Heliyon 9 (2023) e15884

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Anatomical landscape of oral squamous cell carcinoma: A single cancer center study in UAE

Natheer H. Al-Rawi [a,b,*], Ibrahim Y. Hachim [a,c], Mahmood Y. Hachim [d], Abdulrahman Salmeh [b], Asmaa T. Uthman [e], Hesham Marei [e]

[a] Sharjah Institute for Medical Research, University of Sharjah, Sharjah, United Arab Emirates
[b] College of Dental Medicine, University of Sharjah, United Arab Emirates
[c] College of Medicine, University of Sharjah, Sharjah, United Arab Emirates
[d] College of Medicine, Mohammed bin Rashid University of Medicine and Health Sciences, Dubai, United Arab Emirates
[e] College of Dentistry, Gulf Medical University, Ajman, United Arab Emirates

ARTICLE INFO

Keywords:
Oral cancer
Anatomical sites
Bioportal
Oral tongue
Jaw bones
Base of tongue
OSCC

ABSTRACT

Objectives: This study aimed to present demographic and clinicopathological aspects of OSCC identified in Pathology service in the UAE over a 13-year period and compare these findings to a cohort of 523 cases of Head and neck squamous cell carcinoma using the Cancer Genome Atlas's cBioPortal database (http://cbioportal.org).

Material and methods: Histological examination of all hematoxylin and eosin-stained slides and assessment of all demographic and clinical information from laboratory records were performed on all OSCC diagnosed between 2005 and 2018.

Results: Males made up 71.4% of the sample of 231 OSCCs that were evaluated. The patients' average age was 55.38 years. The two most prevalent afflicted sites were the anterior two-thirds of the tongue (57.6%) and the cheek (28.1%). The most prevalent site among smokers were the floor of mouth, cheek, and jaw bones. There was a link between tumor size and numerous anatomical subsites that was shown to be highly significant. OSCC in the FOM was associated with a 25% mortality rate. Patients with OSCC of the anterior tongue and cheek had the best prognosis, with only 15.7% and 15.3% of patients dying during follow-up.

Conclusion: The present investigation found a correlation between the diverse clinicopathological characteristics of the various anatomical subsites in OSCC. Different anatomical subsites also displayed varying degrees of gene mutation.

1. Introduction

Oral cancer is one of the top twenty most prevalent cancers worldwide [1], and its frequency is rising in the Middle East, notably the UAE [2]. The mouth is said to be the sixth most prevalent site for cancer in the human body, however the relative prevalence of oral cancer is widely geographically variable [3], with Asians from the Indian subcontinent having a significantly higher risk than other Asians [3]. Squamous cell carcinoma of the oral cavity (OSCC) accounts for 90% of all occurrences of oral cancer [4,5]. The National Comprehensive Cancer Network (NCCN) reported that OSCC can develop in a variety of oral cavity regions, including the buccal

* Corresponding author. Sharjah Institute for Medical Research, University of Sharjah, Sharjah, United Arab Emirates.
E-mail address: nhabdulla@sharjah.ac.ae (N.H. Al-Rawi).

https://doi.org/10.1016/j.heliyon.2023.e15884
Received 30 December 2022; Received in revised form 12 March 2023; Accepted 25 April 2023
Available online 3 May 2023

mucosa, alveolar ridge, tongue, hard palate, retromolar trigone, floor of the mouth (FOM), and labial mucosa [6].

In the Western world, squamous cell carcinoma (SCC) of the head and neck most often develops on the floor of the mouth or in the oropharynx. The prevalence of human papillomavirus (HPV) infections, as well as the prevalence of alcohol consumption and smoking may explain this finding [6]. In contrast, in the UAE and other Asian regions, SCC is most commonly seen in the mouth's anterior region, including the lip, tongue, and buccal mucosa. The use of tobacco products may be the cause for this, including cigarettes or chewable tobacco [7].

Many researchers have speculated that OSCC at different subsites might be considered as clinicopathologically distinct entities based on varying results [8–10]. Factors such as tumor depth, histological grade, lymph node metastases, and extra nodal extension have all been linked to poor survival in patients with oral cancer, as reported by NCCN [11–13]. However, the NCCN recommendations did not take into consideration the fact that overall survival and disease-free survival rates varied with distinct anatomic subsites of OSCC [11].

The present study aimed to determine whether distinct anatomical subsites of OSCC influence survival and prognosis for OSCC patients in the UAE. In addition, we evaluate their link with the disease's classical clinicopathological features. Using an independent cohort collected from the cBioPortal cancer genomes database, further analysis of the connection between anatomical subsites and clinicopathological features was conducted, in addition to investigating the differential gene expression across the included anatomical subsites. This might offer a clearer understanding of the clinical relevance of anatomical subsites in defining the prognosis, outcome, and behavior of the patient.

