Original Article

Oral cavity cancer treatment outcomes in Western Australia

Thomas Hendriks[1], Felipe Cardemil[1,2], Chady Sader[1]

[1]Department of Otolaryngology and Head and Neck Surgery, Sir Charles Gairdner Hospital, Perth, WA, Australia; [2]Department of Otolaryngology-Head and Neck Surgery, Clinica Las Condes, School of Medicine, Universidad de Chile, Santiago, Chile

Contributions: (I) Conception and design: C Sader, F Cardemil; (II) Administrative support: None; (III) Provision of study materials or patients: C Sader, F Cardemil; (IV) Collection and assembly of data: T Hendriks; (V) Data analysis and interpretation: T Hendriks, F Cardemil; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Thomas Hendriks. Sir Charles Gairdner Hospital, Perth, WA 6159, Australia. Email: thomas.hendriks@health.wa.gov.au.

Background: Oral cavity cancers (OCC) account for a significant proportion of head and neck malignancies and pose a significant disease burden given the poor quality of life outcomes and high mortality rates. We evaluated the treatment outcomes of OCC treated at Sir Charles Gairdner Hospital (SCGH), Western Australia (WA).

Methods: A retrospective cohort study was conducted at one of the largest tertiary hospitals in the state. The hospital-based cancer registry was used as a primary source of data, including cases presented between January 2012 and December 2016. Review of medical records was performed for those patients with missing data. The study was approved by the Institutional Safety Board (ISB) in accordance with the hospital regulations (SCGH).

Results: One hundred and one patients with primary diagnosed OCC received treatment during the period. The majority of patients were male, and most were treated primarily with surgery. Twenty-six patients (25.7%) developed recurrence during follow-up, with a median time to recurrence of 10.5 months. Of the patient with recurrence, 73% (19/26) died because of their recurrence. A total of 38 patients died during follow-up (37.6%), with a 3-year overall survival of 66.3% (95% CI, 55.2–75.2%), and a 3-year disease-specific survival (DSS) of 83.2% (95% CI, 72.2–90.1%).

Conclusions: OCC continues to be a therapeutic challenge for the head and neck surgeon. Given the relatively asymptomatic nature of early disease, OCC diagnosed at a late stage is not uncommon, therefore positive lymph-nodes are important when evaluating survival. This study examines up-to-date treatment outcomes for OCC in WA and highlights the variation in mortality rates observed globally.

Keywords: Oral cavity; cancer; malignancy; carcinoma; survival; treatment outcome

Received: 23 December 2018; Accepted: 25 June 2019; Published: 23 July 2019.

doi: 10.21037/ajo.2019.06.01

View this article at: http://dx.doi.org/10.21037/ajo.2019.06.01

Introduction

Oral cavity cancers (OCC) account for a significant proportion of head and neck malignancies. There has been a gradual decline in incidence globally over the past three decades, however, OCC pose a significant disease burden given the high mortality rates and poor quality of life outcomes. Consequently, appropriate prevention and management is paramount for patients with OCC. The aim of this study is to evaluate the treatment outcomes of OCC treated at a tertiary hospital in Perth, Western Australia (WA).

The oral cavity anatomically extends from the skin-vermilion junction of the lips to the hard and soft palate junction, and frequent sites of malignancy include the tongue (40%) and floor of mouth (30%) (1-3). Squamous cell carcinomas (SCC) represent the majority of the malignant lesions identified in those with OCC (4). Demographic risk factors for the development of OCC include age greater than 50 years old and gender (higher risk in males) and both these

factors are associated with poorer prognosis (5-8). Tumour subsite location within the oral cavity is also important when evaluating treatment outcomes with higher mortality rates seen in cancers involving the oral tongue, buccal region and floor of mouth (8). Smoking and alcohol use are synergistic in oral carcinogenesis and increased consumption impacts overall survival and the incidence of second primary tumours (8-12). The role of human papillomavirus in the development of OCC is still unclear although there is well established evidence of the virus' causality in oropharyngeal SCC (13,14).

