Original Article

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Treatment Interval Effects on Prognoses of Oral Cancer Patients

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Abstract:

Objective: To determine the effect of treatment interval (TI) on the survival of patients with oral cancer at a tertiary healthcare institute.

Material and Methods: The medical records of patients with oral cancer between 2010 and 2018 who complied with the inclusion criteria. The information collected included demographic data, tumor subsite, staging, initial treatment, date of diagnosis, date of treatment, and last follow-up date. TI was defined as the period between the dates of diagnosis and treatment. The impact of the TI was illustrated by the area under the receiver operating characteristic curve. Survival analysis was performed using the Kaplan-Meier curve and compared using the log-rank test. The Cox proportional hazard ratio (HR) was used to describe the correlation between variables. Logistic regression analysis was used to assess the factors associated with TI p-value<0.05 was considered statistically significant.

Results: Out of 1,806 oral cancer patients recruited, 1,565 met the criteria and were analyzed for sensitivity and specificity. The cutoff for the TI was set at 18 days, beyond which patient survival was negatively impacted (HR=1.27; 95% CI=1.01, 1.6), p-value=0.038. The study also found that factors such as religion, advanced staging, radiation therapy, and distance from tertiary hospitals were associated with the TI.

Conclusion: Patients with oral cancer who had a TI of 18 days or more had a statistically significant negative correlation with survival rates compared to those with a TI of less than 18 days. Other factors such as religion, disease stage, primary treatment with radiation, and distance from residence to hospital were associated with TI.

Keywords: oral cancer, treatment interval, treatment delay

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Introduction

Oral cancer is one of the most common cancers worldwide. In 2018, data from the Global Cancer Observatory showed that the annual incidence of oral cancer was 354,864 cases worldwide, with the highest number recorded in Asia. The mortality incidence was 177,384 individuals, accounting for 1.8% of all cancer-related deaths[1]. Over the past decade, the 5-year survival rate for oral cancer has been around 50%[2].

Oral cancer treatment is time-sensitive. Various factors influence cancer care processes. The increase in patient numbers, complexity of the disease, and treatment at tertiary hospitals for advanced stages lead to an increase in the time from diagnosis to treatment[3-6]. This, in turn, has had a detrimental effect on both disease progression and survival rates[7-10]. To date, investigators have aimed to enhance the early detection and treatment of oral cancer while minimizing any delays, all with the goal of improving disease survival rates. However, definitive evidence regarding the optimal time for achieving this goal is still lacking.

The model of pathways to treatment: the Aarhus Statement[11] has categorized time intervals into various segments, with the treatment interval (TI) being a crucial and relevant period to the disease[5,9-14]. Extended TI is associated with the staging[15-18], survival rates[5,10,19-21], and recurrence of the disease[22]. Significantly, a critical measure for evaluating the quality of a hospital lies in the promptness with which treatment is initiated[23]. An extended treatment delay in head and neck cancer increases the mortality risk by 7% for each week of delay[24], and an interval exceeding 30 days or even 20 days has a negative impact on 5-year survival rates[25,26]. However, there exists a considerable variation in the TIs among current studies, ranging from 20 to 120 days.

In recent studies, it has been challenging to draw a conclusion owing to the heterogeneity among studies, insufficient stratification in each interval and lack of clear definitions for the intervals used. Additionally, the healthcare systems in developed countries may differ from those in developing countries, leading to limitations in comparative research and advancement. This study aimed to determine the effects of TI on the survival of patients with oral cancer in a tertiary healthcare institute.

Material and Methods

The Ethics Committee of the Faculty of Medicine, Prince of Songkla University approved this study protocol (REC. 63-254-13-1). All patients diagnosed with oral squamous cell carcinoma from January 2009 to December 2018 were reviewed and those with recurrence or second primary cancer in the oral cavity were excluded.

