentiated** | 18 (72) | 7 (28) | |
| **Tumor invasion (Bryne 1992)** | | | |
| - **Low grade (Bryne score ≤8)** | 61 (67) | 30 (33) | 0.773 |
| - **High grade (Bryne score >8)** | 53 (67.9) | 25 (32.1) | |
| **Surgical margin** | 13 (33.3) | 26 (66.7) | 0.039 |
| - **Clear** | 3 (100) | 0 | |
| - **Involved** | | | |

Table 3: Bivariate analysis of prognostic factors for two-year survival.

| Prognostic factor | Event (+) | OS | *p* value |
|---|---|---|---|
| **Age** | | | |
| - **≤50 years old** | 62 (82.6) | 13 (17.4) | 0.637 |
| - **>50 years old** | 76 (80.8) | 18 (19.2) | |
| **Gender** | | | |
| - **Male** | 73 (84) | 14 (16) | |
| - **Female** | 65 (79.3) | 17 (20.7) | 0.298 |
| **Tumor location** | | | |
| - **Tongue** | 100 (81.3) | 23 (18.7) | |
| - **Buccal mucosa** | 19 (86.4) | 3 (13.6) | |
| - **Mandible-maxilla** | 14 (87.5) | 2 (12.5) | 0.069 |
| - **Palate** | 5 (100) | 0 (0) | |
| - **Gingiva** | 0 (0) | 3 (100) | |
| **T stage** | | | |
| - **T1** | 1 (33.4) | 2 (66.6) | |
| - **T2** | 6 (42.9) | 8 (57.1) | 0.001 |
| - **T3** | 9 (69.3) | 4 (30.7) | |
| - **T4** | 122 (87.7) | 17 (12.3) | |
| **N stage** | | | |
| - **N0** | 43 (75.5) | 14 (24.5) | |
| - **N1** | 37 (78) | 11 (22) | 0.014 |
| - **N2** | 56 (91.9) | 5 (8,1) | |
| - **N3** | 2 (66.6) | 1 (33.4) | |
| **Distant metastasis** | | | |
| - **M0** | 128 (81) | 30 (19) | 0.396 |
| - **M1** | 10 (91) | 1 (9) | |
| **Clinical stage** | | | |
| - **I** | 1 (33.4) | 2 (66.6) | |
| - **II** | 6 (42.8) | 8 (57.2) | 0.001 |
| - **III** | 9 (69.3) | 4 (30.7) | |
| - **IV** | 122 (87.8) | 17 (12.2) | |
| **Tumor differentiation** | | | |
| - **Well differentiated** | 83 (81.4) | 19 (18.6) | |
| - **Moderately differentiated** | 36 (85.7) | 6 (14.3) | 0.833 |
| - **Poorly differentiated** | 19 (76) | 6 (24) | |
| **Tumor invasion (Bryne 1992)** | | | |
| - **Low grade (Bryne score ≤8)** | 75 (82.4) | 16 (17.6) | 0.646 |
| - **High grade (Bryne score >8)** | 63 (80.8) | 15 (19.2) | |
| **Surgical margin** | 21 (53.8) | 18 (46.2) | 0.039 |
| - **Clear** | 3 (100) | 0 | |
| - **Involved** | | | |

clinical stage (HR: 1.749; 95% CI: 1.261–2.425; $p < 0.05$) were also independently associated with the risk of death. The 2-year survival based on tumor size and nodal status are provided in Figure 4 and Figure 5, respectively.

# 4. Discussion

Based on the analysis, the one-year survival of OSCC in Cipto Mangunkusumo Hospital based on clinical stage was 66.7%, 90%, 76.4%, and 53.5%. The two-year survivals were 66.7%, 66.5%, 76.4%, and 36.1% (stage I, II, III, and IV, respectively). The disease-specific survival rate was 66.9%. Based on clinical staging, the