The global incidence of OCC is estimated at 300,000 cases annually and although incidence has declined over the past few decades, OCC still remains one of the top ten most common cancers worldwide (8,15,16). More concerning is the minimal improvement in mortality rates for OCC despite advances in treatment and technology (8,17-20). OCC diagnosed at an early stage is associated with good survival outcomes. Local OCC of the lip, tongue and floor of mouth all have 5-year survival rates >75%, however, when diagnosed at a later stage with regional metastases, survival diminishes to between 38–63% (depending on site) (21). Unfortunately only a minority (approximately 30%) of OCC are diagnosed at an early stage so despite favourable prognosis in these cases, mortality remains high (22). Surgical resection is the mainstay of treatment for OCC and if indicated, the optimal time frame from surgical resection to post-operative radiotherapy should be less than 6 weeks (23,24).

OCC is a common malignancy worldwide and there is an abundance of literature regarding the presentation, work-up, diagnosis and management of OCC. OCC outcomes over the last 5 years in Australia are poorly described and so the aim of this study was to evaluate the treatment outcomes of OCC treated at a tertiary hospital in WA.

Methods

We conducted a retrospective cohort study at Sir Charles Gairdner Hospital (SCGH) in Perth, WA, one of the largest tertiary hospitals in the state. The hospital-based cancer registry was used as a primary source of data, including cases presented between January 2012 and December 2016. Review of medical records was performed for those patients with missing data. One hundred and one patients were included that were treated for OCC during this 5-year period. Patients identified as having OCC recurrence with previous malignancy prior to January 2012 were excluded. Lip malignancies were also not included in this dataset. The study was approved by the Institutional Safety Board (ISB) in accordance with the hospital regulations (SCGH).

Patient characteristics were recorded and included: age, gender, alcohol consumption, smoking history, evidence of recurrence, time between treatment and recurrence, and deceased status. Disease specific data was also recorded and included: tumour site and size, pathology, grade, pathological stage, resection margins, evidence of lymphovascular/neural/bony invasion, cancer progression, primary treatment modality, adjuvant therapy and surgical reconstruction.

The primary outcome was overall survival. Secondary outcomes included disease-specific survival (DSS) and recurrence. Nodal status was defined as the presence of metastasis on neck lymph nodes on clinical presentation, imaging investigations or pathology results. We calculated 3-year survival rates due to the fact that the last patients included had a follow-up of only one year at the time of the analysis and so 5-year estimates were not available for all patients. We included all consecutive patients during that period of time.

As a part of standard of care at SCGH, every patient with OCC is discussed in a multi-disciplinary head and neck oncology meeting (MDT), regarding indication for primary and adjuvant treatment, as well as surveillance and palliative-care.

Statistical analyses

Variables were analysed using Stata12, with mean and standard deviation for normal-distributed continuous variables and relative and absolute frequencies for categorical variables. Fisher's exact test was used for association between categorical variables. Kaplan-Meier curves were used for survival analysis, and log-rank test for assessing differences among variables. For all analysis we considered an alpha of 5%.

Results

A total of 101 patients with primary diagnosed OCC received treatment during the 5-year period (*Table 1*) and were included in the study. The majority of patients were male (55.6%) and the mean age at diagnosis was 64 years. The most common primary site of malignancy was oral tongue (66%) followed by the retromolar trigone (9%).