1.1. Patients and method

From 2005 to 2018, all OSCC-diagnosed registries from the Maxillofacial department at Tawam hospital in Al Ain, United Arab Emirates were acquired and evaluated. Only the most representative histological section was included. Through a rigorous examination of all forms presented with specimens, we were able to collect demographic and clinical data from all patients, including gender, age, time gap before diagnosis (in months), clinical aspect, location, tumor size (in centimeters), and risk factors (smoking). Cases included are those seen in the anterior two-thirds of the tongue (oral tongue), the floor of the mouth (extending to the ventral tongue), the buccal mucosa (including the buccal sulcus and mucobuccal fold), and the jaw bones (including the gingiva, alveolar mucosa, palate and retromolar trigone). Cancers of the lip and oropharynx (base of tongue, throat, or tonsils) were excluded from this analysis. Histological slides were evaluated for diagnostic confirmation and categorization of tumors as well-differentiated (WD), moderately differentiated (MD), or poorly differentiated (PD), as well as in OSCC variant using recently published approved criteria [14].

All information were descriptively analyzed, and statistical analysis was performed using a standard program (Statistical Package for Social Sciences, SPSS version 28.0, Chicago, IL, US), with statistical significance set at $p < 0.05$. Distribution of group variables was compared in crosstabs by Pearson Chi-square and comparison of means was performed with student's t-test. This study was approved by the ethics committee, Tawam Hospital, Al Ain, UAE (protocol number THREC 556).

1.2. Bioinformatics and in silico analysis

We also used a cohort of 523 cases of Head and neck squamous cell carcinoma to investigate the association between anatomical subsites and various clinicopathological parameters, patient outcomes, and differential gene expression using the cBioPortal for Cancer Genomics (http://cbioportal.org) database, which provides a Web resource for exploring, visualizing, and analyzing multidimensional cancer genomics data. (HNSCC) (TCGA, Pan Cancer Atlas).

2. Results

2.1. Distribution of cases according to anatomical sites

Initial study of our 231 OSCC patients revealed that the oral tongue (O tongue) was the most prevalent location (57.6%), followed

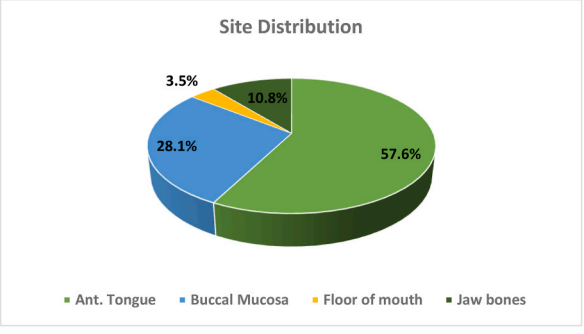

Figure (1). Site distribution of OSCC in UAE population.

by the cheeks (28.1%), Jaw bones (10.8%), and floor of mouth (3.5%) (Fig. 1). There was no statistically significant variation in age between OSCC patients with various anatomical subsites. The present data also indicates that 71.4% of patients were male, whereas just 28.6% were female. Males were afflicted more commonly than females, with a male-to-female ratio of 2.5:1 (Fig. 2).

2.2. Association between OSCC anatomical subsites and smoking

The link between anatomical subsites and smoking was found to be statistically significant ($P < 0.001$) upon stratification of our patients by smoking history. The largest rate of smoking was seen in patients with squamous cell carcinoma of the floor of the mouth (37.5%), buccal mucosa (30.7%), and jaw bones (24%) (Table 1).

Association between OSCC anatomical subsites with classical clinicopathological parameters.

The relationship between anatomical subsites and clinicopathological criteria, such as lymph node (LN) involvement, was studied. LN involvement was shown to have a significant association with anatomical subsites ($P < 0.001$). Lymph nodes involvement was negative (N0) in 50% of OSCC cases in the FOM, followed by the anterior tongue, jawbone region, and the cheek. No significant difference was seen between tumor grade and anatomical subsites ($P = 0.19$).

In addition, a significant relationship ($P < 0.001$) was discovered between tumor size and several anatomical subsites. 33.1% of individuals with OSCC in the anterior tongue had T1 tumors, whereas only 12.5% of patients with OSCC in the FOM had T1 tumors. On the contrary, 52% of patients with OSCC in the jaw bones had T4 tumors.

Additionally, it was shown that anatomical subsites are significantly related to patient outcomes. ($P = 0.01$). OSCC in the FOM was associated with a 25% death rate. In contrast, individuals with OSCC of the anterior tongue had the most favorable prognosis, with an 84.3% survival rate at the time of follow-up (at 3–5 years). (Table 1).

2.3. Association between OSCC anatomical subsites with classical histopathological parameters

A dataset of 523 Head and neck squamous cell carcinomas was evaluated and compared to our cohort using a bioinformatics-based method. A unique correlation was discovered between anatomical subsites and tumor growth. The TCGA Pan Cancer data set demonstrated that most cases of cancer of the anterior two-thirds of the tongue fell into the T2 and T3 categories; however, in the present investigation, one-third of cases fell into the T1 group. In the present study, over forty percent of cases affecting the buccal mucosa belonged to the T4 group, whereas in the "TCGA Pan cancer" data set, T2 represented the majority of cases in the buccal mucosa (36.8%). The Pan Cancer group had somewhat larger cancers on the floor of the mouth, especially at the T4 stage. (45.5% vs. 37.5%). In both groups, T4 was the most common stage tumor size for jaw bone cancer. (figure 3).

