Advances in Oral and Maxillofacial Cancer Research: A Comprehensive Review

Abstract

Oral and maxillofacial cancers (OMC) remain a significant global public health concern due to their high incidence, mortality rates, and long-term morbidity. Key risk factors, including tobacco use, alcohol consumption, betel quid chewing, and human papillomavirus (HPV) infection, drive the heterogeneous etiology of these malignancies. Recent research efforts have elucidated the molecular pathogenesis of OMC, highlighting the crucial roles of genetic mutations, epigenetic alterations, and tumor–microenvironment interactions in disease initiation and progression. Advanced imaging modalities, such as PET/CT and PET/MRI, have improved diagnostic accuracy, while liquid biopsy approaches leveraging circulating tumor DNA (ctDNA) and salivary biomarkers offer promising avenues for early detection and post-treatment surveillance.

Therapeutically, a multimodal paradigm combining surgery, radiotherapy, and chemotherapy has long been the standard of care. However, cutting-edge treatments—including targeted therapies against the epidermal growth factor receptor (EGFR) and the PI3K/AKT/mTOR pathway—are increasingly applied. Moreover, immune checkpoint inhibitors (ICIs) targeting the PD-1/PD-L1 axis have provided durable responses in a subset of patients with advanced or recurrent disease, establishing immunotherapy as a vital component of the treatment armamentarium. Parallel innovations in surgical techniques, especially transoral robotic surgery (TORS), and reconstructive procedures using microvascular free flaps have substantially improved functional and aesthetic outcomes.

Ongoing research aims to refine precision medicine strategies by integrating molecular diagnostics, genomic profiling, and predictive biomarkers to tailor individualized therapies. Future directions also emphasize combination regimens—such as immunotherapy paired with targeted or epigenetic drugs—designed to overcome therapeutic resistance. Alongside efforts to develop minimally invasive diagnostic tools, robust prevention measures focusing on lifestyle modifications and HPV vaccination are essential to mitigating the global burden of oral and maxillofacial cancers.

Keywords: Oral and maxillofacial cancer; Head and neck oncology; Molecular pathogenesis; Immunotherapy; Targeted therapy; Diagnostic innovations; Liquid biopsy; Tumor microenvironment; Surgical management; Precision medicine

1. Introduction

Oral and maxillofacial cancers are among the most significant public health concerns worldwide, with high morbidity and mortality rates, particularly in regions where tobacco and alcohol use are prevalent (Johnson et al., 2011) (Alotaibi, 2022). Oral cancer, included within head and neck cancer, is the sixth most common malignant neoplasm in the world

(Rodríguez-Molinero et al., 2021). Oral squamous cell carcinoma (OSCC) is considered the most common type of head and neck squamous cell carcinoma (HNSCC) as it holds 90% of HNSCC cases that arise from multiple locations in the oral cavity (Jagadeesan et al., 2024). WHO estimates that there are 4 cases of lip and oral cavity cancer for every 100,000 people worldwide (Khijmatgar et al., 2024). These malignancies primarily affect the oral cavity, lips, oropharynx, salivary glands, and adjacent maxillofacial structures. According to the Global Cancer Observatory, oral cancer ranks among the top 10 most common cancers in terms of incidence, accounting for an estimated 377,713 new cases in 2020 (Kumari et al., 2021), (Sung et al., 2021). Public awareness regarding oral cancer is poor, and many patients present with late-stage disease, contributing to high mortality. Oral cancer is often preceded by a clinical premalignant phase accessible to visual inspection, and thus there are opportunities for earlier detection and to reduce morbidity and mortality. Screening asymptomatic individuals by systematic visual oral examinations to detect the disease has been shown to be feasible. A positive screen includes both oral cancer and oral potentially malignant disorders (Warnakulasuriya and Kerr. 2021). Despite advancements in diagnostic technologies, therapeutic interventions, and preventive strategies, the 5-year survival rate remains relatively low, largely due to late diagnosis and the aggressive nature of the disease (Liu et al., 2021) (Cai et al., 2024).