The electronic medical records of patients with oral cancer who met the inclusion criteria were reviewed. The information gathered included demographic data such as age, sex, religion and smoking or betel nut use. Smokers and betel nut users were categorized as nonsmokers or nonusers, ex-smokers or ex-users, and current smokers or users. In this study, 'ex-smokers' or 'ex-users' were defined as individuals with a history of cessation for at least one year. Cancer staging conformed to the 7th edition of the American Joint Committee on cancer staging manual. Data on treatment modalities, pretreatment laboratory results, and dates of diagnosis and treatment were collected. Blind techniques were applied to label the hospital number of each patient, ensuring the confidentiality of personal data. The date of diagnosis was defined as the date when the pathological report was issued. The date of treatment was defined as the day of commencing definitive treatment, either surgery or radiation. TI was defined as the period between the dates of diagnosis and treatment. The distance from the patient's residence to the study site was recorded using postal codes and measured in kilometers along the actual road.

Statistical analysis

All statistical analyses were performed using R statistical software version 3.3.1 (Vienna, Austria). Continuous variables were presented as either means or medians. Discrete variables were expressed as percentages. The area under the receiver operating characteristic curve was used to evaluate the relationship between the TI and survival rate.

Hazard ratios (HR) for 5-year survival were evaluated using univariate and multivariate Cox proportional hazard regressions. Kaplan-Meier curves were used to assess survival rates, which were compared using the log-rank test. Adjustments for confounders were made for age, race, tobacco and betel nut use, primary subsite, staging, and health insurance status. To determine the relationship between the factors and the TI, Pearson's chi-square test and odds ratios (OR) were used to compare discrete variables. HRs and 95% confident interval (CIs) were calculated, and p-value<0.05 was considered statistically significant. Analysis for the limited or disproportionate number of the index subjects applied the matching technique to control for confounding.

Results

Patient characteristics

A total of 1,565 patients met the inclusion criteria. Of these, the majority were male (59.7%). The most common subsite of cancer was the tongue (625 patients, 40%). There were 68.1% in the advanced stage. The median distance from the patient's residence to the study site was 193 kilometers. The demographic data of patients with oral cancer are presented in Table 1.

Table 1 Demographic data of the study population

Characteristics	N=1,565 (%)
Gender	
Male	934 (59.7)
Female	631 (40.3)
Age, mean (S.D.)	63.5 (14.5)
Religion	
Buddhism	1,390 (88.8)
Islam	160 (10.2)
Other	15 (1.0)
Occupation	
Agriculture	551 (35.2)
Employer	355 (22.7)
Government officer	84 (5.4)
Others	575 (36.7)
Smoking	
No	655 (41.8)
Ex-smoker	596 (38.1)
Currently	314 (20.1)
Betel nut use	
No	893 (57.1)
Ex-user	252 (16.1)
Currently	420 (26.8)
Tumor subsite	
Tongue	625 (39.9)
Buccal mucosa	194 (12.4)
Alveolar ridge	245 (15.6)
Floor of mouth	214 (13.9)
Hard palate	103 (6.5)
Lip	80 (5.1)
Retromolar trigone	99 (6.3)
Unknown	5 (0.3)
Aim	
Curative	1,253 (80.1)
Palliative	268 (17.1)
Unknown	44 (2.8)
Blood test	
Hemoglobin: mean (S.D.)	11.7 (1.9)
White blood cell: mean (S.D.)	9,200 (5.4)
Albumin: mean (S.D.)	3.9 (0.7)
Occupation	
Government officer	84 (5.4)
Agriculture and fisheries	551 (35.2)
Employee	355 (22.7)
Household work and others	575 (36.7)
Distance from tertiary care	
≤200 km	1,002 (64.1)
>200 km	562 (35.8)
Unknown	1 (0.1)

Table 1 (countinued)

Characteristics	N=1,565 (%)
Health insurance	
UC	1,112 (71.1)
CSMBS	262 (16.7)
Out of pocket	94 (6.0)
SSS	58 (3.7)
Other	32 (2.0)
Unknown	7 (0.5)
Stage	
Early	427 (27.3)
Advanced	1,138 (72.7)
Treatment	
Surgery	669 (42.7)
Radiation	358 (22.9)
No treatment	538 (34.4)

S.D.=standard deviation, UC=universal coverage, CSMBS=civil servant medical benefit scheme, SSS=social security scheme

Survival analysis

The median TI was 41 (21, 67.75) days. The receiver operating characteristic curve analysis showed that a TI of 18 days had a significant impact on the survival rate. Sensitivity and specificity were 82% and 29%, respectively (Figure 1).