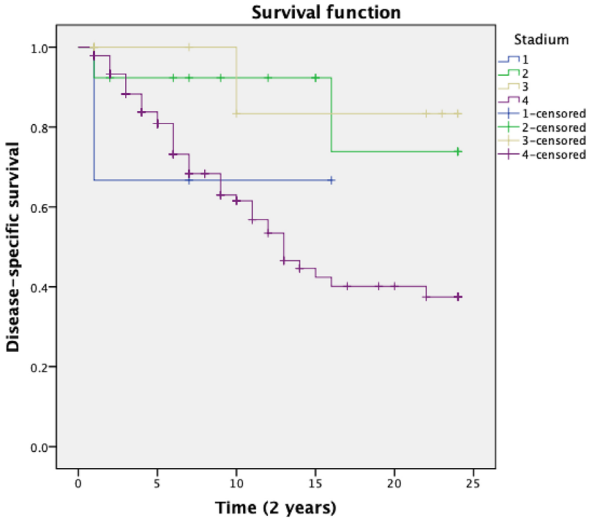



Figure 3: Disease-specific survival based on clinical staging.

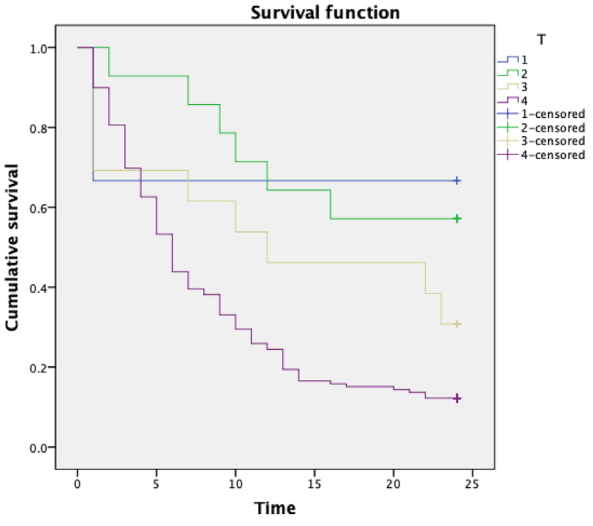



Figure 4: Two-year survival based on tumor size.

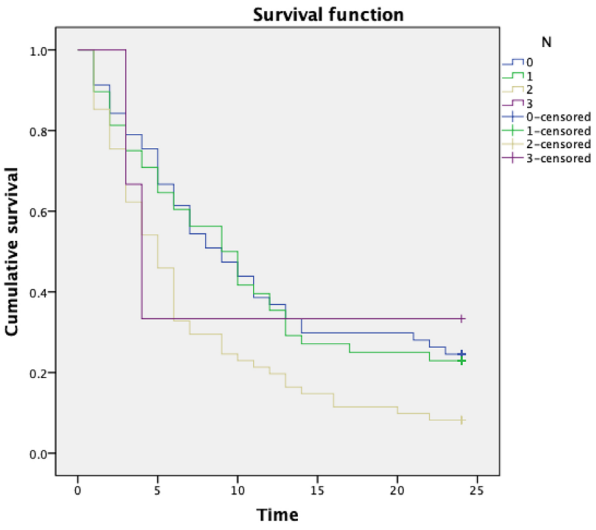



Figure 5: Two-year survival based on nodal status.

Table 4: One-year survival multivariate analysis.

| Variable | HR | 95% CI | *p* value | $R^2$ |
|---|---|---|---|---|
| **Tumor location** | 1.077 | 0.93-1.24 | 0.294 | 0.137 |
| **T stage** | 1.730 | 1.17-2.54 | 0.005 | |
| **N stage** | 1.231 | 0.99-1.52 | 0.055 | |
| **Clinical stage** | 1.730 | 1.17-2.54 | 0.005 | |

Abbreviations: HR, hazard ratio; CI, confidence interval.