Of all patients, 89.1% were treated primarily with

Table 1 Patient and disease specific characteristics

Patient characteristics	N=101 (%)
Male	56 (55.6)
Female	45 (44.4)
Age at diagnosis (years), [mean (range)]	64.4 [19–94]
Primary tumour location	
Tongue	67 (66.0)
Retromolar trigone	10 (10.0)
Floor of mouth	9 (9.0)
Gingiva (upper or lower)	9 (9.0)
Buccal	4 (4.0)
Hard palate	2 (2.0)
Tumour size (mm), [mean (range)]	26.9 [0.5–84]
Recurrence	26 (25.7)
Locoregional	23 (88.5)
Distant	3 (11.5)
Time to recurrence (months), [mean (range)]	11 [1–48]
Histopathology	
Squamous cell carcinoma	99 (98.0)
Adenoid cystic carcinoma	1 (1.0)
Verrucous carcinoma	1 (1.0)
Smoking history	
Current smoker	26 (25.7)
Ex-smoker	30 (29.7)
Non-smoker	20 (19.8)
Unknown	25 (24.8)
Alcohol consumption history	
Heavy	17 (16.8)
Moderate	10 (9.9)
Light	19 (18.8)
Non-drinker	15 (14.9)
Unknown	40 (39.6)
Margin status	
Involved resection margins	16 (15.8)
Unknown margins	22 (21.8)
Average closest margin (mm), n=63	3.8 [0.1–12]

surgery and 66.3% received adjuvant or palliative radiation therapy. Pathological staging was as follows (% patients): I: 37.6; II: 11.9; III: 8; IV/IVA: 39.7; IVB: 1.9; IVC: 0.9. Thirty-five patients (34.7%) had pathologically positive lymph nodes and only one patient had distance metastases at diagnosis. Resection margins were involved in 15.8% of patients. Lymphovascular invasion (LVI) was present in 11 patients, perineural invasion present in 31 and bony invasion present in five. The decision to treat patients with adjuvant therapy (radiotherapy or chemoradiotherapy) was made after discussion at MDT with post-operative histopathological results available.

Forty-four patients (43.6%) received microvascular free flap reconstruction, the most common being anterolateral thigh (ALT) (n=16) and radial forearm (RFFF) (n=15).

Sixty-seven patients (66%) received radiotherapy at some part of their treatment. Of these, 56 underwent primary surgery and the received adjuvant post-operative radiation therapy, and a small proportion of patients (n=10) received radiotherapy without any surgical intervention. Of the series, 33 patients (32.6%) underwent surgery with no need for post-operative radiotherapy. There was one patient that did not receive any surgery or adjuvant therapy due to death soon after initial diagnosis (within 2 weeks). The majority of patients received surgery with post-operative radiotherapy as curative intent treatment, however six patients received palliative radiotherapy and no surgical intervention. These patients all had large tumour burdens and were at least staged IVA. Twenty-eight patients (27.7%) received adjuvant chemotherapy in addition to radiotherapy and the most common agent used was cisplatin. Management of the neck varied and was dependent on discussion at the MDT and with the patient. A majority of patients received comprehensive neck dissections (77%) if appropriate although patient factors and co-morbidities precluded some patients from surgical management of the neck.

One quarter of the patients (25.7%, n=26) developed a recurrence during the follow up, with a median time to recurrence of 11 months (range, 1–48). Locoregional metastatic recurrence was most common (n=23). Of the patients with recurrence, 73% (19/26) died and subsequent analysis identified that recurrence was associated with significantly worse overall survival (P=0.001). The presence of LVI was significantly associated with recurrence (P=0.02) however PNI was not (P=0.052). There were no significant associations between gender and recurrence (P=0.50),

Table 2 Three-year disease-specific survival according to stage in patients with OCC

Stage	Survival (%)	95% CI (%)
I	93.5	76.5–98.3
II	75	40.8–91.1
III	84.7	33.4–97.8
IVA	73.2	43.4–88.9

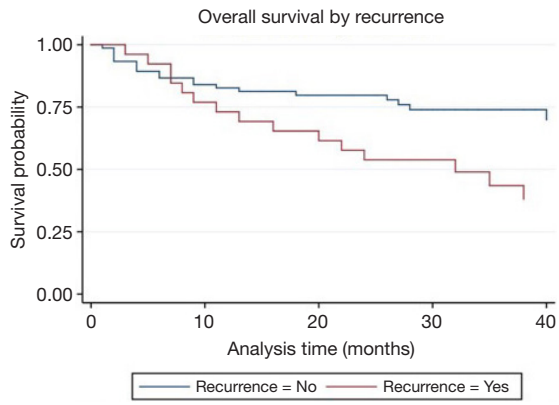

Figure 1 Overall survival by recurrence on a series of patients with OCC (log-rank P=0.001).