The median follow-up duration was 24.83 months. Overall survival was 34.3 months. In the group with TI <18 days (n=212), the median survival was 40.4 months (CI 35.4-66.7), while the TI ≥18 days (n=746) group had a median survival time of 25.3 months (CI=23.2-30) (Figure 2). In the subgroup analysis, the optimal cut points for TI from the receiver operating characteristic (ROC) curve were identified as 19 days for the early-stage group (area under the curve (AUC)=0.534 [0.469-0.598], sensitivity=0.69, specificity=0.44) and 28 days for the advanced stage group (AUC=0.528 [0.478-0.578], sensitivity=0.79, specificity=0.28).

Factors affecting the TI

In the TI ≥18 days group, several significant factors affecting patient outcomes were discovered. Religion was one factor since Islamic patients tended to receive treatment later than Buddhist patients (OR, 2.21; CI 1.13-4.3, p-value= 0.012). Patients who were currently smoking tended to delay treatment initiation longer than non-smokers (OR, 1.17, CI 0.49-2.8, p-value=0.72). Conversely, betel nut users tended to receive treatment earlier than non-users (OR, 0.55, CI 0.55-0.94, p-value=0.03).

Patients in the advanced stage, along with those whose initial treatment was radiation, received delayed treatment versus those in the early stage and treated with surgery (OR, 2.21, CI 1.45-3.36, p-value<0.001 and OR, 31.86, 11.49-88.31 p-value<0.001). Out-of-pocket expenses could result in a higher chance of receiving treatment earlier compared to patients with universal coverage (OR, 0.41; CI 0.17-0.98, p-value=0.033). Additionally, the distance between the patient's residence and the hospital played a role. Patients residing more than 200 kilometers away had delayed treatment (OR, 1.78; CI 1.15-2.75, p-value=0.01) (Table 2).

Apart from the aforementioned factors, sex, age, primary subsite, occupation, and laboratory test results showed no statistically significant relationships with TI.

Multivariate analysis of the relationships among variables affecting survival outcome

The confounder-adjusted logistic regression analysis found that patients with a TI ≥18 had a significantly higher risk of mortality than patients with a TI <18 days (HR, 1.30; CI 1.04-1.6, p-value=0.023). Age was significantly associated with survival rates, with an increase in age correlating to an increased mortality risk (HR, 1.01; CI 1.01-1.02, p-value=0.005). Patients with current betel nut use (HR, 1.36; CI 1.08-1.7, p-value=0.01) had an increased

mortality risk. Similarly, in advanced-stage cases, there was also a higher mortality risk (HR, 1.61; CI 1.32-2.0, p-value<0.001). Additionally, out-of-pocket expenses were related to an approximately 3 times lower mortality risk (HR, 0.44, CI 0.24-0.8, p-value 0.007) than universal coverage. Religion and distance from the patient's residence to the study site were not significantly associated with the survival rate.

Table 2 Relationship between factors analyzed and TI ≥18 days

Characteristics	Adjusted OR (Odd ratio)	95% CI	p-value
Gender			
Female	1 (reference)		0.46
Male	1.33	0.63-2.85	
Age (years)			
>65	1 (reference)		
≤65	1.1	0.7-1.87	0.59
Religion			0.01
Buddhism	1 (reference)		
Islam	2.21	1.13-4.3	0.02
Smoking			0.60
No	1 (reference)		
Ex-smoker	0.87	0.42-1.84	0.72
Currently	1.17	0.49-2.8	0.72
Betel nut use			0.09
No	1 (reference)		
Ex-user	0.80	0.45-1.41	0.44
Currently	0.55	0.55-0.94	0.03
Primary subsites			0.26
Tongue	1 (reference)		
Buccal mucosa	1.43	0.68-3.01	0.35
Alveolar ridge	1.59	0.86-2.97	0.14
Floor of mouth	1.53	0.82-2.87	0.18
Hard palate	0.70	0.29-1.69	0.43
Lip	1.56	0.57-4.23	0.38
Retromolar trigone	4.16	0.87-19.76	0.07
Stage			
Advanced	1.00 (reference)		
Early	2.21	1.45-3.36	<0.001
Blood test			
Hemoglobin	0.90	0.79-1.03	0.11
White blood cell	1.01	0.97-1.06	0.55
Albumin	1.02	0.73-1.41	0.92
Initial treatment			
Surgery	1.00 (reference)		
Radiation	31.86	11.49-88.31	<0.001
Initial treatment			
Surgery	1.00 (reference)		
Radiation	31.86	11.49-88.31	<0.001