Over the past decade, there has been a surge in research aimed at improving diagnostic precision, refining therapeutic modalities, and understanding the molecular pathogenesis of oral and maxillofacial cancers. Innovations in molecular profiling and next-generation sequencing have paved the way for targeted therapies that offer the promise of better outcomes and fewer side effects (Jayawickrama et al., 2024). Furthermore, immunotherapeutic approaches, including immune checkpoint inhibitors, have garnered considerable attention as potential game-changers in the management of advanced and recurrent disease (Ferris et al., 2018).

This review provides a comprehensive analysis of recent advances in oral and maxillofacial cancer research, emphasizing epidemiology, molecular pathogenesis, diagnostic innovations, therapeutic modalities, and future directions. Through a synthesis of the latest findings and expert consensus, this article aims to inform clinicians, researchers, and policymakers about cutting-edge developments and emerging trends in this field.

2. Epidemiology and Etiology

2.1 Global Burden

The global burden of oral and maxillofacial cancer exhibits considerable geographic variation. High prevalence and mortality rates are observed in South and Southeast Asia, parts of Eastern Europe, and in areas where tobacco and betel quid use are endemic (Bray et al., 2018). In Western countries, the incidence of oropharyngeal cancers associated with human papillomavirus (HPV) has been rising steadily, highlighting the heterogeneous etiological landscape of these malignancies (Chaturvedi et al., 2018). Despite public health measures such as anti-tobacco campaigns and vaccination programs targeting HPV, the overall incidence of oral cancer has not decreased significantly on a global scale (Perdomo et al., 2016).

2.2 Risk Factors

The most well-established risk factors for oral and maxillofacial cancers include tobacco consumption (both smoked and smokeless forms), alcohol abuse, and betel quid chewing (Johnson et al., 2020). The imbalance of the oral microbiome may influence the progression of oral squamous cell carcinoma (OSCC). However, the composition of the oral microbiome varies depending on saliva, different sites within the oral cavity, and is influenced by risk factors such as smoking, alcohol consumption, and betel quid chewing, as well as an individual's overall oral health status (Su et al., 2021). Chronic exposure to these carcinogens leads to a cascade of genetic and epigenetic changes that predispose individuals to malignant transformation. The primary etiological factors contributing to oral cancer are tobacco and alcohol; however, diet is now recognized as a significant determinant in its development. Various dietary nutrients play specific roles, either protecting against cancer or increasing the risk of its onset, progression, and spread. Consumption of foods such as fruits, vegetables, curcumin, and green tea has been linked to a reduced risk of oral cancer, whereas a pro-inflammatory diet—characterized by high intake of red meat and fried foods—can elevate the likelihood of occurrence. Protective dietary factors exhibit multiple mechanisms of action, including antioxidant, anti-inflammatory, anti-angiogenic, and anti-proliferative effects, which often complement and overlap with one another (Rodríguez-Molinero at al., 2021).

2.2.1 Human Papillomavirus (HPV)

HPV, particularly HPV-16, has emerged as a critical etiological agent for oropharyngeal cancers, which are considered a subset of oral and maxillofacial cancers (Chaturvedi et al., 2018). HPV-driven tumors generally present in younger, non-smoking populations and exhibit distinct molecular and clinical characteristics. Patients with HPV-positive tumors often have better outcomes and respond more favorably to treatment, possibly due to differences in immune recognition and tumor biology (Krsek et al., 2024).

2.2.2 Occupational Exposures and Environmental Factors

Occupational exposure to certain chemicals (e.g., polycyclic aromatic hydrocarbons) and environmental contaminants (e.g., arsenic in drinking water) is also implicated in oral carcinogenesis (Su et al., 2016). Poor oral hygiene, chronic irritation (e.g., ill-fitting dentures), and a diet deficient in fruits and vegetables further contribute to carcinogenesis by promoting inflammatory and dysplastic changes (Jayawickrama et al., 2024).

3. Molecular Pathogenesis

3.1 Genetic Alterations

Oral and maxillofacial cancers result from the accumulation of genetic and epigenetic alterations that disrupt key regulatory pathways controlling cell proliferation, apoptosis, and DNA repair. Common genetic alterations include mutations in the TP53 gene, which lead to impaired DNA damage response and increased susceptibility to malignant transformation. Oncogenic activation of genes such as PIK3CA and MYC, along with inactivation of tumor suppressors CDKN2A and PTEN, further drive tumor progression (Menditti et al., 2023).