Approximately fifty percent of OSCC patients with varied anatomical locations in the Pan Cancer cohort had no LN involvement (N0), which was relatively comparable to the results of the present study (Supp. Figure 2).

In terms of histological grade, nearly fifty percent of OSCCs at various locations were well-differentiated in our sample. However, greater than half the sample in the Pan Cancer cohort was of the moderately differentiated type (Supp. Figure 3).

Evaluation of the association between OSCC anatomical subsites and patient outcome in the Pan Cancer data set found a substantial variation in patient outcome dependent on location. Patients with OSCC of the FOM and jaw bones had the worst outcomes (52.3–58.9% mortality). In comparison, individuals with oral tongue OSCC had the greatest prognosis, with a median survival time of 65.77 months. In the present study, Jaw bones and FOM also had the worst prognosis, although the death rate was lower than that reported in the Pan Cancer data set (20–25%) (Fig. 3).

Different anatomical subsites in OSCC showed a distinct molecular profile and mutation signatures.

The current findings demonstrated a unique clinicopathological profile of OSCC at various anatomical subsites. This may be due to the size, anatomical position, and lymphatic drainage routes. However, we also set to determine if this different clinicopathological

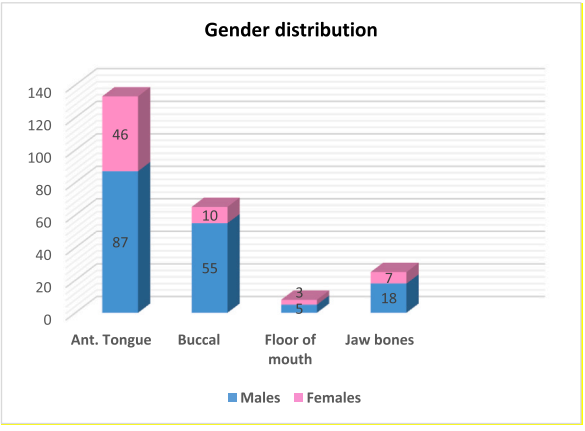

Figure (2). Gender distribution per anatomical subsites (percentages).

Table 1
The association between different anatomical subsites and clinicopathological parameters.

Site		Ant. Tongue	Cheek	Floor of mouth	Jaw bones	P value
	No.	133	65	8	25	
	%	57.6	28.1	3.5	10.8	
Age	**Mean**	**56.13**	**52.31**	**59.25**	**58.16**	**0.43**
	SD	**13.06**	**13.66**	**17.01**	**12.71**	
Gender						
Male	**No.**	**87**	**55**	**5**	**18**	**P < 0.01**
	%	**65.4**	**84.6**	**62.5**	**72**	
Female	**No.**	**46**	**10**	**3**	**7**	
	%	**34.5**	**15.3**	**37.5**	**28**	
Nationality						
Emirati	**No.**	**36**	**12**	**4**	**8**	P < 0.05
	%	**27**	**18.4**	**50**	**32**	
Expat	**No.**	**97**	**43**	**4**	**17**	
	%	**73**	**66.1**	**50**	**68**	
Smoking status						
Smoke	**No.**	**25**	**20**	**3**	**6**	**P < 0.001**
	%	**18.8**	**30.7**	**37.5**	**24**	
No smoke	**No.**	**108**	**35**	**5**	**12**	
	%	**81.2**	**53.8**	**62.5**	**48**	
Recurrence status						
Recurrence	**No.**	**33**	**11**	**0**	**5**	
	%	**24.8**	**16.9**	**0**	**20**	
Mortality						
Dead	**No.**	**21**	**10**	**2**	**5**	**P < 0.05**
	%	**15.7**	**15.3**	**25**	**20**	
Alive	**No.**	**112**	**45**	**6**	**20**	
	%	**84.3**	**69.2**	**75**	**80**	
LN Status						
N0	**No.**	**61**	**25**	**4**	**11**	**P < 0.001**
	%	**45.8**	**35.3**	**50**	**44**	
N1	**No.**	**31**	**18**	**0**	**4**	
	%	**23.3**	**27.7**	**0**	**16**	
N2	**No.**	**25**	**14**	**1**	**5**	
	%	**18.7**	**21.5**	**12.5**	**20**	
N3	**No.**	**5**	**2**	**2**	**2**	
	%	**3.7**	**3**	**25**	**8**	
Nx	**No.**	**11**	**6**	**1**	**3**	
	%	**8.2**	**9.2**	**12.5**	**12**	
Tumor size						
T1	**No.**	**44**	**13**	**1**	**7**	**P < 0.01**
	%	**33.1**	**20**	**12.5**	**28**	
T2	**No.**	**33**	**13**	**3**	**1**	
	%	**24.8**	**20**	**37.5**	**4**	
T3	**No.**	**18**	**8**	**1**	**1**	
	%	**13.5**	**12.3**	**12.5**	**4**	
T4	**No.**	**19**	**26**	**3**	**13**	
	%	**14.3**	**40**	**37.5**	**52**	
Tx	**No.**	**15**	**5**	**0**	**3**	
	%	**11.3**	**7.6**	**0**	**12**	
Histological Grade						
G1	**No.**	**77**	**38**	**4**	**14**	**p > 0.05**
	%	**64.2**	**63.3**	**50**	**63.6**	
G2	**No.**	**40**	**21**	**2**	**5**	
	%	**33.3**	**35**	**25**	**22.7**	
G3	**No.**	**3**	**1**	**2**	**3**	
	%	**2.5**	**16.7**	**25**	**13.7**	