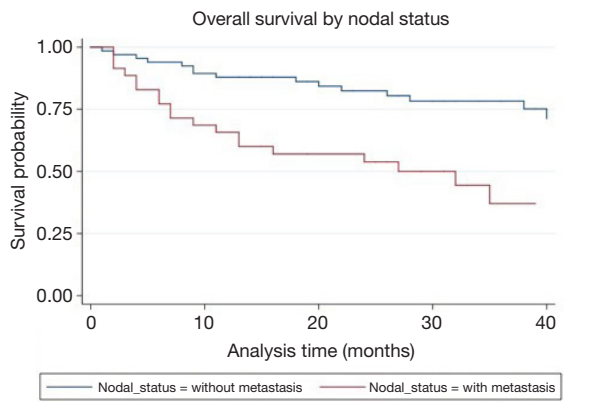

Figure 2 Overall survival by nodal status on a series of patients with OCC (log-rank P=0.004).

pathological stage and recurrence (P=0.41) or tumour site and recurrence (P=0.68). There was no difference in the mean age between patients with recurrence and for those that did not develop recurrence (P=0.84).

A total of 38 patients died during the follow-up (37.6% of the group), with a 3-year overall survival of 66.3% (95% CI, 55.2–75.2%), and a 3-year DSS of 83.2% (95% CI, 72.2–90.1%). The 3-year DSS for patients with stage I was 93.5%, while for patients with stage IVA was 73.2% (*Table 2*). LVI and PNI were not associated with poorer overall survival (P=0.23 and P=0.07 respectively). Gender was not associated with overall survival (P=0.83), And there was no difference in age between survivors and non-survivors (P=0.29). However, there was a statistically significant association between tumour site and survival (P=0.04), with 100% mortality in those with primary buccal site malignancies (n=4). Forty percent of both the tongue and retromolar trigone tumour location patients died whilst mortality was lower for tumours of the floor of mouth and gingiva (22.2% and 11.1% respectively). All patients with hard palate tumours survived. When analysing survival, there was a statistically significant difference in overall survival according to recurrence (P=0.001) (*Figure 1*) and nodal status (P=0.004) (*Figure 2*). There was no difference in DSS according to recurrence or nodal status. and there was no difference in recurrence depending on nodal status.

Discussion

Oral cancer poses a significant disease burden and global 5-year overall survival rates are estimated at 50% (25). There is however, significant variation in treatment outcomes worldwide. In North America, OCC survival continues to improve, whereas in other regions survival rates have remained stable or declined. The main proposed causes for improvement include more advanced adjuvant therapy options (superior radiation therapy, standardised protocols and enhanced knowledge of adjuvant therapy), access to greater reconstruction options that allow more comprehensive resections, improved imaging technology which offers more accurate staging prior to treatment, and regionalisation of services (26-28). The global incidence of OCC also appears to be steadily declining however there is some evidence that incidence in younger individuals may in fact be increasing. Our study assessed OCC treatment outcomes at a tertiary hospital in Perth, WA and our findings are in align with data from North America demonstrating improvement in overall survival in patients suffering from OCC.

Warnakulasuriya's review in 2009 revealed an increasing incidence of oral cancer in Western Europe and Japan during the last 20 years and higher mortality rates in Eastern Europe (8). There was also an increase in mortality and incidence of OCC among younger individuals. Data

released by Cancer Research UK demonstrated similar results with increasing age-standardised mortality rates by up to 21% during the last decade and predicted increases of up to 35% by 2035 (28). Conversely, Gupta *et al.* and Montero *et al.* recently revealed an overall downward trend in mortality for those with oral cancer in the USA (27,29). In fact overall 5-year survival rates increased from 52.7% in 1975 to 68.8% as of 2010 (28,30). The reduction in smoking habits has likely contributed to the overall decline in global incidence of OCC. However, an ageing population in addition to an increase in alcohol consumption particularly amongst the younger generation may be partly responsible for the global variation in mortality rates.