Table 2 (continued)

Characteristics	Adjusted OR (Odd ratio)	95% CI	p-value
Health insurance			0.16
UC	1.00 (reference)		
CSMBS	1.34	0.74–2.42	0.33
SSS	1.05	0.42–2.65	0.91
Out of pocket	0.41	0.17–0.98	0.04
Other	1.76	0.42–7.36	0.44
Occupation			
Government officer	1.00 (reference)		
Agriculture–fisheries	1.42	0.55–3.68	0.47
Employer	1.42	0.52–3.87	0.49
other	1.44	0.53–3.91	0.47
Distance			
≤200 km	1.00 (reference)		
>200 km	1.78	1.15–2.75	0.01

UC=universal coverage, CSMBS=civil servant medical benefit scheme, SSS=social security scheme, CI=confident interval

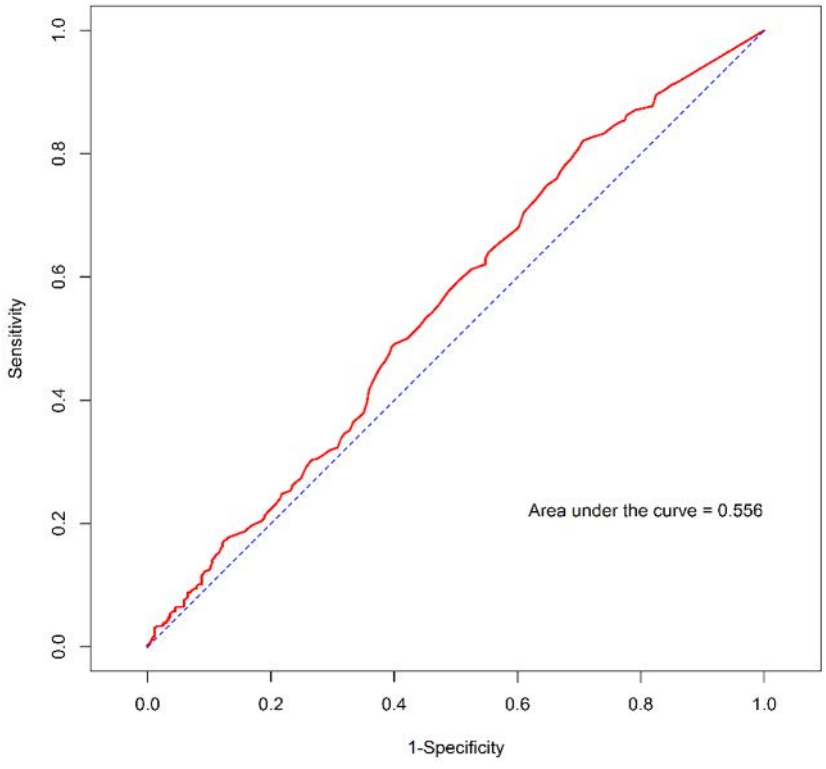

Figure 1 ROC curve for the impacted TI value

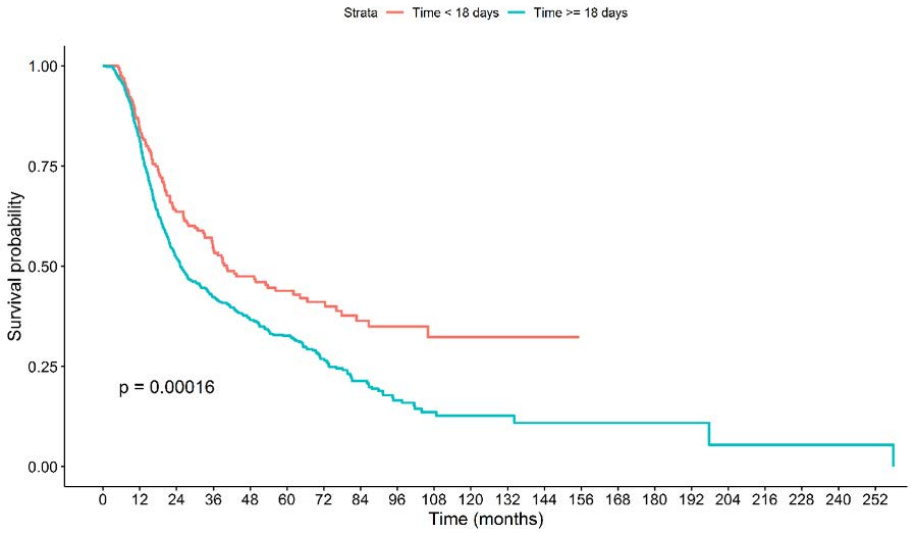

Figure 2 Survival rates for the TI <18 and ≥18 days groups

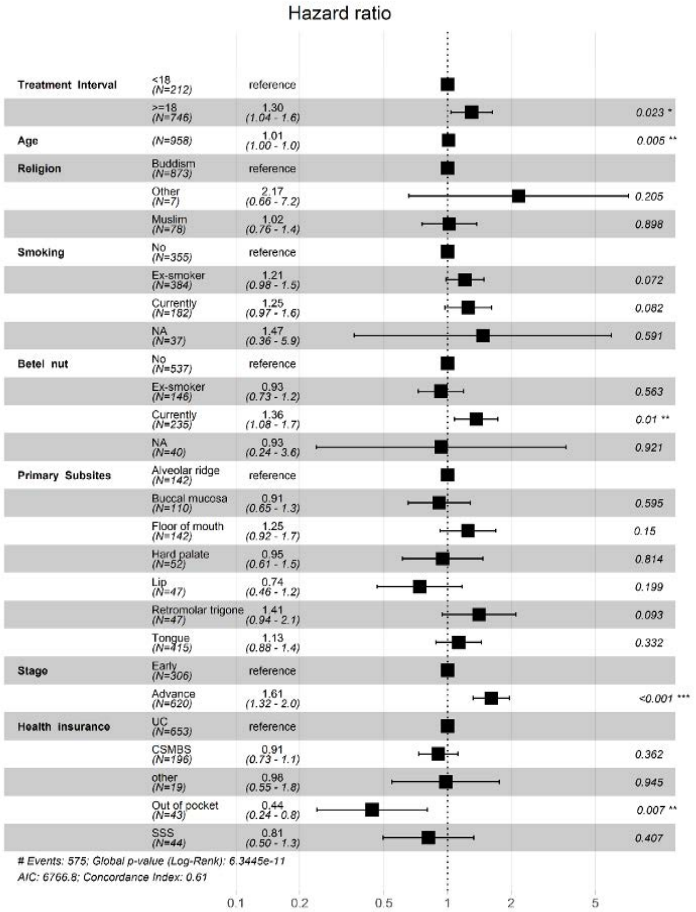

Figure 3 The multivariate analysis presents the relationships between variables and mortality

Discussion

Delays in diagnosis and treatment are widely recognized as negative prognostic factors for oral cancer. Reducing delays in cancer care can lead to improved treatment outcomes. The objective of our study was to determine the definitive TI affecting the survival of patients with oral cancer. The study population was predominantly male, with a history of smoking diagnosed at an advanced stage, and an average age of approximately 60 years. These characteristics are typical of patients with oral cancer in developing countries.

Our study found that a TI ≥18 days significantly affected the 5-year survival rates after adjusting for confounding variables. This finding corresponds to previous studies by Liao at al. and Tsai et al., who reported that TI ≥120 or even 90 days significantly increased the risk (HR, 1.32; CI 1.19-1.47 and HR, 1.28; CI 1.14-1.45) versus TI ≤20–30 days[25,26]. Chen et al. postulated that to improve the survival rate, the entire process from diagnosis to surgery or radiation should be completed within 11 weeks since they found that delaying treatment beyond this timeframe reduced survival rates (HR, 1.34; CI 0.53-3.36, p-value=0.89)[27]. Polesel et al. reported that the 5-year overall survival rate decreased from 62% for TI <30 days to 39% for TI >90 days (p-value<0.01)[28]. A systematic review demonstrated that delayed TI negatively affects disease prognosis and patient survival rates. The review found that treatment initiation ranges from 20 to 120 days or even beyond; nevertheless, there is no universally accepted delay period, due to the variations in population groups and healthcare systems across different studies[29]. Our study determined that the cutoff TI is 18 days, which is shorter than that in other studies. Possible causes are more aggressive tumor behavior and disease severity at the initial stage.