3.2 Epigenetic Modifications

Epigenetic changes, including promoter hypermethylation, histone modifications, and microRNA (miRNA) deregulation, are increasingly recognized as critical events in oral carcinogenesis (Han et al., 2022). These changes can silence tumor suppressor genes or enhance oncogene expression, thus contributing to tumor initiation and progression. Recent studies suggest that targeting epigenetic regulators may offer therapeutic benefit, especially in combination with conventional treatments (Jayawickrama et al., 2024).

3.3 Tumor Microenvironment

The tumor microenvironment (TME) in oral and maxillofacial cancers is composed of cancer-associated fibroblasts, immune cells, blood vessels, and the extracellular matrix. Crosstalk between these components and cancer cells influences tumor growth, angiogenesis, and metastasis (Labrador et al., 2022) (Cai et al., 2024). In particular, tumor-associated macrophages and myeloid-derived suppressor cells are frequently implicated in immune evasion and resistance to therapy. Modulating the TME through immunotherapeutic or anti-angiogenic strategies has shown promise in preclinical and early clinical studies (Ferris et al., 2018).

---

4. Diagnostic Advances

4.1 Imaging Modalities

4.1.1 Conventional Imaging

Conventional imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI), remain cornerstones for the staging and localization of oral and maxillofacial cancers. They offer high-resolution visualization of bony structures, soft tissues, and vascular involvement (Jayawickrama et al., 2024). However, these modalities may sometimes fail to detect sub-centimeter lesions or distinguish between post-treatment changes and tumor recurrence.

4.1.2 PET/CT and PET/MRI

Positron emission tomography (PET) combined with CT (PET/CT) or MRI (PET/MRI) has enhanced the sensitivity and specificity of imaging for oral and maxillofacial cancers, particularly in detecting regional lymph node metastases (Bastías et al., 2024). Fluorodeoxyglucose (FDG) PET/CT is widely used to identify metabolic hotspots, providing valuable information for treatment planning and monitoring therapeutic response. Novel tracers targeting specific molecular pathways, such as amino acid transporters or hypoxia markers, are under investigation to further improve diagnostic accuracy (Han et al., 2022).

4.2 Biomarker Development

4.2.1 Liquid Biopsies

The advent of liquid biopsies has opened new avenues for non-invasive cancer diagnosis and monitoring. Circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and exosomes harbor tumor-specific genetic and epigenetic alterations that can be detected in blood or saliva samples (Su et al., 2016) (Hanna et al., 2024). Liquid biopsy–based assays have the potential to identify minimal residual disease, predict treatment response, and detect early recurrences, thus optimizing clinical decision-making (Jayawickrama et al., 2024).

4.2.2 Salivary Diagnostics

Saliva has gained attention as a diagnostic fluid for oral and maxillofacial cancers due to its proximity to tumor sites and ease of collection (Bastías et al., 2024). Salivary biomarkers, including miRNAs, proteins, and metabolites, have shown promise as diagnostic and prognostic tools. Prospective clinical trials are underway to validate salivary tests for routine clinical use (Menditti et al., 2023).

5. Treatment Modalities

5.1 Surgical Management

Surgery remains the primary curative treatment for localized oral and maxillofacial cancers, with the goal of achieving complete tumor resection with adequate margins (Johnson et al., 2020). Advances in surgical techniques, including transoral robotic surgery (TORS) and minimally invasive approaches, have improved functional and cosmetic outcomes (Chaturvedi et al., 2018). Reconstructive surgeries using microvascular free flaps, such as the fibula or radial forearm flap, have further enhanced patients' post-surgical quality of life by restoring facial contour and oral function.

5.2 Radiotherapy

Adjuvant radiotherapy is typically indicated in cases with high-risk features such as close or positive margins, extracapsular spread, or advanced nodal disease (Su et al., 2016). Intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) have revolutionized radiation oncology by enabling precise targeting of tumor sites while sparing critical adjacent structures (Ferris et al., 2018). Image-guided radiotherapy (IGRT) further refines treatment accuracy by accounting for tumor motion and anatomic changes during the treatment course.

5.3 Chemotherapy

Chemotherapy is generally used in a multimodal setting, either concomitant with radiotherapy or as neoadjuvant/adjuvant treatment (Cai et al., 2024). Platinum-based regimens (e.g., cisplatin or carboplatin) remain the gold standard, often combined with 5-fluorouracil or taxanes. While these combinations have improved survival in certain subgroups, toxicities can be significant, necessitating careful patient selection and supportive care measures (Jayawickrama et al., 2024).