In Australia, there have been several large epidemiological studies published assessing OCC incidence, trends and mortality between the 1980's and mid 2000's. Sugerman *et al.* assessed over 2,000 patients with OCC. The most common sites of malignancy being the lip followed by tongue, occurring more frequently in males and in those above the age of 60 (30). Incidence remained stable during the study period with some variation between anatomical site (increase in lip and decrease in floor of mouth cancers). Mortality rates in lip and tongue malignancies in the study decreased (30). Farah *et al.* reported similar findings between 1982 and 2008 assessing over 60,000 new cancer cases (lip, oral cavity and oropharynx). Overall incidence and mortality remained stable however there was a small increase in incidence of tongue cancer which was also associated with poorer outcomes as compared to the other oral cancer anatomical sites (31). Although difficult to draw conclusions in our cohort given the absence of lip and oropharyngeal malignancies, it is important to acknowledge the significant burden of tongue specific oral cancer.

Abreu conducted a retrospective epidemiological study in WA between 1982 and 2006 demonstrating highest mortality rates in malignancies involving the tongue however overall mortality rates were down-trending. Incidence also remained stable (32). The results of this study closely resemble ours in that OCC is seen most frequently in elderly men and responsible for higher mortality rates when involving the tongue. In contrast to the European data, Australian statistics are suggestive of an overall reduction in incidence of OCC and stable or down-trending mortality rates.

Unfortunately, a vast majority of OCC diagnoses are made at a later stage with patients presenting with nodal disease. This is especially important given nodal involvement is the most important prognostic factor with regards to OCC outcomes (33,34). The prognosis of advanced stage disease remains poor, in contrast to relatively high survival rates in patients with early stage disease. There is limited data in Australia assessing these outcomes specifically, so the present study contributes significantly in this regard.

In this cohort, just over 50% (n=51) of the patients were initially diagnosed with at least pathological stage III disease, which is in keeping with the US National Cancer Institute SEER data demonstrating regional disease in 47% of OCC malignancies (22). The survival outcomes vary significantly between early and advanced disease with 5-year survival rates estimated at 83.7% for localised disease compared to 64.2% in regional disease (22). A recent publication out of the Memorial Sloan Kettering Cancer Center assessed 1,800 patients with OCC revealing a 5-year overall survival rate of 62.5% and overall survival by stage: I: 78.5%; II: 68.4%; III: 64.5% and IV: 34.5% (28). The results from our study are certainly comparable with this data demonstrating good prognosis with early stage cancers without nodal involvement but marked deterioration in survival associated with regional disease (*Figure 2*). Interestingly, there was no significant correlation between pathological stage and recurrence in our cohort despite strong evidence supporting nodal disease and factors (including size, number, ratio) as predictors of recurrence (35-37). There was however a statistically significant association between tumour site and overall survival with 100% mortality for buccal tumour site malignancies. Although there were only four cases of buccal site tumours in our cohort, it is well acknowledged that this subsite is associated with aggressive disease and higher mortality (38-40).

Recurrence was low in our cohort (25%) and more often than not occurring within 18 months of initial diagnosis. This can be likened to recurrence patterns demonstrated in the literature (41-44). Our study also explored the associations between histopathological factors, recurrence and overall survival. Perineural invasion is widely accepted as a predictive prognostic indicator of recurrence and increased mortality however our study was in contrast to this, with no significant associations demonstrated (40,45-47). LVI is also recognised as a marker of prognosis given the potential for nodal metastases however to what extent remains largely unclear (48-51). Adel and Chen *et al.* papers concluded that although strongly correlated with poorer overall survival, LVI is not an independent prognostic factor in those with early stage OCC (51,52).

