Survival Rates According to Tumour Location in Patients With Surgically Treated Oral and Oropharyngeal Squamous Cell Carcinoma

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Abstract. *Background/Aim:* We evaluated survival rates in surgically-treated oral and oropharyngeal squamous cell carcinoma patients at our clinic, and determined whether survival differed by tumour locations. *Patients and Methods:* In a retrospective study, tumour lesions in 1,486 patients were categorized into 6 groups according to tumour location. *Patients' age, sex, tumour-node-metastasis classification, resection status, 5-year and disease-specific survival rates were statistically analysed between groups. Results:* A significantly inferior disease-specific and lower 5-year survival rates for tumours located at the base of the tongue and oropharynx, and maxilla, due to higher T-stage and incomplete resection status were shown. *Cervical lymph node metastasis and distant metastatic spread were more frequently observed with base of the tongue and oropharynx lesions. Conclusion:* Attentive inspection and precise clinical examinations of specific oral and oropharyngeal regions are crucial for early diagnosis and treatment. Oral and oropharyngeal tumour locations play important roles in disease prognosis.

Oral and oropharyngeal cancer occur in approximately 5% of patients with malignant neoplasms and is the tenth most common cancer in the world (1, 2). Squamous cell carcinoma is the most frequent malignancy, accounting for 90% of oral and oropharyngeal cancer cases, followed by other cancers such as adenocarcinoma and mesenchymal tumours (2, 3). The most important risk factors of tumorigenesis are alcohol and tobacco consumption (4, 5). In particular, the effects multiply when both are consumed

together (6). Other important risk factors include poor oral hygiene with plaque accumulation and chronic inflammation and permanent traumatic irritation of the mucosa due to poorly fitted dental prosthesis or sharp-edged dental fillings (7, 8). Other possible triggers of malignant mucosal degeneration include malnutrition and dietary agents, therapeutic irradiation, and betel nut chewing (9, 10).

Oral and oropharyngeal squamous cell carcinoma grows as an exophytic or endophytic mass. In most cases, lesion growth is not accompanied by pain or functional compromise. Therefore, regular inspection of the oral and oropharyngeal mucosa plays an important role in the early diagnosis of cancer (11, 12). Tumours in specific areas of the oral cavity, that are not easy to inspect, such as the base of the tongue and the oropharynx, often grow unnoticed without symptoms and eventually metastasize (13, 14). Therefore, tumour location is a crucial factor influencing diagnosis and treatment. General therapeutic strategies include surgical resection, radiotherapy, and/or chemotherapy. With oral and oropharyngeal squamous cell carcinoma, disease-specific survival differs significantly between early- and advanced-stage disease (15). Mean overall 5-year survival rates range between 45% and 50% (16). To determine whether survival rates differ between specific locations and, therefore, to understand if tumour location plays a role in disease prognosis, a large number of patients need to be investigated. However, data concerning this are limited in the literature.

In this retrospective study, we estimated survival rates in patients with oral and oropharyngeal cancer who were surgically treated at our clinic, and determined whether survival differed according to tumour location.

Patients and Methods

We retrospectively analysed the data of 1,486 patients with primary oral and oropharyngeal squamous cell carcinoma who were surgically treated at our clinic. Data were acquired from the clinical cancer register of the Tumour Center at Hannover Medical School (Hannover, Germany).

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Key Words: Squamous cell carcinoma, oral cancer, oropharyngeal cancer, survival rates, tumor location, surgical treatment.

Table I. Demographic characteristics of patients with oral and oropharyngeal squamous cell carcinoma according to tumour location.

Tumour location	Patients, n (%)	Age (years), mean (SD)	Men, %	Women, %
Mouth floor and mandible	840 (56.5)	57.1 (10.7)	78.0	22.0
Maxilla	93 (6.3)	65.7 (14.3)	54.8	45.2
Palate	126 (8.5)	57.7 (10.3)	71.4	28.6
Anterior tongue	223 (15.0)	59.0 (13.4)	63.2	36.8
Base of the tongue and oropharynx	135 (9.1)	55.4 (10.7)	79.3	20.7
Buccal mucosa and oral vestibule	69 (4.6)	65.2 (15.6)	46.4	53.6
Total	1,486 (100.0)	60.0 (12.5)	72.4	27.6

SD: Standard deviation.