profile found in the various anatomical subsites of OSCC is related with a separate molecular abnormality.

Using the cBioPortal database, we investigated the OSCC anatomical subsites with the most altered genes. Across all subsites, TP53 and CASP8 were revealed to be the most altered genes. Other than TP53 and CASP8, OSCC in the buccal mucosa also demonstrated a reasonably high mutation frequency in a set of genes comprising ABCB6, ARHGAP32, C9, CREB5, SMARCC2, VPS33A, CENPF, and DLC1 (Fig. 4).

The mRNA markers that were most differentially expressed at each anatomical subsite were also analyzed. The most common type of alteration is the overexpression of mRNA with a range in frequency from 1.15 to 15.87%. As revealed by our findings, each OSCC anatomical subsite has a distinct molecular profile. The main differentially expressed genes (DEGs) per anatomical location are reported in Table 2 & Supp. Table 1.

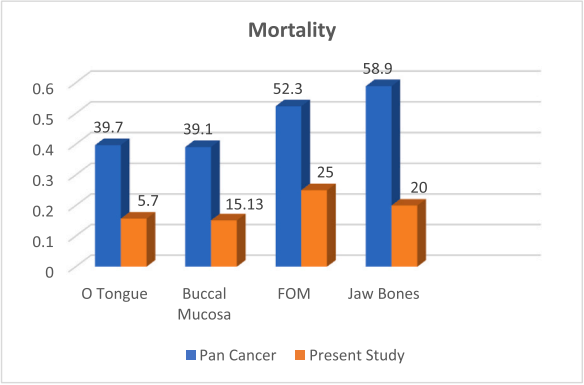

Figure (3). Mortality rates among different anatomical sites (percentages).

ACTIN1, CARD 10, and CAV 1, as well as ARCN1 and DNAJ2, were the most under expressed genes in buccal cancer. Among others, IGFBP2 and PHLDB2 were the most overexpressed genes in the floor of the mouth. The two genes most overexpressed in jaw bones cancer are AHNAK2 and CDK6. In cancer of the anterior two-thirds of the tongue, DLGAP4 and COL4A6 were most overexpressed. Supp. Table 1 demonstrated the heterogeneous nature of gene expressions at different sites of the oral cavity.

3. Discussion

The goal of this study was to provide a 13-year anatomical profile of OSCC in the UAE population and to compare it to Western cohorts. In the present study, OSCC was found in the anterior two-thirds of the tongue in around 57.6% of instances, and in another 28.1%, it was found in the buccal mucosa. These findings were consistent with previous studies conducted in the United Arab Emirates [2], Libya [15], India [16],China [17], and Taiwan [18], among other locations in Asia and the MENA [18].

Despite the variability in the prevalence of oral cancer (OC) in other anatomic subsites, a literature review of OC cases in Arab countries found that the tongue was the most common site of OC in most Arab countries. Cultural, dietary, and environmental factors were cited as possible causes of this site predilection [19]. The higher visibility of these anatomic subsites in the anterior oral cavity could have also contributed to their higher rate of diagnosis. Several studies have revealed that OSCC of the buccal mucosa is more common than OSCC of the tongue in Southeast Asia. This may be because smokeless tobacco products like betel quid and areca nut are more popular in this region [19,20]. While similar habits, such as Shammah and khat usage, are prevalent in the MENA area, their prevalence is lower. In Western countries, a distinct trend was seen, with the anterior tongue (20–40%) and the FOM (15–20%) being the most prevalent sites of oral squamous cell carcinoma (OSCC) compared to buccal mucosa, which is significantly less commonly