Table 5: Two-year survival multivariate analysis.

| Variable | HR | 95% CI | p value | $R^2$ |
|---|---|---|---|---|
| **Tumor location** | 1.048 | 0.918-1.196 | 0.489 | 0.188 |
| **T stage** | 1.749 | 1.261-2.425 | 0.001 | |
| **N stage** | 1.212 | 0.997-1.474 | 0.049 | |
| **Clinical stage** | 1.749 | 1.261-2.425 | 0.001 | |

Abbreviations: HR, hazard ratio; CI, confidence interval.

disease-specific survival rate for stage I, II, III, and IV were 66.7%, 73.8%, 83.3%, and 37.5%, respectively. The one-year survival for the stage II group is higher than stage I in this study because 1 out of 3 subjects died within the first year of observation, which gave a more significant result than the stage II group (1 dead out of 13 subjects). In the second year of follow-up, there were two more subjects who died in the stage II group, so the two-year survival rate decreased. These findings were not consistent with previous studies in which the survival rate decreased as the clinical stage increased[5,8,11]. The one-year and two-year overall survival in our study (58.6% and 43.1%) were consistent with other countries that have characteristics similar to those of Indonesia, especially for advanced-stage patients who came late to our facility as a result of patients delaying treatments[3,4,8,11]. Another cause for the small number of early-stage patients who visited Cipto Mangunkusumo Hospital was the fact that those patients were already treated in lower-level healthcare facilities. Even though Indonesia is a country with good literacy, information about OSCC is still very limited for the general population Many people still don't have enough knowledge to identify early-stage lesions of OSCC, so they only recognize the disease when the lesion has grown bigger or has caused significant disturbance to their daily activities. The low survival rate in our study

was also caused by the patients' irregular visits to the clinic for continuing the course of therapy. Their reasons varied from fear of the side effects of chemotherapy or surgery, a decision to decline continued therapy, difficulty with transportation, and limited financial support. The survival rate closest to our study was from India, which was less than 35%[8].

The disease-specific survival in this study for OSCC was 66.9%, with the lowest survival rate in the stage IV group (37.5%). Based on the study conducted by Sim et al in South Korea, the stage IV disease-specific survival was 71.6%, while the early stage patients could achieve a 100% disease-specific survival rate[12]. The results in that study were correlated with pathological staging and lymph node involvement. Generally, advanced-stage OSCC is more likely to have lymph node involvement, a positive margin in surgery, and more comorbidities. In patients who underwent surgery, the level of complications would be higher than that of those in the lower stages. Hence, mortality was higher in advanced-stage patients[3].

OSCC distribution based on age was in concordance with previous studies. The majority of patients were >50 years old (55.6%). Age did not affect one-year and two-year survival ($p$ = 0.448 and $p$ = 0.637). A lower survival rate was found in the ≤50-year-old age group than the >50 years old age group (17.3% vs. 19.1%, respectively). This might be attributed to the uneven distribution of clinical stages, in which the majority of patients were in the advanced stage. Taghavi et al. presented several cohort studies in which the survival rate was lower in male patients <50 years old[13]. Suresh et al. reported higher OS and DFS in patients <65 years old with an HR of 2.3[14]. The older the patient, the higher the risk for OSCC as a result of the length of exposure to carcinogenic agents and potential DNA damage[6].

Gender distribution in this study was in concordance with the epidemiology of oral cancer in Asia in which the majority of patients were male with a 1.5–4:1 ratio male to female[15]. Warnakulasuriya also noted that the trends for oral cancer have fallen, and the ratio of male to female patients has declined (1.5:1)[16]. In the present study, gender did not affect one-year and two-year survival ($p$ = 0.396 and $p$ = 0.298). Suresh et al. reported no significant difference in five-year disease-specific survival based on gender (male 82.5% vs. female 84.6%) [14]. However, there was a significant decrease in survival rate in male patients with the following risk factors: alcohol consumption, smoking, and advanced clinical stage[14].