The differing cut points for TI identified in our subgroup analysis, 19 days for early stage and 28 days for advanced stage, emphasize the necessity for prompt management in early-stage oral cancer, as any delay can adversely impact survival. However, these values should be further studied in a multivariate analysis in order to ascertain their significance.

To illustrate the relationship between different variables and TI, we found that Islam was associated with more delayed treatment than Buddhism. The Muslim belief that life can be a divine gift may influence their decision to seek medical care. Consequently, patients may opt for treatment later[30,31]. Advanced disease stage with initial radiation treatment correlated with delayed treatment, which is in line with prior studies, and reflects the complexity of the patient preparation and care processes[5,24,28,31]. Additionally, the time required for consultations with various specialists, such as diagnostic radiologists, radiation oncologists, and pathologists, may contribute to each step. Dental evaluation and oral preparation take time, leading to delayed radiation administration[32]. The longer TI in advanced-stage patients may be caused by a higher likelihood of patients seeking alternative treatments, potentially delaying standard care[33]. Finally, the distance between the patient's residence and the hospital also delayed treatment, consistent with previous findings, indicating that the need to travel extended distances for treatment impacts disease prognosis and can result in irrational treatment decisions[34].

In addition to TI, many other factors associated with oral cancer mortality have been discovered. An increase in age and presentation in advanced stages are associated with an increased mortality risk. These findings clearly illustrate the effects of age-related health conditions and greater disease extent. Patients with current betel nut use have an increased risk of mortality. Wen et al. have reported the effects of betel nuts and smoking on oral cancer risk.

In addition to oral cancer, significant increases were observed among chewers for cancers of the esophagus, liver, pancreas, larynx, lungs, and all other cancers. Chewing and smoking interact synergistically and shorten patients' life span by nearly 6 years[35]. Out-of-pocket expenses significantly reduced the risk of mortality versus the universal coverage type, possibly because it led to a faster access to treatment than universal coverage. Fujiwara et al. also reported that private insurance facilitated faster access to treatment and implied a higher quality of life[36]. This may reflect the overwhelming number of patients under the universal coverage system, which is a bottleneck in the treatment process.

To date, our study included a large sample size in southeast Asia, with an estimation of appropriate TI values representing the survival of oral cancer patients. However, this study has some limitations. First, it is a retrospective study. The mortality data collection relied on cross-verification through civil registration. If no record of death was found, the patient was assumed to be alive. This could introduce selection bias and potential misclassification, especially in cases where the registration data are incomplete. Second, there may be other unanalyzed confounding factors that could affect the survival rates. Nevertheless, all the solid confounders that could affect survival were adjusted for in this study. Third, owing to the substantial sample size, attributed to the study institution being the largest center in southern Thailand, instances of missing and under-recorded data occurred, potentially resulting in some information not being accurately documented.

This study is significant because of the lack of a universally accepted TI cut-off point. Identifying the factors influencing TI is also crucial because it is a priority to decrease the time by controlling adjustable factors following treatment. However, a lack of consensus could impede the timely planning of hospital care and treatment. Noticeably, the measures from our study could have a profound effect on the survival of patients with oral cancer, potentially leading to the establishment of a universal standard metric for the time to treatment. Given the numerous studies focused on improving the quality of cancer care, it is necessary to establish goals and benchmarks for treatment. Besides TI, diagnostic delay (the first symptoms and signs to diagnosis) and adjuvant delay (the date of surgical treatment to the start of adjuvant treatment) also influence oral cancer treatment outcomes. However, these 2 delays are beyond the objectives of this study. Further research should include an investigation into these delays.