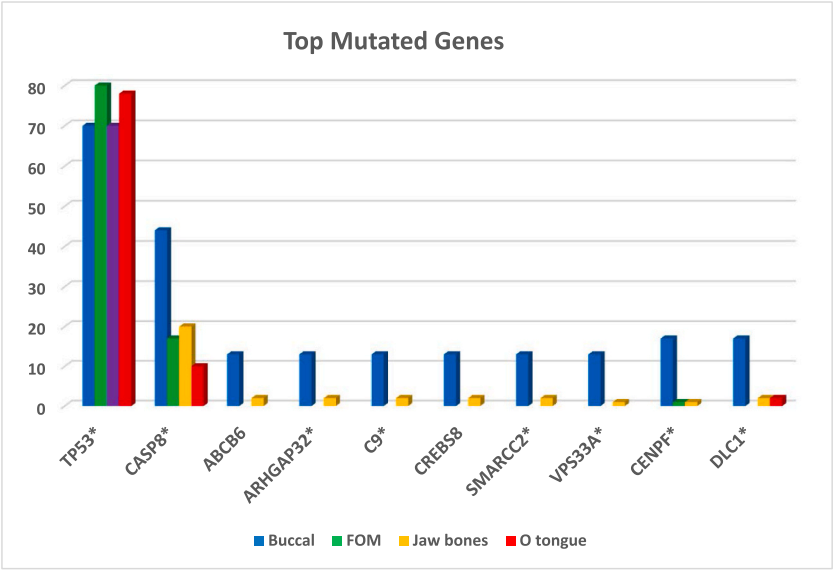

Figure (4). Top mutated genes in different anatomical subsites of OSCC in HNSCC cohort obtained from TCGA, Pan Cancer Atlas using the cBioPortal for Cancer Genomics database.

Table 2
Leading DEGs per anatomical site obtained from various anatomical subsites of OSCC in HNSCC cohort obtained from TCGA, Pan Cancer Atlas using the cBioPortal for Cancer Genomics database.

Anatomical Subsite	Leading DEGs
Buccal Mucosa	ACTN1, AGPAT4, APBB2, ARCN1, BOK, CARD10, CAV1, CAVIN1, CHPF, and DNAJA2
Floor of Mouth	ARL4D, IGF2BP2, IMPDH1, PHLDB2, RNF217, SLC3A2, SMOX, WDFY2, and ZDHHC9.
Jaw bones	AHNAK2, BTBD11, CAMSAP2, CD44, CDK6, CDSN, COL12A1, CPA4, DMKN, and F2RL1
Oral Tongue	ACTA1, AMIGO2, CAP2, CAV2, CAVIN4, CDA, CDH13, COL4A6, CSPG4, and DLGAP4

affected [21]. Multiple investigations undertaken in Europe [20,22], Australia [22], and the Americas reached comparable conclusions [22,23]. This might be attributed to different etiology, with smoking and heavy alcohol use being the culprit rather than smokeless tobacco habits as was observed in Asia and the MENA region.

Oral cancer's site preference can be explained by the histological characteristics of the afflicted tissues and the related etiological variables. As previously mentioned, the tongue was the most common location of OSCC, and OSCC of the tongue was allegedly the most prevalent kind of oral cancer. Histologically, the tongue consists primarily of muscle tissues with a dense arterial and lymphatic supply, rendering it susceptible to invasion and metastases [24]. Furthermore, the tongue, FOM, and buccal mucosa are particularly vulnerable to carcinogens because their thin, non-keratinized mucosa provides little protection against the diffusion of mutagenic chemicals [2]. Such epithelia also have a greater tissue turnover rate than the keratinized gingiva and hard palate, hence raising the chance of cytogenic mutations and consequent malignant transformation [25]. In addition to their inherent susceptibility to cancer, these tissues are constantly bathed in carcinogens that mix with saliva and accumulate within the oral cavity (in the tongue and FOM region in the case of smoking and alcohol consumption) and buccal vestibule (in the case of smokeless tobacco habits, thereby affecting the buccal mucosa) [2]. This is supported by the findings of the current study, in which stratification of cases by smoking history revealed a significant correlation between anatomical subsites and smoking, with the highest prevalence of smoking observed in individuals with OSCC of the floor of the mouth. Though even without tobacco and alcohol usage, the anterior two-thirds of the tongue remain the most likely location for oral cancer [20]. As a whole, this may clarify why the tongue is the most prevalent location for oral cancer in most nations, as well as the reported difference in site preference between the East and the West.

Globally, OSCC predominantly affects males, with variable male-to-female (M:F) ratio ranging in recent studies from 14:1 to 3:2 [26,27] This could be due to the tendency of males to partake in risky habits more frequently than their female counterparts [28], especially in the Arab World, where smoking and alcohol consumption are deemed more stigmatizing for females [19]. In the present study, the M:F ratio was found to be 2.5:1, similar, although a little higher than that observed in studies based in Iraq (2:1) and Jordan (1.8–2.1:1) [2]. This was however significantly lower than that observed in a previous UAE-based study, where the M:F ratio was found to be 4.1:1 [2].