Tumours were categorized into six groups according to location, based on the International Statistical Classification of Diseases and Related Health Problems, tenth revision as follows (17): mouth floor and mandible; maxilla; palate; anterior tongue; base of the tongue and oropharynx; and buccal mucosa and oral vestibule. Patients with malignant neoplasms other than squamous cell carcinoma and those with tumours located in other anatomical regions were excluded.

Patients' age, sex, Union for International Cancer Control tumour-node-metastasis (TNM) classification (T, primary tumour size; N, regional lymph nodes; and M, distant metastasis based on clinical or pathological investigations), resection status (R), 5-year survival rate, and disease-specific survival rate were statistically analysed between the six tumour groups. Stages T1 and T2 tumours were analysed together, as were stages T3 and T4 tumours. With respect to regional lymph node metastasis, cases were considered lymph node-positive (N+) or lymph node-negative (N0). With respect to distant metastasis, cases were considered to have trans-regional metastasis (M1) or no metastasis (M0). Complete tumour removal with free resection margins was documented as R0 resection (R0), tumour removal with microscopically visible infiltration of the resection margins was documented as R1 resection (R1), and tumour removal with macroscopically visible tumour remnants was documented as R2 resection (R2).

The 5-year survival rate, which represents the proportion of patients still alive after a 5-year follow-up, and disease-specific survival rate, which represents the time interval between diagnosis and tumour-related death, were investigated using the product-limit method of Kaplan and Meier. Data for patients who died from non-tumour-related conditions and those who were lost to follow-up were excluded. Significant differences (*p*-value) among the groups were evaluated using log-rank tests, Chi-square tests, Student's *t*-tests, and the Bonferroni-Holm method. A *p*-value less than 0.05 was considered statistically significant.

All statistical analyses were conducted using Statistical Package for the Social Sciences for Windows (software version 20; SPSS Inc., Chicago, IL, USA), SigmaPlot 10 (Systat Software Inc., San Jose, CA, USA), and Microsoft Office Excel 2010 (Microsoft Corporation, Redmond, WA, USA).

Results

In total, 1,486 patients with primary oral and oropharyngeal squamous cell carcinoma were analysed. The majority of tumours were located on the floor of the mouth and mandible

(*n*=840), followed by the anterior tongue (*n*=223), base of the tongue and oropharynx (*n*=135), palate (*n*=126), maxilla (*n*=93), and buccal mucosa and oral vestibule (*n*=69) (Table I).

The mean age at the time of diagnosis was 60.0 (range=55.4 [tumours located at the base of the tongue and oropharynx] to 65.7 [tumours located in the maxilla]) years. Tumours involving the mouth floor and mandible, palate, anterior tongue, and base of the tongue and oropharynx occurred more frequently in patients within the age range of 50.0 to 60.0 years, while those involving the maxilla and buccal mucosa and oral vestibule occurred more frequently in patients aged ≥60.0 years (Table I).

In total, 72.4% of patients were men, with a male to female ratio of 27.6:1.0. Male predominance was observed in all groups except the lesions in the buccal mucosa and oral vestibule group with a male to female ratio of 0.9:1.0 (Table I).

Lesions involving the maxilla and base of the tongue and oropharynx had higher T-stage (T3-4), whereas those involving the anterior tongue, buccal mucosa and oral vestibule, mouth floor and mandible, and palate had lower T-stage (T1-2), at the time of diagnosis. Accordingly, regional lymph node metastasis (N+) and a greater extent of distant metastasis (M1) were more frequent in patients with lesions of the base of the tongue and oropharynx than in those with lesions at other sites (N0, M0) (Table II).

R0 resection was achieved more frequently in patients with lesions involving the mouth floor and mandible and anterior tongue, whereas R1 and R2 resections were achieved more frequently in patients with lesions involving the maxilla and base of the tongue and oropharynx (Table II).