The tongue was the most common anatomical site of the tumor in this study (72.8%). This result was in concordance with Thavarool et al. in which the tongue was also the most prevalent site (51.4%)[8]. Tumors on the palate had the lowest survival rate (0%), followed by those located on the mandible-maxilla (12.5%) and buccal mucosa (13.6%). These findings showed poorer outcomes in the anatomic locations mentioned compared to other locations. All subjects with a tumor on the gingiva were still alive at the end of observation. Tumor site is associated with the predominant risk factors in a certain geographic area[13]. Tumors that are difficult to access also worsen prognosis[16]. Carcinomas on the lip mucosa have a good prognosis. Carcinomas on the anterior two-thirds of the tongue, the floor of the mouth, and lower alveolar ridge have a poor prognosis due to the high risk of metastasis to adjacent lymph nodes[14,17]. In this study, tumor site did not influence one-year and two-year survival of OSCC ($p$ = 0.121 and $p$ = 0.069). This can be attributed to the uneven distribution of subjects with tumors located on the buccal mucosa, mandible-maxilla, palate, and gingiva, with the majority being on the tongue. Dissanayaka reported a five-year survival rate for patients with tumors on the buccal mucosa at 65.9% (vs. 34.1% in patients with a tumor on the tongue)[7]. An occult micrometastasis is more likely to occur in a tumor on the tongue[7]. Lymph node involvement was histologically found in 59–64% of patients with tumors on the tongue, retromolar trigonum, and oropharynx (vs. 22% in patients with tumors on the buccal mucosa and 7% on gingiva-alveolar)[17].

T and N stage diagnoses influenced survival in this study, but the N stage was not statistically significant in a multivariate one-year survival analysis ($p$ = 0,055). Taghavi et al. concluded that T and N stages significantly affected the survival of oral cancer[13]. In the present study, there was a decrease of mean survival in nodal involvement (7–10 months in N2 and N3 vs. 11–12 months in N0 and N1). Patients with N2 were 1.4 times more likely to die ($p$ = 0.059) compared to those with N0. Liang Lo et al. reported that the five-year survival rate of the N0, N1, N2, and N3 stages were 65.8%, 38%, 40%, and 20%, respectively ($p$ = 0.0234)[6]. Tumors on the alveolus/gingiva were most commonly infiltrated with lymph node metastasis (45.7%) followed by tumors on the floor of the mouth (34.8%)[6]. OSCC is one of the most difficult carcinomas to control because of the high local invasion and cervical lymph node dissemination, especially in tumors located on the tongue and floor of the mouth[18]. Lymphatic involvement indicates that the tumor has spread systemically. The incremental increase of nodal status will increase mortality[18].

The majority of OSCC patients in this study were in stage IV (82.2%) with T4, N2, and M0. This result showed that most patients in Cipto Mangunkusumo Hospital had advanced disease. Liang Lo et al. reported equal proportions of patients in stage I, II, III, and IV (27.5%,

25.4%, 25.9%, and 21.2%, respectively)[6]. In this study, as the stage increased, the OS rate decreased ($p$ = 0.001). Tumor staging (T), nodal involvement (N), and clinical stage affect one-year and two-year survival ($p$ = 0.001; $p$ = 0.014; $p$ = 0.001, respectively). Multivariate analysis showed that nodal involvement (N) and clinical stage affect one-year and two-year survival (p = 0.049; $p$ = 0.001). Subjects in stage IV were 3.4 times more likely to die but the difference in survival rate was statistically insignificant ($p$ = 0.225). Liang Lo et al. reported a decrease in the five-year survival rate based on stage I, II, III, and IV (75%, 65.6%, 49%, and 30%, respectively)[6]. These differences in survival rate based on clinical stages imply that TNM staging is an independent prognostic factor.

This study showed no correlation between histopathological factors and survival of OSCC. This can be attributed to the advanced disease and high mortality in the present study. The majority of subjects had a well-differentiated tumor (60.4%), which is similar to the results of Dissanayaka et al. in which 61.5% of subjects had a well-differentiated tumor and 38.5% had a moderately differentiated tumor[7]. In this study, a higher one-year survival rate was found with the well-differentiated tumor ($p$ = 0.810); the two-year survival rate was found to be the highest on the poorly differentiated tumor ($p$ = 0.833). Robert et al. noted a distinctive genetic predisposition to drug resistance on well-differentiated tumors[19]. Liang Lo et al. reported the five-year survival rate on well, moderately, and poorly differentiated tumors as 49.1%, 69.7%, and 36.8%, respectively ($p$ < 0.0291)[6]. Asio et al. reported the two-year survival rate on well, moderately, and poorly differentiated tumors as 64.9%, 50.1%, and 26.4%, respectively ($p$ < 0.001)[11]. These findings concluded that poorly differentiated tumors have higher mortality than well and moderately differentiated tumors.