The M:F ratio did not differ substantially between anatomical subsites in this investigation. The same held true for the average age of the patients, which remained reasonably steady throughout the various anatomical subsites, ranging from 52.31 to 59.25 years. This high mean age implies cumulative exposure to carcinogens, such as smoking and drinking, throughout a lifetime. Recent studies, however, indicate that the average age of oral cancer patients is decreasing, while the incidence rate is rising among younger populations. This tendency has been noted particularly among those who began smoking as adolescents, however OSCC has also been detected in young populations with no smoking or drinking history, suggesting a possible distinct etiological route via HPV infection [2].

According to the Centers for Disease Control and Prevention (CDC), cancers of the oral cavity and pharynx combined have increased in incidence between 2007 and 2016 despite the overall decrease in tobacco use and incidence of tobacco-associated cancers in the United States (US) [29]. Despite a decline in oral cancer cases in various anatomical subsites, including the lip, FOM, and hard palate, the incidence of cancer in the cheek and salivary gland has remained stable. It is suspected that a rise in smokeless tobacco habit is the cause of this trend, particularly at the cheek. The incidence of oral cancer in the anterior tongue and gum also increased, although they were not HPV-associated [29].

In addition to investigating the clinicopathological variation across the different anatomical subsites, it was also prudent to investigate the oncogenes that drive carcinogenesis and have the potential to be employed as prognostic variables and therapeutic targets. Recent advances in high-throughput multi-omic technologies have enabled full molecular profiling of tumor samples to discover drivers of oncogenesis and progression, which may lead to the development of targeted oncotherapeutics which influence prognosis and survival of oral cancer at different anatomical subsites [30]. For example, NCBP2 and TFRC expression had been recently associated with increased mortality in patients with OSCC, with targeted NCBP2 depletion showing promising results as a novel oncotherapy for the suppression cell migration, invasion, and proliferation [30]. Furthermore, the recent identification of SERPINH1 as a protein with notable cell-surface expression in the oncogenesis of head-and-neck-SCCs has aided the development of a novel photothermal assisted targeted oncotherapy via gold nanostars combined with the searched SERPINH1 antibody; thereby illustrating the potential of key genes as biomarkers and therapeutic targets for OSCC [31].

Interestingly, our bioinformatic analysis revealed that genes alteration is variable among different anatomical subsites. 16 out of 47 (27.65%) of altered genes were in the form of high mRNA expression (>5% frequency).

Dysregulated genes in each anatomic site were also analyzed in this study, ACTN1 levels, one of the most prominent DEGS in OSCC in buccal mucosa, were shown to be substantially linked with the clinical stage and lymph node metastases, and a high ACTN1 protein level was associated with a poor prognosis. Additionally, suppression of ACTN1 might inhibit OSCC cell growth and metastasis [32].

Furthermore, CARD10, a gene that is differently expressed in OSCCs of the buccal mucosa, was shown to play a crucial role in tumor growth by activating the transcription factor NFkB [33]. Accumulation of CAV1-TME, which also differentially expressed in carcinoma of buccal mucosa was shown to have negative prognostic value in OSCC of the tongue [34].

Additionally, our analysis revealed that polymorphism of IGF2BP2 gene that is differentially expressed in carcinoma of FOM [35] was found to be associated with less favorable oral cancer clinical characteristics [36]. DLGAP4 and COL4A6 that were found to be differentially expressed in carcinoma of anterior 2/3 of the tongue were found to be associated with poor overall survival in cancer, and the COL4A family was discovered to be a major component of the basement membrane (BM) that has recently been found to be involved in tumor angiogenesis and progression [37].

The present study serves as a foundation for the understanding of OSCCs of different subsites as clinicopathologically, genetically, and molecularly distinct entities, which could facilitate further research into the disease's underlying etiology and processes. Furthermore, preventive, diagnostic, and treatment outcomes could be improved by developing subsite-specific molecular targets based on the unique genetic and molecular aberrations across the different subsites.

However, it is important to note that the present study faces several limitations. To start with, the labial mucosa had to be excluded as there was no apparent distinction between SCC of the labial mucosa and SCC of the external lip (which does not belong to the oral cavity) in our pathology registry. Secondly, the gingiva, alveolar mucosa, palate and retromolar trigone were not considered as distinct subsites but grouped together under "jawbones", which may have hindered the specificity of the results. Furthermore, the follow-up duration was not completely uniform, varying between 3 and 5 years. Moreover, the study suffered from a restricted sample size, which could impede the statistical confidence and accuracy of its conclusions. Lastly, the genetic mutation information was derived from a western cohort, and therefore may not accurately represent the genetic aberrations that would be seen in our UAE-based sample.

4. Conclusion

The present findings demonstrated a potential link between the diverse clinicopathological characteristics of the several anatomical subsites in OSCC and the specific genetic dysregulation detected in each anatomical subsite. The identification of such molecular biomarkers may not only be crucial for expanding our understanding of the beginning and progression of OSCC, but also for the development of novel markers for more selective therapies that may target derangements in each anatomical subsite.

Author contribution statement

Natheer H Al-Rawi: Conceived and designed the experiments; Performed the experiment; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Ibrahim Y Hachem; Mahmood Y Hachem: Conceived and designed the experiments; Analyzed and interpreted the data.