Conclusion

Oral cancer patients with a TI of 18 days or more had a statistically significant negative correlation with survival rates compared to those with a TI of less than 18 days. Factors associated with TI include religion, disease stage, primary treatment with radiation, and distance from residence to hospital.

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Conflict of interest

The authors declare no conflicts of interest.

References

1. 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.
2. Kumar M, Nanavati R, Modi T, Dobariya C. Oral cancer: Etiology and risk factors: a review. J Cancer Res Ther 2016;12:458.

3. Brouha XDR, Tromp DM, Koole R, Hordijk GJ, Winnubst JAM, de Leeuw JRJ. Professional delay in head and neck cancer patients: analysis of the diagnostic pathway. Oral Oncol 2007;43:551–6.
4. Kowalski LP, Carvalho AL. Influence of time delay and clinical upstaging in the prognosis of head and neck cancer. Oral Oncol 2001;37:94–8.
5. Murphy CT, Galloway TJ, Handorf EA, Wang L, Mehra R, Flieder DB, et al. Increasing time to treatment initiation for head and neck cancer: an analysis of the national cancer database: head and neck treatment time. Cancer 2015;121:1204–13.
6. Murphy CT, Galloway TJ, Handorf EA, Egleston BL, Wang LS, Mehra R, et al. Survival impact of increasing time to treatment initiation for patients with head and neck cancer in the United States. J Clin Oncol 2016;34:169–78.
7. Pulte D, Brenner H. Changes in survival in head and neck cancers in the late 20th and early 21st century: a period analysis. The Oncologist 2010;15:994–1001.
8. Jensen AR, Nellemann HM, Overgaard J. Tumor progression in waiting time for radiotherapy in head and neck cancer. Radiother Oncol 2007;84:5–10.
9. Gómez I, Seoane J, Varela-Centelles P, Diz P, Takkouche B. Is diagnostic delay related to advanced-stage oral cancer? a meta-analysis. Eur J Oral Sci 2009;117:541–6.
10. Seoane J, Alvarez-Novoa P, Gomez I, Takkouche B, Diz P, Warnakulasiruya S, et al. Early oral cancer diagnosis: the Aarhus statement perspective. a systematic review and meta-analysis: early oral cancer diagnosis: a meta-analysis. Head Neck 2016;38:e2182–9.
11. Weller D, Vedsted P, Rubin G, Walter FM, Emery J, Scott S, et al. The Aarhus statement: improving design and reporting of studies on early cancer diagnosis. Br J Cancer 2012;106:1262–7.
12. Varela-Centelles P, Lopez-Cedrun J, Fernandez-Santroman J, Alvarez-Novoa P, Luaces-Rey R, Pombo-Castro M, et al. Assessment of time intervals in the pathway to oral cancer diagnosis in north-western Spain. Relative contribution of patient interval. Med Oral Patol Oral Cirugia Bucal 2017;22:e478–83.
13. Gigliotti J, Madathil S, Makhoul N. Delays in oral cavity cancer. Int J Oral Maxillofac Surg 2019;48:1131–7.
14. Kerdpon D, Jantharapattana K, Sriplung H. Factors related to diagnostic delay of oral squamous cell carcinoma in southern Thailand: revisited. Oral Dis 2018;24:347–54.
15. Wang K, Song BH, Gilde JE, Darbinian JA, Weintraub MLR, Wu TJ. Diagnostic pathway of oral cavity cancer in an integrated health care system. Perm J 2018;22:17–152.
16. Schutte HW, Heutink F, Wellenstein DJ, van den Broek GB, van den Hoogen FJA, Marres HAM, et al. Impact of time to diagnosis and treatment in head and neck cancer: a systematic review. Otolaryngol Neck Surg 2020;162:446–57.
17. Monteiro de Oliveira Novaes JA, William WN. Prognostic factors, predictive markers and cancer biology: the triad for successful oral cancer chemoprevention. Future Oncol 2016;12:2379–86.
18. Lopez-Cedrún JL, Varela-Centelles P, Otero-Rico A, Vázquez-Mahía I, Seoane J, Castelo-Baz P, et al. Overall time interval ("total diagnostic delay") and mortality in symptomatic oral cancer: a U-shaped association. Oral Oncol 2020;104:104626.
19. Sorensen JR, Johansen J, Gano L, Sørensen JA, Larsen SR, Andersen PB, et al. A "package solution" fast track program can reduce the diagnostic waiting time in head and neck cancer. Eur Arch Otorhinolaryngol 2014;271:1163–70.
20. Mundi N, Theurer J, Warner A, Yoo J, Fung K, MacNeil D, et al. The impact of seasonal operating room closures on wait times for oral cancer surgery. Curr Oncol 2018;25:67.
21. Tong XJ, Shan ZF, Tang ZG, Guo XC. The impact of clinical prognostic factors on the survival of patients with oral squamous cell carcinoma. J Oral Maxillofac Surg 2014;72:e1-10.
22. Morelatto RA, Herrera MC, Fernández EN, Corball AG, López de Blanc SA. Diagnostic delay of oral squamous cell carcinoma in two diagnosis centers in Córdoba Argentina: diagnostic delay of oral carcinoma. J Oral Pathol Med 2007;36:405–8.
23. Takes RP, Halmos GB, Ridge JA, Bossi P, Merkx MAW, Rinaldo A, et al. Value and quality of care in head and neck oncology. Curr Oncol Rep 2020;22:92.
24. Van Harten MC, Hoebers FJP, Kross KW, van Werkhoven ED, van den Brekel MWM, van Dijk BAC. Determinants of treatment waiting times for head and neck cancer in the Netherlands and their relation to survival. Oral Oncol 2015;51:272–8.
25. Liao CT, Chen HN, Wen YW, Lee SR, Ng SH, Liu TW, et al. Association between the diagnosis-to-treatment interval and overall survival in Taiwanese patients with oral cavity squamous cell carcinoma. Eur J Cancer 2017;72:226–34.
26. Tsai WC, Kung PT, Wang YH, Huang KH, Liu SA. Influence of time interval from diagnosis to treatment on survival for