The majority of subjects had a low-grade tumor (53.8%), which was similar to the results of Dissayanake et al. in which 51% of subjects had Bryne scores of 9–12 and 49% of subjects had Bryne scores of 13–20.7. In this study, there was no significant difference in the survival rate of subjects with low-grade tumors (Bryne score ≤8) and high-grade tumors (Bryne score >8). One-year survival rate was higher on low-grade tumors compared to high-grade tumors (33% vs. 32.1%; $p$ = 0.773). The two-year survival rate was higher on high-grade tumors compared to low-grade tumors (19.2% vs. 17.6%; $p$ = 0.646). These findings can be attributed to the majority of subjects being in the late–stage. Previous studies showed poorer prognosis with higher Bryne scores[20,21]. The relationship between Bryne score and survival of OSCC has been described in past studies. Wagner et al. showed that a high Bryne score is associated with higher mortality and metastasis risk. Bryne grade III (score 13–16) was correlated with a low disease-specific survival rate ($p$ < 0.05)[20].

The surgical margin did not affect the overall survival of OSCC significantly in this study. Subjects with a clear margin had a survival rate of 46.2%, none of the subjects with involved margin survived ($p$ = 0.039). This can be attributed to the condition of the patients in which the majority were in the advanced stage. Surgery that leaves residual tumors can increase local recurrence and decrease prognosis. Zanoni et al. concluded that surgical margin was an independent prognostic factor of OS and disease-specific survival based on multivariate analysis[9]. Patients with clear margins had a five-year survival rate of 73.3%, those with close margins had 63%, and those with involved margins had 37.6% ($p$ < 0.001)[9]. Liu et al. noted that a surgical margin of <5 mm is associated with a lower survival rate only in patients with tumors located on the gingiva (HR 3.01; 95% CI 1.31–6.91) and buccal mucosa (HR 1.66; 95% CI 1.12–2.46) [22]. However, Hasegawa stated that survival of OSCC is not related to surgical margin[23]. An inadequate surgical margin does not increase locoregional recurrence. The difference in this finding can be attributed to the uneven distribution of tumor sites. The current multimodality treatment also aids surgery in which a clear margin is not achieved.

This is the first study conducted in our center to analyze the survival of OSCC and its correlating factors. There are several limitations to our study. First, there was a large number of loss-to-follow-up patients because the study was a retrospective study, so we only obtained data from medical records or follow-up by phone. Second, Cipto Mangunkusumo Hospital, as the national referral hospital, meant the majority of OSCC patients were those who were already in the late stage, hence there was a significant imbalance among the stages of the subject group. Thus, this also meant that the distribution for each variable was not proportional.

In conclusion, the one-year and two-year overall survival rates of OSCC in Cipto Mangunkusumo Hospital were 58.6% and 43.1%. The disease-specific survival rate was 66.9%. Clinical stage, tumor size, and lymph node involvement were the most significant prognostic factors of OSCC.

## Conflict of Interest and Source of Funding

The authors affirm neither conflict of interest nor funding source in this study.

## References


[1] Miranda-Filho A, Bray F. Global patterns and trends in cancers of the lip, tongue and mouth. Oral Oncol. 2020;102:104551.

[2] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68:394–424.

[3] Wang B, Zhang S, Yue K, Wang XD. The recurrence and survival of oral squamous cell carcinoma: a report of 275 cases. Chin J Cancer. 2013;32: 614–8.

[4] Le Campion A, Ribeiro CMB, Luiz RR, da Silva Junior FF, Barros HC, Dos Santos KC, et al. Low Survival Rates of Oral and Oropharyngeal Squamous Cell Carcinoma. Int J Dent. 2017;2017:5815493.

[5] Lohia N, Bhatnagar S, Singh S, Prashar M, Subramananiam A, Viswanath S, et al. Survival trends in oral cavity cancer patients treated with surgery and adjuvant radiotherapy in a tertiary center of Northern India: Where do we stand compared to the developed world? SRM J Res Dental Sci. 2019;10:26–31.

[6] Lo WL, Kao SY, Chi LY, Wong YK, Chang RC. Outcomes of oral squamous cell carcinoma in Taiwan after surgical therapy: factors affecting survival. J Oral Maxillofac Surg. 2003;61:751–8.