Abdulrahman Salmeh: Analyzed and interpreted the data; Wrote the paper.

Asmaa T Uthman; Hesham Marei: Conceived and designed the experiments; Wrote the paper.

Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e15884.

References

[1] Y. Ghantous, A. Elnaaj, Global incidence and risk factors of oral cancer, Harefuah 156 (10) (2017) 645–649.
[2] R. Anis, K. Gaballah, Oral cancer in the UAE: a multicenter, retrospective study, Libyan J. Med. 8 (1) (2013).
[3] J.P. Shah, Z. Gil, Current concepts in management of oral cancer–surgery, Oral Oncol. 45 (4–5) (2009) 394–401.
[4] L.D.R. Thompson, World Health Organization classification of tumours: pathology and genetics of head and neck tumours, Ear Nose Throat J. 85 (2) (2006) 74–75.
[5] T. Tanaka, R. Ishigamori, Understanding carcinogenesis for fighting oral cancer, JAMA Oncol. 2011 (2011).
[6] M. Yakin, B. Seo, H. Hussaini, A. Rich, K. Hunter, Human papillomavirus and oral and oropharyngeal carcinoma: the essentials, Aust. Dent. J. 64 (1) (2019) 11–18.
[7] D.D.L. Dantas, C.C.F. Ramos, A. de LL. Costa, LB de Souza, L.P. Pinto, Clinical-pathological parameters in squamous cell carcinoma of the tongue, Braz. Dent. J. 14 (2003) 22–25.

[8] W.W. Su, C. Su, D. Chang, S. Chuang, S.L. Chen, C. Hsu, et al., Impact of varying anatomic sites on advanced stage and survival of oral cancer: 9-year prospective cohort of 27 717 cases, Head Neck 41 (5) (2019) 1475–1483.

[9] Z. Farhood, M. Simpson, G.M. Ward, R.J. Walker, N. Osazuwa-Peters, Does anatomic subsite influence oral cavity cancer mortality? A SEER database analysis, Laryngoscope 129 (6) (2019) 1400–1406.

[10] S.-A. Liu, C.-C. Wang, R.-S. Jiang, F.-Y. Lee, W.-J. Lin, J.-C. Lin, Pathological features and their prognostic impacts on oral cavity cancer patients among different subsites–A singe institute's experience in Taiwan, Sci. Rep. 7 (1) (2017) 1–9.

[11] D. Adelstein, M.L. Gillison, D.G. Pfister, S. Spencer, D. Adkins, D.M. Brizel, et al., NCCN guidelines insights: head and neck cancers, version 2.2017, J. Natl. Compr. Cancer Netw. 15 (6) (2017) 761–770.

[12] S.K. Mukherji, D. Armao, V.M. Joshi, Cervical nodal metastases in squamous cell carcinoma of the head and neck: what to expect, Head Neck J. Sci. Spec. Head Neck 23 (11) (2001) 995–1005.

[13] P.C. Caldeira, A.M.L. Soto, M.C.F. de Aguiar, C.C. Martins, Tumor depth of invasion and prognosis of early-stage oral squamous cell carcinoma: a meta-analysis, Oral Dis. 26 (7) (2020) 1357–1365.

[14] L. Barnes, J. Eveson, P. Reichart, D. Sidransky, World Health Organization Classification of Tumours: Pathology and Genetics of Head and Neck Tumours, 2005.

[15] K. Subhashraj, M. Orafi, K.V. Nair, R. El-Gehani, M. Elarbi, Primary malignant tumors of orofacial region at Benghazi, Libya: a 17 years review, Cancer Epidemiol. 33 (5) (2009) 332–336.

[16] R. Mehrotra, S. Pandya, A.K. Chaudhary, M. Kumar, M. Singh, Prevalence of oral pre-malignant and malignant lesions at a tertiary level hospital in Allahabad, India, Asian Pac. J. Cancer Prev. APJCP 9 (2) (2008) 263–265.

[17] X.-X. Bai, J. Zhang, L. Wei, Analysis of primary oral and oropharyngeal squamous cell carcinoma in inhabitants of Beijing, China—a 10-year continuous single-center study, BMC Oral Health 20 (1) (2020) 1–7.

[18] N.-C. Lin, S.-I. Hsien, J.-T. Hsu, M.Y.C. Chen, Impact on patients with oral squamous cell carcinoma in different anatomical subsites: a single-center study in Taiwan, Sci. Rep. 11 (1) (2021) 1–9.

[19] A. Al-Jaber, L. Al-Nasser, A. El-Metwally, Epidemiology of oral cancer in Arab countries, Saudi Med. J. 37 (3) (2016) 249.

[20] J.S. Jensen, K.K. Jakobsen, C. Mirian, J.T. Christensen, K. Schneider, A. Nahavandipour, et al., The copenhagen oral cavity squamous cell carcinoma database: protocol and report on establishing a comprehensive oral cavity cancer database, Clin. Epidemiol. 11 (2019) 733.