With respect to survival, patients with lesions involving the buccal mucosa and oral vestibule exhibited the highest 5-year survival rate (68.2%), followed by patients with lesions involving the anterior tongue (62.8%). The lowest 5-year survival rate was exhibited by patients with lesions involving the base of the tongue and oropharynx (38.8%). The mean overall survival rate was 54.1% (Table III). Disease-specific survival was evaluated over a long-term follow-up period of ≥18.0 years. The disease-specific survival rate was significantly

Table II. Tumour characteristics of patients with oral and oropharyngeal squamous cell carcinoma according to location.

Location n (%)	Primary tumour size			Regional lymph nodes			Distant metastatic spread			Resection status			
	T1-2	T3-4	Total	N0	N+	Total	M0	M1	Total	R0	R1	R2	Total
Mouth floor and mandible	492 (60.6)	320 (39.4)	812 (100.0)	457 (56.1)	358 (43.9)	815 (100.0)	808 (99.1)	7 (0.9)	815 (100.0)	702 (92.6)	38 (5.0)	18 (2.4)	758 (100.0)
Maxilla	39 (41.9)	54 (58.1)	93 (100.0)	60 (64.5)	33 (35.5)	93 (100.0)	91 (98.9)	1 (1.1)	92 (100.0)	62 (72.9)	14 (16.5)	9 (10.6)	85 (100.0)
Palate	93 (76.2)	29 (23.8)	122 (100.0)	76 (61.3)	48 (38.7)	124 (100.0)	124 (100.0)	0 (0.0)	124 (100.0)	105 (91.3)	7 (6.1)	3 (2.6)	115 (100.0)
Anterior tongue	181 (83.8)	35 (16.2)	216 (100.0)	154 (70.3)	65 (29.7)	219 (100.0)	218 (99.5)	1 (0.5)	219 (100.0)	201 (95.7)	6 (2.9)	3 (1.4)	210 (100.0)
Base of the tongue and oropharynx	40 (31.7)	86 (68.3)	126 (100.0)	36 (28.6)	90 (71.4)	126 (100.0)	121 (96.8)	4 (3.2)	125 (100.0)	80 (80.0)	6 (6.0)	14 (14.0)	100 (100.0)
Buccal mucosa and oral vestibule	48 (73.8)	17 (26.2)	65 (100.0)	48 (73.8)	17 (26.2)	65 (100.0)	65 (100.0)	0 (0.0)	65 (100.0)	62 (89.9)	5 (7.2)	2 (2.9)	69 (100.0)
Data available	893 (64.6)	541 (35.4)	1,434 (100.0)	832 (60.4)	611 (39.6)	1,442 (100.0)	1,427 (99.1)	13 (0.9)	1,440 (100.0)	1,212 (90.6)	76 (5.7)	49 (3.7)	1,337 (100.0)
Data missing	–	–	52	–	–	44	–	–	46	–	–	–	149
Total	–	–	1,486	–	–	1,486	–	–	1,486	–	–	–	1,486

inferior for lesions involving the base of the tongue and oropharynx than for those involving the mouth floor and mandible ($p=0.0108$), anterior tongue ($p=0.0015$), palate ($p=0.0204$), and buccal mucosa and oral vestibule ($p=0.0141$). Lesions involving the anterior tongue were associated with a significantly higher disease-specific survival rate than those involving the mouth floor and mandible ($p=0.0087$) and maxilla ($p=0.0088$) (Table IV and Figure 1).

Discussion

To date, only a limited number of studies have investigated the influence of tumour location on the survival of patients with oral and oropharyngeal cancer. In this study, we determined whether disease-specific survival differs according to tumour locations in patients with oral and oropharyngeal squamous cell carcinoma. Patients' age, sex, TNM classification, resection status, and 5-year survival rate were additionally assessed between tumour groups.

With respect to the distribution of tumour locations, the mouth floor and mandible were the most commonly involved (56.5%), followed by the anterior tongue (15.0%), and base of the tongue and oropharynx (9.1%). These data are comparable to those reported for a group of 1,021 patients in a study by Platz *et al.* (18), who showed that 40.0%, 12.9%, 11.7%, 9.3%, 5.2%, and 3.2% of lesions were located in the mouth floor and mandible, maxilla, anterior tongue, buccal mucosa, palate, and base of the tongue and oropharynx, respectively. The results of the German-Swiss-Austrian Group on Maxillofacial Tumours (DOSAK) tumour register (19)

Table III. Five-year survival rates according to tumour location in patients with oral and oropharyngeal squamous cell carcinoma.