[7] Dissanayaka WL, Pitiyage G, Kumarasiri PV, Liyanage RL, Dias KD, Tilakaratne WM. Clinical and histopathologic parameters in survival of oral squamous cell carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol. 2012;113:518–25.

[8] Thavarool SB, Muttath G, Nayanar S, Duraisamy K, Bhat P, Shringarpure K, et al. Improved survival among oral cancer patients: findings from a retrospective study at a tertiary care cancer centre in rural Kerala, India. World J Surg Oncol. 2019;17:1–7.

[9] Zanoni DK, Montero PH, Migliacci JC, Shah JP, Wong RJ, Ganly I, et al. Survival outcomes after treatment of cancer of the oral cavity (1985–2015). Oral Oncol. 2019;90:115–21.

[10] Carrillo JF, Cano A, Ramirez-Ortega MC, Chanona JG, Aviles A. A aetrospective cohort study of prognostic factors in patients with squamous cell carcinoma of the oral cavity and oropharynx. *Med Clin (Barc)*. 2014;4:1–10.

[11] Asio J, Kamulegeya A, Banura C. Survival and associated factors among patients with oral squamous cell carcinoma (OSCC) in Mulago hospital, Kampala, Uganda. Cancers Head Neck 2018;3(1):1–10.

[12] Sim YC, Hwang JH, Ahn KM. Overall and disease-specific survival outcomes following primary surgery for oral squamous cell carcinoma: Analysis of consecutive 67 patients. J Korean Assoc Oral Maxillofac Surg. 2019;45(2):83–90.

[13] Taghavi N, Yazdi I. Prognostic factors of survival rate in oral squamous cell carcinoma: clinical, histologic, genetic and molecular concepts. Arch Iran Med. 2015;18:314–9.

[14] Suresh GM, Koppad R, Prakash BV, Sabitha KS, Dhara PS. Prognostic indicators of oral squamous cell carcinoma. Ann Maxillofac Surg. 2019;9:364–70.

[15] Krishna Rao SV, Mejia G, Roberts-Thomson K, Logan R. Epidemiology of oral cancer in Asia in the past decade—an update (2000–2012). Asian Pac J Cancer Prev. 2013;14:5567–77.

[16] Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. Oral Oncol. 2009;45:309–16.

[17] Woolgar JA. Histopathological prognosticators in oral and oropharyngeal squamous cell carcinoma. Oral Oncol. 2006;42:229–39.

[18] Ho AS, Kim S, Tighiouart M, Gudino C, Mita A, Scher KS, et al. Metastatic lymph node burden and survival in oral cavity cancer. J Clin Oncol. 2017;35:3601–9.

[19] Robert BM, Dakshinamoorthy M, Ganapathyagraharam Ramamoorthy B, Dhandapani M, Thangaiyan R, Muthusamy G, et al. Predicting tumor sensitivity to chemotherapeutic drugs in oral squamous cell carcinoma patients. Sci Rep [Internet]. 2018;8(1):15545. Available from: https://doi.org/10.1038/s41598-018-33998-4.

[20] Wagner VP, Webber LP, Curra M, Klein IP, Meurer L, Carrad VC, et al. Bryne's grading system predicts poor disease-specific survival of oral squamous cell carcinoma: a comparative study among different histological grading systems. Oral Surg, Oral Med, Oral Path and Oral Radiol. 2017;5:1–10.

[21] Ankurgoyal, Bharat V, Mamta. Comparitive Analysis of Broder & Bryne's grading of squamous cell carcinoma in different anatomical sites. IOSR-JRME. 2018;8:55–8.

[22] Liu SA, Wang CC, Jiang RS, Lee FY, Lin WJ, Lin JC. Pathological features and their prognostic impacts on oral cavity cancer patients among different subsites - A singe institute's experience in Taiwan. Sci Rep. 2017;7:7451.

[23] Hasegawa T, Tanakura M, Takeda D, Sakakibara A, Akashi M, Minamikawa T, et al. Risk factors associated with distant metastasis in patients with oral squamous cell carcinoma. Otolaryngol Head Neck Surg. 2015;152:1053–60.