[21] F. Bray, J. Ferlay, I. Soerjomataram, R.L. Siegel, L.A. Torre, A. Jemal, Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA A Cancer J. Clin. 68 (6) (2018) 394–424.

[22] O.G. Rikardsen, I.-H. Bjerkli, L. Uhlin-Hansen, E. Hadler-Olsen, S.E. Steigen, Clinicopathological characteristics of oral squamous cell carcinoma in Northern Norway: a retrospective study, BMC Oral Health 14 (1) (2014) 1–9.

[23] F.R. Pires, A.B. Ramos, JBC de Oliveira, A.S. Tavares, PSR da Luz, Santos TCRB dos. Oral squamous cell carcinoma: clinicopathological features from 346 cases from a single oral pathology service during an 8-year period, J. Appl. Oral Sci. 21 (2013) 460–467.

[24] I.O. Bello, Y. Soini, T. Salo, Prognostic evaluation of oral tongue cancer: means, markers and perspectives (II), Oral Oncol. 46 (9) (2010) 636–643.

[25] L.L. Feller, R.R.A.G. Khammissa, B.B. Kramer, J.J. Lemmer, Oral squamous cell carcinoma in relation to field precancerisation: pathobiology, Cancer Cell Int. 13 (1) (2013) 1–8.

[26] Y.-C. Lee, C.-K. Young, H.-T. Chien, S.-C. Chin, A. Iandelli, C.-T. Liao, et al., Characteristics and outcome differences in male and female oral cavity cancer patients in Taiwan, Medicine (Baltim.) 100 (44) (2021).

[27] B.M. Alshehri, Trends in the incidence of oral cancer in Saudi Arabia from 1994 to 2015, World J. Surg. Oncol. 18 (1) (2020) 1–6.

[28] M. Bouckaert, T.I. Munzhelele, L. Feller, J. Lemmer, R.A.G. Khammissa, The clinical characteristics of oral squamous cell carcinoma in patients attending the Medunsa Oral Health Centre, South Africa, Integr. Cancer Sci. Ther. 3 (2016) 575–578.

[29] T.D. Ellington, S.J. Henley, V. Senkomago, M.E. O'Neil, R.J. Wilson, S. Singh, et al., Trends in incidence of cancers of the oral cavity and pharynx—United States 2007–2016, Morb. Mortal. Wkly. Rep. 69 (15) (2020) 433.

[30] R. Arora, L. Haynes, M. Kumar, R. McNeil, J. Ashkani, S.C. Nakoneshny, et al., NCBP2 and TFRC are novel prognostic biomarkers in oral squamous cell carcinoma, Cancer Gene Ther. (2023) 1–14.

[31] L. Cai, Y. Wang, X. Peng, W. Li, Y. Yuan, X. Tao, et al., Gold nanostars combined with the searched antibody for targeted oral squamous cell carcinoma therapy, ACS Biomater. Sci. Eng. 8 (6) (2022) 2664–2675.

[32] G. Xie, L. Zhao, Q. Chen, D. Tang, Q. Chen, H. Lu, et al., High ACTN1 is associated with poor prognosis, and ACTN1 silencing suppresses cell proliferation and metastasis in oral squamous cell carcinoma, Drug Des. Dev. Ther. 14 (2020) 1717.

[33] L. Peng, K. He, Z. Cao, L. Bi, D. Yu, Q. Wang, et al., CARD10 promotes the progression of renal cell carcinoma by regulating the NF-κB signaling pathway, Mol. Med. Rep. 21 (1) (2020) 329–337.

[34] M. Vered, M. Lehtonen, L. Hotakainen, E. Pirilä, S. Teppo, P. Nyberg, et al., Caveolin-1 accumulation in the tongue cancer tumor microenvironment is significantly associated with poor prognosis: an in-vivo and in-vitro study, BMC Cancer 15 (1) (2015) 1–12.

[35] D. Li, Y. Guo, S. Tian, C. Zhu, C. Sun, CAV2 regulates Mir-4723/Wnt7A signalling Axis through endocytosis and epithelial-Mesenchymal transition to promote proliferation, invasion, and metastasis of pancreatic cancer cells, J. Cancer 13 (7) (2022) 2200.

[36] C.-H. Chou, C.-Y. Chang, H.-J. Lu, M.-C. Hsin, M.-K. Chen, H.-C. Huang, et al., IGF2BP2 polymorphisms are associated with clinical characteristics and development of oral cancer, Int. J. Mol. Sci. 21 (16) (2020) 5662.

[37] X. Zeng, H.Y. Wang, Y.P. Wang, S.Y. Bai, K. Pu, Y. Zheng, Q.H. Guo, Q.L. Guan, R. Ji, Y.N. Zhou, COL4A family: potential prognostic biomarkers and therapeutic targets for gastric cancer, Transl. Cancer Res. 9 (9) (2020 Sep) 5218.