Location	5-year survival rate (%)
Buccal mucosa and oral vestibule	68.2
Anterior tongue	62.8
Mouth floor and mandible	57.1
Palate	55.0
Maxilla	42.4
Base of the tongue and oropharynx	38.8

showed that the incidence of oral and oropharyngeal squamous cell carcinoma was approximately 88.0% in patients with oral and 4.0% in patients with oropharyngeal cancer, respectively. The high proportion of squamous cell carcinoma, particularly in the mouth floor and mandible, may be explained by the major exposure of the oral cavity to carcinogens, such as tobacco and alcohol, and the longer interaction time between these agents and the mucosa (20).

With respect to the 5-year survival rate, we found remarkable discrepancies among the six groups, with an overall median 5-year survival rate of 54.1%. Patients with lesions involving the base of the tongue and oropharynx (38.8%) and maxilla (42.4%) had survival rates of <50.0%. In particular, disease-specific survival was significantly inferior for lesions involving the base of the tongue and oropharynx than for those involving the mouth floor and mandible, anterior tongue, palate, and buccal mucosal and oral vestibule. Other studies have shown similar findings.

Table IV. Statistical comparisons of disease-specific survival among patients with oral and oropharyngeal squamous cell carcinoma for different locations.

Location	Mouth floor and mandible	Maxilla	Palate	Anterior tongue	Base of the tongue and oropharynx	Buccal mucosa and oral vestibule
Mouth floor and mandible	–	$p=0.2717$	$p=0.7806$	$p=0.0087$	$p=0.0108$	$p=0.1245$
Maxilla	$p=0.2717$	–	$p=0.2006$	$p=0.0088$	$p=0.6380$	$p=0.0856$
Palate	$p=0.7806$	$p=0.2006$	–	$p=0.1328$	$p=0.0204$	$p=0.2300$
Anterior tongue	$p=0.0087$	$p=0.0088$	$p=0.1328$	–	$p=0.0015$	$p=0.8966$
Base of the tongue and oropharynx	$p=0.0108$	$p=0.6380$	$p=0.0204$	$p=0.0015$	–	$p=0.0141$
Buccal mucosa and oral vestibule	$p=0.1245$	$p=0.0856$	$p=0.2300$	$p=0.8966$	$p=0.0141$	–

Listl *et al.* (21) evaluated 15,792 patients with oral cancer and reported a median 5-year survival rate of 54.6%, while Howaldt *et al.* (19) assessed 9,002 cases of oral and oropharyngeal carcinoma from the DOSAK tumour register and reported a median 5-year survival rate of 52.4%. Conversely, Rösli *et al.* (22) reported a higher 5-year survival rate of 68.8% in a series of 427 patients. With respect to different tumour locations, Rao *et al.* (23) reported 5-year survival rates of 23.4%, 34.3%, 35.8%, 16.6%, 14.7%, 21.7%, 34.4%, 27.6%, and 37.3% for a series of 5,595 patients with tumours involving the mouth floor, mandible, anterior tongue, dorsal tongue, oropharynx, maxilla, hard palate, soft palate, and buccal mucosa, respectively. The survival rates of patients in that study, who were from India, were notably lower than those reported by other authors. This may be attributed to the higher rates of tobacco consumption and betel nut chewing in the reviewed study population, as well as the fact that the majority of tumours were diagnosed at an advanced stage. Nevertheless, survival was poorer for patients with maxillary lesions and base of the tongue and oropharyngeal lesions than for those with anterior tongue and mandibular lesions, which is concordant with our results. These findings may be explained by the fact that the former tumour sites are not easy to inspect clinically, which results in a late diagnosis in the majority of cases, when an unnoticed infiltration of neighbouring structures, as for example the maxillary sinus or the hypopharynx, already took place and complete tumour resection is impeded. In support of the theory of unnoticed and hidden growth depending on tumour location, lesions involving the base of the tongue and oropharynx exhibited tumour-positive regional lymph nodes (N+), as well as distant metastasis (M1), in an appreciable number of cases in the present study. These findings are consistent with those of Hasegawa *et al.* (24), who showed that N-stage tumours are a significant risk factor for the development of distant metastasis. In this connection, neck recurrence after surgery was found to be the most important risk factor for a lower 5-year survival rate in another study (25).