This study adds to the existing literature supporting

improvements in mortality rates over the past 20–30 years especially in comparison to Europe and the UK. Our results are similar to that of North America demonstrating relatively good prognosis in early stage disease but poorer prognosis with more advanced disease. Three-year overall survival in our cohort was 66.3% which is certainly comparative to that of North America and significantly better than outcomes from some of the larger studies worldwide (28). Survival according to stage in our study was encouraging compared to previous data with overall excellent 3-year DSS of 93.5% for stage I and 73.2% for stage IVA malignancies. Unfortunately nodal metastases drastically reduced overall survival in our cohort and this is well known based on previous literature. Recurrence was low (25.7%) but significantly associated with an increase in overall mortality in this cohort, analogous to other published papers (28,41,53).

The study utilises a relatively large sample size and includes comprehensive analysis of current data relating to oral cavity SCC which has been lacking in recent years in Australia. This study has several limitations including the retrospective nature of the study design which inherently introduces biases and that data was collected at a single centre institution. Depth of tumour invasion was not available in this cohort which was unfortunate given the importance of the role of adjuvant therapy and potential recurrence in patients with greater depths of invasion. Smoking and alcohol consumption history where available was collected but poorly captured in the hospital-based cancer registry and/or medical notes and so analyses of these variables was not performed. Similarly, resection margins were unknown in almost a quarter of the cohort so multi-variate analysis was not performed in order to prevent potential bias and invalid conclusions.

Conclusions

OCC continues to be a therapeutic challenge for the head and neck surgeon despite advances in surgical treatments and adjuvant therapies. Incidence appears to be decreasing slowly worldwide although emerging data suggests geographical variation. Fortunately, in Australia, mortality rates have improved as demonstrated by several large epidemiological studies over the past 20–30 years. Our study supports this notion through analysis of up-to-date treatment outcomes in those with OCC in a large tertiary hospital in Western Australia. Given the relatively asymptomatic nature of early disease, OCC diagnosed at a late stage is not uncommon therefore positive lymph-nodes are important when evaluating survival. Tumour location and histopathological markers are also significant in determining overall prognosis in patients with OCC. This study is one of few in recent years in Australia assessing OCC treatment outcomes and these results, whilst encouraging, highlight the importance of prevention and early detection of OCC in otolaryngology.

Acknowledgments

Funding: None.

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ajo.2019.06.01). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Safety Board (ISB) in accordance with the hospital regulations (SCGH). Informed consent was waived due to the retrospective nature of the study.

References

1. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol 2010;17:1471-4.
2. Bagan J, Sarrion G, Jimenez Y. Oral cancer: clinical features. Oral Oncol 2010;46:414-7.