oral cavity cancer: a nationwide cohort study. PLOS ONE 2017;12:e0175148.

27. Chen MM, Harris JP, Orosco RK, Sirjani D, Hara W, Divi V. Association of time between surgery and adjuvant therapy with survival in oral cavity cancer. Otolaryngol Neck Surg 2018;158:1051–6.
28. Polesel J, Furlan C, Birri S, Giacomarra V, Vaccher E, Grando G, et al. The impact of time to treatment initiation on survival from head and neck cancer in north-eastern Italy. Oral Oncol 2017; 67:175–82.
29. Graboyes EM, Kompelli AR, Neskey DM, Brennan E, Nguyen S, Sterba KR, et al. Association of treatment delays with survival for patients with head and neck cancer: a systematic review. JAMA Otolaryngol Neck Surg 2019;145:166–77.
30. Hellyer P. The role of religious beliefs in oral cancer diagnosis and treatment. Br Dent J 2022;233:42.
31. Saka-Herrán C, Jané-Salas E, Mari-Roig A, Estrugo-Devesa A, López-López J. Time-to-treatment in oral 48 cancer: causes and implications for survival. Cancers 2021;13:1321.
32. Patel UA, Brennan TE. Disparities in head and neck cancer: assessing delay in treatment initiation. The Laryngoscope 2012;122:1756–60.
33. Truant T, Porcino A, Ross B, Wong M, Hilario C. Complementary and alternative medicine (CAM) use in advanced cancer: a systematic review. J Support Oncol 2013;11:105–13.
34. Ambroggi M, Biasini C, Del Giovane C, Fornari F, Cavanna L. Distance as a barrier to cancer diagnosis and treatment: review of the literature. Oncologist 2015;20:1378–85.
35. Wen CP, Tsai MK, Chung WS, Hsu HL, Chang YC, Chan HT, et al. Cancer risks from betel quid chewing beyond oral cancer: a multiple-site carcinogen when acting with smoking. Cancer Causes Control 2010;21:1427.
36. Fujiwara RJT, Judson BL, Yarbrough WG, Husain Z, Mehra S. Treatment delays in oral cavity squamous cell carcinoma and association with survival: treatment delays in oral cavity cancer. Head Neck 2017;39:639–46.