With respect to primary tumour size, the majority of the base of the tongue and oropharyngeal lesions and maxillary lesions were in advanced stages (T3-4) at the time of diagnosis. Furthermore, tumour-free margins (R0 resection) were not achieved in a considerable proportion of patients with involvement at these sites (this was a precondition for recurrence) (26). Wang *et al.* (27) evaluated 275 patients with oral squamous cell carcinoma and reported a significantly lower 5-year survival rate in patients with recurrence than in those without recurrence (31.8% vs. 79.9%, respectively).

With respect to patients' age, base of the tongue and oropharyngeal lesions were considerably more common in younger patients, whereas maxillary lesions appeared more frequently in older patients in the present study. The aetiology and molecular basis of those tumours may differ between younger and older patients (28), although these differences still require further investigation.

Liao *et al.* (29) collected data from 827 patients with oral cavity cancer, with 5 year survival rates of 80.0%, 79.4%, 74.9%, and 77.8% for lesions involving the mouth floor, tongue, palate, and buccal mucosa, respectively. These rates are considerably higher than those reported in the present study, even though the disease stages were comparable between the two studies. A plausible explanation for this discrepancy is lacking.

In the present study, squamous cell carcinoma of the buccal mucosa and oral vestibule, which was, interestingly, more common in women than men, was associated with the highest 5-year survival rate (68.2%), followed by tumours of the anterior tongue (62.8%). Shaw *et al.* (30) evaluated 482 patients with oral carcinoma and reported a survival rate of 70.0% for patients with lesions in the buccal region, while Bachar *et al.* (31) reported a 5-year disease-specific survival rate of 76.4% for surgically treated patients with carcinomas in the buccal mucosa. The high survival rates for lesions involving the buccal mucosa in both studies are almost comparable with that of the present study (68.2%). Zhang *et al.* (32) reported a 5-year survival rate of 64.8% for tongue lesions in middle-aged patients, which is comparable to that

Figure 1. Disease-specific survival according to tumour location in patients with oral and oropharyngeal squamous cell carcinoma. Distinct tumour locations are represented by different coloured lines. The number of patients confirmed as having died from the disease and total number of patients are indicated in parentheses.

of the present study (62.8%). These findings confirm the utility of tumour location in determining the prognosis of patients with head and neck cancer.

In the present study, disease-specific survival was significantly higher for lesions involving the anterior tongue than for those involving the mouth floor and mandible ($p=0.0087$) and maxilla ($p=0.0088$), possibly because lesions involving the anterior tongue are mostly visible in the early clinical stages and can be treated early. In support of this theory, we showed that oral squamous cell carcinoma of the anterior tongue and buccal mucosa and oral vestibule were detected at much earlier stages and smaller sizes (T1-2) than carcinoma involving other sites. Moreover, tumours of the anterior tongue were completely resected (R0) in the majority of cases.

As only surgically treated oral and oropharyngeal squamous cell carcinomas were included, the lack of data concerning 5-year- and disease-specific survival rates with

regard to other treatment modalities, such as for example primary radio- or radiochemotherapy, has to be stated as an important limitation of the present study. Therefore, further analysis of a large cohort of patients including those treatments could supplement and improve our results. Furthermore, the influence of known risk factors in tumorigenesis, for example alcohol and tobacco consumption, poor oral hygiene, or betel nut chewing (4-10), which were not evaluated in the present study in detail, should be factored into analysis. In addition, infection with human papilloma virus (HPV), which is associated with oropharyngeal carcinomas in many cases and known as factor with impact on treatment and prognosis (33), has to be taken into account when considering location as a prognostic factor. As patients virological status was not surveyed during our data analysis, further investigation including this parameter are of high interest and should be pushed forward to validate tumour location as an independent factor in disease prognosis.