3. Rivera C. Essentials of oral cancer. Int J Clin Exp Pathol 2015;8:11884-94.
4. Ernani V, Saba NF. Oral Cavity Cancer: Risk Factors, Pathology, and Management. Oncology 2015;89:187-95.
5. Boyle P, Ferlay J. Cancer incidence and mortality in Europe, 2004. Ann Oncol 2005;16:481-8.
6. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. Oral Oncol 2009;45:309-16.
7. Chen SW, Zhang Q, Guo ZM, et al. Trends in clinical features and survival of oral cavity cancer: fifty years of experience with 3,362 consecutive cases from a single institution. Cancer Manag Res 2018;10:4523-35.
8. Jadhav KB, Gupta N. Clinicopathological prognostic implicators of oral squamous cell carcinoma: need to understand and revise. N Am J Med Sci 2013;5:671-9.
9. Dissanayaka WL, Pitiyage G, Kumarasiri PV, et al. Clinical and histopathologic parameters in survival of oral squamous cell carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol 2012;113:518-25.
10. Hashibe M, Brennan P, Benhamou S, et al. Alcohol drinking in never users of tobacco, cigarette smoking in never drinkers, and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. J Natl Cancer Inst 2007;99:777-89.
11. Koontongkaew S. The tumor microenvironment contribution to development, growth, invasion and metastasis of head and neck squamous cell carcinomas. J Cancer 2013;4:66-83.
12. Chen YK, Huang HC, Lin LM, et al. Primary oral squamous cell carcinoma: an analysis of 703 cases in southern Taiwan. Oral Oncol 1999;35:173-9.
13. Gillison ML, Koch WM, Capone RB, et al. Evidence for a causal association between human papillomavirus and a subset of head and neck cancers. J Natl Cancer Inst 2000;92:709-20.
14. Lingen MW, Xiao W, Schmitt A, et al. Low etiologic fraction for high-risk human papillomavirus in oral cavity squamous cell carcinomas. Oral Oncol 2013;49:1-8.
15. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:E359-86.
16. Shiboski CH, Shiboski SC, Silverman S Jr. Trends in oral cancer rates in the United States, 1973-1996. Community Dent Oral Epidemiol 2000;28:249-56.
17. da Silva SD, Ferlito A, Takes RP, et al. Advances and applications of oral cancer basic research. Oral Oncol 2011;47:783-91.
18. Deng H, Sambrook PJ, Logan RM. The treatment of oral cancer: an overview for dental professionals. Aust Dent J 2011;56:244-52, 341.
19. Mehrotra R, Gupta DK. Exciting new advances in oral cancer diagnosis: avenues to early detection. Head Neck Oncol 2011;3:33.
20. Society AC. Survival Rates for Oral Cavity and Oropharyngeal Cancer by Stage 2016 [updated 8th August 2016]. Available online: https://www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/detection-diagnosis-staging/survival-rates.html
21. Institute NC. Cancer Stat Facts: Oral Cavity and Pharynx Cancer 2014. Available online: https://seer.cancer.gov/statfacts/html/oralcav.html
22. Hinerman RW, Mendenhall WM, Morris CG, et al. Postoperative irradiation for squamous cell carcinoma of the oral cavity: 35-year experience. Head Neck 2004;26:984-94.
23. National Comprehensive Cancer Network clinical practice guidelines in oncology, head and neck cancers [Internet]. 2012. [cited 16th April 2018].
24. Greenlee RT, Murray T, Bolden S, et al. Cancer statistics, 2000. CA Cancer J Clin 2000;50:7-33.
25. Eskander A, Goldstein DP, Irish JC. Health Services Research and Regionalization of Care-From Policy to Practice: the Ontario Experience in Head and Neck Cancer. Curr Oncol Rep 2016;18:19.
26. Eskander A, Merdad M, Irish JC, et al. Volume-outcome associations in head and neck cancer treatment: a systematic review and meta-analysis. Head Neck 2014;36:1820-34.
27. Montero PH, Patel SG. Cancer of the oral cavity. Surg Oncol Clin N Am 2015;24:491-508.
28. Research UC. Oral cancer statistics. Available online: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oral-cancer#heading-One
29. Gupta N, Gupta R, Acharya AK, et al. Changing Trends in oral cancer - a global scenario. Nepal J Epidemiol 2016;6:613-9.
30. Sugerman PB, Savage NW. Oral cancer in Australia: 1983-1996. Aust Dent J 2002;47:45-56.
31. Farah CS, Simanovic B, Dost F. Oral cancer in Australia 1982-2008: a growing need for opportunistic screening and prevention. Aust Dent J 2014;59:349-59.
32. Abreu LP, Kruger E, Tennant M. Oral cancer in Western Australia, 1982-2006: a retrospective epidemiological