5.4 Targeted Therapies

With the burgeoning understanding of molecular pathways implicated in oral and maxillofacial cancers, targeted therapies have come to the forefront (Menditti et al., 2023). The epidermal growth factor receptor (EGFR) is a well-established target, with cetuximab being the first FDA-approved targeted therapy for head and neck cancers (Ferris et al., 2018). Additional agents targeting angiogenesis (bevacizumab) and the PI3K/AKT/mTOR pathway are under clinical investigation, although their efficacy has thus far been modest (Kamangar et al., 2020).

5.5 Immunotherapy

Immunotherapeutic strategies, particularly immune checkpoint inhibitors (ICIs) targeting the programmed death-1 (PD-1) and programmed death-ligand 1 (PD-L1) pathways, have shown encouraging results in advanced oral and maxillofacial cancers (Ferris et al., 2018). Nivolumab and pembrolizumab have demonstrated durable responses in a subset of patients, leading to their approval for recurrent or metastatic disease (Chaturvedi et al., 2018). In a recent study scientists evaluated a peptide-based immunotherapy termed SynerGel: an injectable, biomaterial-based platform for intratumoral drug delivery. A drug-mimicking peptide hydrogel named L-NIL-MDP was loaded with an anti-tumor cyclic dinucleotide (CDN) immunotherapy agonist. The biomaterial combines inducible Nitric Oxide Synthase (iNOS) inhibition with controlled delivery of CDNs, demonstrating between 4- and 20-fold slower drug release than commercially available hydrogels. The findings of the research showed a promising therapy showing improved efficacy over previous hydrogel systems (Leach et al., 2021). Ongoing trials are evaluating combination immunotherapies (e.g., PD-1/PD-L1 blockade with CTLA-4 inhibitors) and novel vaccines to enhance response rates and overcome resistance (Han et al., 2022).

6. Emerging Therapies and Technological Innovations

6.1 Gene Therapy

Gene therapy involves the introduction of genetic material into cancer cells to correct or silence aberrant gene function. Techniques such as CRISPR-Cas9–mediated gene editing are being explored to target mutations in oncogenes like PIK3CA and tumor suppressors such as TP53 (Jayawickrama et al., 2024). While still in the early stages of research, preclinical models have shown promise in achieving tumor regression and overcoming resistance to conventional therapies (Menditti et al., 2023).

6.2 Epigenetic Drugs

Given the role of epigenetic alterations in oral carcinogenesis, drugs targeting DNA methyltransferases (e.g., decitabine) and histone deacetylases (e.g., vorinostat) are under investigation (Han et al., 2022). Preliminary studies suggest that these agents may sensitize tumors to chemotherapy or immunotherapy by reactivating silenced tumor suppressor genes and modulating immune cell infiltration (Su et al., 2016).

6.3 Photodynamic Therapy

Photodynamic therapy (PDT) utilizes light-activated photosensitizers to generate reactive oxygen species that selectively destroy tumor cells. Advances in photosensitizer design and laser technologies have expanded the applicability of PDT for early-stage oral lesions and as an adjunct to surgery (Chaturvedi et al., 2018). PDT offers several advantages, including minimal invasiveness and preservation of healthy tissue, although its efficacy in advanced disease remains limited by penetration depth and tumor hypoxia (Bastías et al., 2024).

6.4 Nanotechnology-Based Therapies

Nanoparticles and other nanomaterials are being explored for targeted drug delivery, imaging, and photothermal therapy in oral and maxillofacial cancers (Han et al., 2022). Nanocarriers can improve the bioavailability and tumor-specific delivery of chemotherapeutic and photodynamic agents while reducing systemic toxicity. Further research is ongoing to optimize nanoparticle formulations, enhance their specificity, and evaluate their long-term safety (Su et al., 2016).