Nevertheless, the results of our study suggest that the survival rates in patients with oral and oropharyngeal cancer are strongly dependent on tumour location, which is also associated with other tumour-specific parameters such as the TNM classification and resection status, particularly in patients with advanced malignancies. Therefore, careful inspection of the oral mucosa is crucial for early diagnosis and treatment. Additionally, the early application of assisting imaging methods, like ultrasound, computed tomography or MR imaging, should be considered early in case of doubt. In this context, our findings may motivate clinicians to conduct precise clinical and technical examinations of specific areas in the oral cavity and oropharynx. Moreover, our findings suggest the prognostic significance of tumour location in patients with oral and oropharyngeal squamous cell carcinoma. Further investigation concerning the course of the disease in conjunction with the tumour location should be performed in larger cohorts, especially with inclusion of tumour-associated risk factors, virological status, and non-surgical treatment, to validate its prognostic impact and maybe adjust diagnostic and therapeutic strategies.

Ethical Approval

Ethical approval was obtained by the Ethics Committee of Hannover Medical School (Hannover, Germany), Reference number: 7832_BO_K_2018.

Conflicts of Interest

The Authors have no conflict of interest to declare. All Authors have reviewed the manuscript and have agreed to the submission.

Authors' Contributions

PJ: Analysis of data and drafting the article; JD: Creation of tables and figure; RZ: Creation of tables and figure; RS: Statistical analysis of data; MJ: Acquisition of data; NCG: Literature review and revising the manuscript critically for important intellectual content; FT: Literature review and revising the manuscript critically for important intellectual content; SS: Design of the study and final approval of data analysis.

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References

- Rivera C: Essentials of oral cancer. *Int J Clin Exp Pathol* 8(9): 11884-11894, 2015. PMID: 26617944.
- Warnakulasuriya S: Global epidemiology of oral and oropharyngeal cancer. *Oral Oncol* 45(4-5): 309-316, 2009. PMID: 18804401. DOI: 10.1016/j.oraloncology.2008.06.002
- Wolff KD, Follmann M and Nast A: The diagnosis and treatment of oral cavity cancer. *Dtsch Arztebl Int* 109(48): 829-835, 2012. PMID: 23248713. DOI: 10.3238/arztebl.2012.0829
- Petersen PE: Oral cancer prevention and control—the approach of the World Health Organization. *Oral Oncol* 45(4-5): 454-460, 2009. PMID: 18804412. DOI: 10.1016/j.oraloncology.2008.05.023
- Neville BW and Day TA: Oral cancer and precancerous lesions. *CA Cancer J Clin* 52(4): 195-215, 2002. PMID: 12139232. DOI: 10.3322/canjclin.52.4.195
- Zygogianni AG, Kyrgias G, Karakitsos P, Psyrris A, Kouvaris J, Kelekis N and Kouloulis V: Oral squamous cell cancer: early detection and the role of alcohol and smoking. *Head Neck Oncol* 3: 2, 2011. PMID: 21211041. DOI: 10.1186/1758-3284-3-2
- Rosenquist K, Wennerberg J, Schildt EB, Bladström A, Göran Hansson B and Andersson G: Oral status, oral infections and some lifestyle factors as risk factors for oral and oropharyngeal squamous cell carcinoma. A population-based case-control study in southern Sweden. *Acta Otolaryngol* 125(12): 1327, 2005. PMID: 16303683. DOI: 10.1080/00016480510012273
- Sadighi Shamami M, Sadighi Shamami M and Amini S: Periodontal Disease and Tooth Loss as Risks for Cancer: A Systematic Review of the Literature. *Iran J Cancer Prev* 4(4): 189-198, 2011. PMID: 26322197
- Sapkota A, Hsu CC, Zaridze D, Shangina O, Szeszenia-Dabrowska N, Mates D, Fabiánová E, Rudnai P, Janout V, Holcatova I, Brennan P, Boffetta P and Hashibe M: Dietary risk factors for squamous cell carcinoma of the upper aerodigestive tract in central and eastern Europe. *Cancer Causes Control* 19: 1161, 2008. PMID: 18512121. DOI: 10.1007/s10552-008-9183-0
- Jacob BJ, Straif K, Thomas G, Ramadas K, Mathew B, Zhang ZF, Sankaranarayanan R and Hashibe M: Betel quid without tobacco as a risk factor for oral precancers. *Oral Oncol* 40(7): 697-704, 2004. PMID: 15172639. DOI: 10.1016/j.oraloncology.2004.01.005
- Spalthoff S, Holtmann H, Krüskemper G, Zimmerer R, Handschel J, Gellrich NC and Jehn P: Regular Dental Visits: Influence on Health-Related Quality of Life in 1,607 Patients with Oral Squamous Cell Carcinoma. *Int J Dent* 2017: 9638345, 2017. PMID: 28638411. DOI: 10.1155/2017/9638345
- MacCarthy D, Nunn J, Healy CM, Stassen LF, Gorman T, Martin B, Toner M, Clarke M, Dougall A, McLoughlin J, Kelly A, Waldron C, O'Sullivan M, Doyle C and Flint S: Outcomes from the first mouth cancer awareness and clinical check-up day in the Dublin Dental University Hospital. *J Ir Dent Assoc* 58(2): 101-108, 2012. PMID: 22611791.
- Pitiphat W, Diehl SR, Laskaris G, Cartsos V, Douglass CW and Zavras AL: Factors associated with delay in the diagnosis of oral cancer. *J Dent Res* 81(3): 192-197, 2002. PMID: 11876274. DOI: 10.1177/0810192
- Kowalski LP, Franco EL, Troloni H, Fava AS, de Andrade Sobrinho J, Ramos G, Oliveira BV and Curado MP: Lateness of diagnosis of oral and oropharyngeal carcinoma: factors related to the tumour, the patient and health professionals. *Eur J Cancer B Oral Oncol* 30(3): 167-173, 1994. PMID: 7920162. DOI: 10.1016/0964-1955(94)90086-8
- Bloebaum M, Poort L, Böckmann R and Kessler P: Survival after curative surgical treatment for primary oral squamous cell