study. J Oral Pathol Med 2010;39:376-81.
33. Shah JP, Cendon RA, Farr HW, et al. Carcinoma of the oral cavity. factors affecting treatment failure at the primary site and neck. Am J Surg 1976;132:504-7.
34. Shah JP. Cervical lymph node metastases--diagnostic, therapeutic, and prognostic implications. Oncology (Williston Park, NY) 1990;4:61-9; discussion 72, 6.
35. Sharma P, Shah SV, Taneja C, et al. A prospective study of prognostic factors for recurrence in early oral tongue cancer. J Clin Diagn Res 2013;7:2559-62.
36. Son HJ, Roh JL, Cho KJ, et al. Nodal factors predictive of recurrence and survival in patients with oral cavity squamous cell carcinoma. Clin Otolaryngol 2018;43:470-6.
37. Bachar G, Goldstein DP, Barker E, et al. Squamous cell carcinoma of the buccal mucosa: outcomes of treatment in the modern era. Laryngoscope 2012;122:1552-7.
38. Diaz EM Jr, Holsinger FC, Zuniga ER, et al. Squamous cell carcinoma of the buccal mucosa: one institution's experience with 119 previously untreated patients. Head Neck 2003;25:267-73.
39. Liu SA, Wang CC, Jiang RS, et al. 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.
40. Liu CH, Chen HJ, Wang PC, et al. Patterns of recurrence and second primary tumors in oral squamous cell carcinoma treated with surgery alone. Kaohsiung J Med Sci 2013;29:554-9.
41. Wang B, Zhang S, Yue K, et al. The recurrence and survival of oral squamous cell carcinoma: a report of 275 cases. Chin J Cancer 2013;32:614-8.
42. Fan S, Tang QL, Lin YJ, et al. A review of clinical and histological parameters associated with contralateral neck metastases in oral squamous cell carcinoma. Int J Oral Sci 2011;3:180-91.
43. Kernohan MD, Clark JR, Gao K, et al. Predicting the prognosis of oral squamous cell carcinoma after first recurrence. Arch Otolaryngol Head Neck Surg 2010;136:1235-9.
44. Brandwein-Gensler M, Teixeira MS, Lewis CM, et al. Oral squamous cell carcinoma: histologic risk assessment, but not margin status, is strongly predictive of local disease-free and overall survival. Am J Surg Pathol 2005;29:167-78.
45. Fagan JJ, Collins B, Barnes L, et al. Perineural invasion in squamous cell carcinoma of the head and neck. Arch Otolaryngol Head Neck Surg 1998;124:637-40.
46. Soo KC, Carter RL, O'Brien CJ, et al. Prognostic implications of perineural spread in squamous carcinomas of the head and neck. Laryngoscope 1986;96:1145-8.
47. Huang TY, Hsu LP, Wen YH, et al. Predictors of locoregional recurrence in early stage oral cavity cancer with free surgical margins. Oral Oncol 2010;46:49-55.
48. Jardim JF, Francisco AL, Gondak R, et al. Prognostic impact of perineural invasion and lymphovascular invasion in advanced stage oral squamous cell carcinoma. Int J Oral Maxillofac Surg 2015;44:23-8.
49. Lin YT, Chien CY, Lu CT, et al. Triple-positive pathologic findings in oral cavity cancer are related to a dismal prognosis. Laryngoscope 2015;125:E300-5.
50. Michikawa C, Uzawa N, Kayamori K, et al. Clinical significance of lymphatic and blood vessel invasion in oral tongue squamous cell carcinomas. Oral Oncol 2012;48:320-4.
51. Adel M, Kao HK, Hsu CL, et al. Evaluation of Lymphatic and Vascular Invasion in Relation to Clinicopathological Factors and Treatment Outcome in Oral Cavity Squamous Cell Carcinoma. Medicine (Baltimore) 2015;94:e1510.
52. Chen TC, Wang CP, Ko JY, et al. The impact of perineural invasion and/or lymphovascular invasion on the survival of early-stage oral squamous cell carcinoma patients. Ann Surg Oncol 2013;20:2388-95.
53. da Silva SD, Hier M, Mlynarek A, et al. Recurrent oral cancer: current and emerging therapeutic approaches. Front Pharmacol 2012;3:149.

doi: 10.21037/ajo.2019.06.01
Cite this article as: Hendriks T, Cardemil F, Sader C. Oral cavity cancer treatment outcomes in Western Australia. Aust J Otolaryngol 2019;2:20.