- carcinoma. *J Craniomaxillofac Surg* 42(8): 1572-1576, 2014. PMID: 24636353. DOI: 10.1016/j.jcms.2014.01.046
- 16 Jerjes W, Upile T, Petrie A, Riskalla A, Hamdoon Z, Vourvachis M, Karavidas K, Jay A, Sandison A, Thomas GJ, Kalavrezos N and Hopper C: Clinicopathological parameters, recurrence, locoregional and distant metastasis in 115 T1-T2 oral squamous cell carcinoma patients. *Head Neck Oncol* 2: 9, 2010. PMID: 20406474. DOI: 10.1186/1758-3284-2-9
- 17 World Health Organization. ICD-10: International Statistical Classification of Diseases and Related Health Problems: Tenth Revision. Geneva: World Health Organization; 2007.
- 18 Platz H, Fries R, Hudec M, Min Tjoa A and Wagner RR: The prognostic relevance of various factors at the time of the first admission of the patient. Retrospective DOSAK study on carcinoma of the oral cavity. *J Maxillofac Surg* 11: 3-12, 1983. PMID: 6572685. DOI: 10.1016/S0301-0503(83)80005-8
- 19 Howaldt HP, Vorast H, Blecher JC, Reicherts M and Kainz M. [Results of the DOSAK tumor register]. *Mund Kiefer Gesichtschir* 4(Suppl 1): S216-S225, 2000. DOI: 10.1007/PL00014543
- 20 Fries R, Platz H, Wagner RR, Stickler A, Grabner H, Kränzl B, Krekeler G, Kriens O, Leijhanec J, Mehnert H, Scharf F, Schroll K, Schulz P, Waldhart E, Wepner F and Zisser G: Carcinoma of the oral cavity: on the prognostic significance of the primary tumour site (by organs) in the oral cavity. *J Maxillofac Surg* 8: 25-37, 1980. PMID: 6929862. DOI: 10.1016/S0301-0503(80)80070-1
- 21 Listl S, Jansen L, Stenzinger A, Freier K, Emrich K, Holleczeck B, Katalinic A, Gondos A, Brenner H and the GEKID Cancer Survival Working Group: Survival of patients with oral cavity cancer in Germany. *PLoS One* 8: e53415, 2013. PMID: 23349710. DOI: 10.1371/journal.pone.0053415
- 22 Rösli C, Tschudi DC, Studer G, Braun J and Stoeckli SJ: Outcome of patients after treatment for a squamous cell carcinoma of the oropharynx. *Laryngoscope* 119(3): 534-540, 2009. PMID: 19235752. DOI: 10.1002/lary.20033
- 23 Rao DN, Shroff PD, Chattopadhyay G and Dinshaw KA: Survival analysis of 5595 head and neck cancers--results of conventional treatment in a high-risk population. *Br J Cancer* 77: 1514-1518, 1998. PMID: 9652771. DOI: 10.1038/bjc.1998.249
- 24 Hasegawa T, Tanakura M, Takeda D, Sakakibara A, Akashi M, Minamikawa T and Komori T: Risk factors associated with distant metastasis in patients with oral squamous cell carcinoma. *Otolaryngol Head Neck Surg* 152(6): 1053-1060, 2015. PMID: 25883102. DOI: 10.1177/0194599815580980
- 25 Liu CH, Chen HJ, Wang PC, Chen HS and Chang YL: Patterns of recurrence and second primary tumors in oral squamous cell carcinoma treated with surgery alone. *Kaohsiung J Med Sci* 29(10): 554-559, 2013. PMID: 24099110. DOI: 10.1016/j.kjms.2013.03.001
- 26 Sutton DN, Brown JS, Rogers SN, Vaughan ED and Woolgar JA: The prognostic implications of the surgical margin in oral squamous cell carcinoma. *Int J Oral Maxillofac Surg* 32(1): 30-34, 2003. PMID: 12653229. DOI: 10.1054/ijom.2002.0313
- 27 Wang B, Zhang S, Yue K and Wang XD: The recurrence and survival of oral squamous cell carcinomas: a report of 275 cases. *Chin J Cancer* 32(11): 614-618, 2013. PMID: 23601241. DOI: 10.5732/cjc.012.10219
- 28 Dos Santos Costa SF, Brennan PA, Gomez RS, Fregnani ER, Santos-Silva AR, Martins MD, de Castro-Junior G, Rahimi S and Fonseca FP: Molecular basis of oral squamous cell carcinoma in young patients: Is it any different from older patients? *J Oral Pathol Med* 47(6): 541-546, 2018. PMID: 28922483. DOI: 10.1111/jop.12642
- 29 Liao CT, Chang JT, Wang HM, Ng SH, Hsueh C, Lee LY, Lin CH, Chen IH, Huang SF, Cheng AJ and Yen TC: Analysis of risk factors of predictive local tumor control in oral cavity cancer. *Ann Surg Oncol* 15(3): 915-922, 2008. PMID: 18165878. DOI: 10.1245/s10434-007-9761-5
- 30 Shaw RJ, McGlashan G, Woolgar JA, Lowe D, Brown JS, Vaughan ED and Rogers SN: Prognostic importance of site in squamous cell carcinoma of the buccal mucosa. *Br J Oral Maxillofac Surg* 47(5): 356-359, 2009. PMID: 19054598. DOI: 10.1016/j.bjoms.2008.09.017
- 31 Bachar G, Goldstein DP, Barker E, Lea J, O'Sullivan B, Brown DH, Gullane PJ, Gilbert RW, Xu W, Su J and Irish JC: Squamous cell carcinoma of the buccal mucosa: outcomes of treatment in the modern era. *Laryngoscope* 122(7): 1552-1557, 2012. PMID: 22689284. DOI: 10.1002/lary.23296
- 32 Zhang YY, Wang DC, Su JZ, Jia LF, Peng X and Yu GY: Clinicopathological characteristics and outcomes of squamous cell carcinoma of the tongue in different age groups. *Head Neck* 39(11): 2276-2282, 2017. PMID: 28842932. DOI: 10.1002/hed.24898
- 33 Syrjänen S: The role of human papillomavirus infection in head and neck cancers. *Ann Oncol* 21(Suppl 7): vii243-vii245, 2010. PMID: 20943622. DOI: 10.1093/annonc/mdq454

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