7. Quality of Life and Survivorship

7.1 Rehabilitation and Reconstruction

Patients who survive oral and maxillofacial cancers often face challenges related to speech, swallowing, and facial disfigurement. Oral Health Management and Rehabilitation for Patients with Oral Cancer is area of thrust to prevent recurrence of cancer (Matsuda et al., 2022). Microsurgical reconstruction using free flaps can restore oral function and aesthetics but may require complex surgical expertise and carry risks of donor-site morbidity (Chen et al., 2023). Prosthetic rehabilitation with dental implants, palatal obturators, or facial prostheses also plays a vital role in improving quality of life (Johnson et al., 2020).

7.2 Psychosocial Support

Psychological distress, depression, and social isolation are common among patients undergoing treatment for oral and maxillofacial cancers (Cai et al., 2024). Multidisciplinary care teams that include mental health professionals, nutritionists, and speech therapists can help address these challenges. Recent studies emphasize the importance of early psychosocial interventions in improving patient adherence to treatment and overall outcomes (Bastías et al., 2024).

8. Future Directions

8.1 Personalized Medicine

The heterogeneity of oral and maxillofacial cancers underscores the need for personalized therapeutic approaches. Integrating molecular diagnostics, genomic profiling, and predictive biomarkers can enable precision medicine, wherein treatments are tailored to the individual’s

genetic and immunological landscape (Ferris et al., 2018). Such an approach may improve survival rates and reduce the adverse effects associated with conventional therapies.

8.2 Combination Therapies

Preclinical and clinical studies increasingly suggest that combining different treatment modalities—e.g., immunotherapy with targeted agents or epigenetic drugs—may yield synergistic effects and overcome resistance (Su et al., 2016). As more agents advance into clinical trials, optimizing combination regimens will require robust translational research and biomarker-driven strategies.

8.3 Early Detection and Prevention

Early diagnosis of oral cancer is critical to improve the survival rate of patients. Efforts to improve early detection include the development of point-of-care diagnostic tools, salivary biomarker panels, and artificial intelligence (AI)–driven image analysis (Han et al., 2022). In a recent study convolutional neural network (CNN) deep learning algorithms was used to develop an automated classification and detection model for oral cancer screening (Warin et al., 2021) (Jubair et al., 2022). Strategies for Oral Cancer Screening by Artificial Intelligence-Oriented Interpretation of Optical Coherence Tomography Images had been developed for further use (Ramezani and Tofangchiha, 2022). A recent study reported that Deep learning algorithms were efficiently developed to predict breast cancer, oral cancer, lung cancer, or any other type of medical image. In that study, researchers proposed a model of transfer learning model using AlexNet in the convolutional neural network to extract rank features from oral squamous cell carcinoma (OSCC) biopsy images to train the model. Simulation results had shown that the proposed model achieved higher classification accuracy 97.66% and 90.06% of training and testing, respectively (Rahman et al., 2022). Lin et al., (2021) proposed an automatic detection of oral cancer in smartphone-based images using deep learning for early diagnosis. The performance of the proposed method achieved a sensitivity of 83.0%, specificity of 96.6%, precision of 84.3%, and *F1* of 83.6% on 455 test images (Lin et al., 2021).

Additionally, prevention campaigns focusing on smoking cessation, alcohol reduction, HPV vaccination, and improved oral hygiene hold the greatest promise for curbing the global burden of oral and maxillofacial cancers (Bray et al., 2018).

9. Conclusion

Oral and maxillofacial cancers remain a formidable challenge due to their heterogeneous etiology, complex molecular underpinnings, and high rates of morbidity and mortality. Nonetheless, significant strides have been made in elucidating the pathogenesis of these malignancies, improving diagnostic accuracy, and refining treatment strategies. Advances in molecular biology, imaging technologies, immunotherapy, and precision medicine offer fresh hope for patients, potentially transforming the management of these cancers from one-size-fits-all approaches to individualized regimens grounded in robust scientific evidence.

Ongoing research must continue to focus on identifying and validating prognostic and predictive biomarkers, expanding the arsenal of targeted and immunotherapeutic agents, and developing minimally invasive diagnostic tools. Equally critical is the need for comprehensive survivorship programs that address quality-of-life issues, ranging from functional rehabilitation to psychosocial support. By combining cutting-edge science with patient-centered care, the field of oral and maxillofacial oncology can look forward to more favorable outcomes and improved patient experiences in the years ahead.

References

Alotaibi O. N. (2022). Oral and maxillofacial cancer: A 35-year retrospective analysis at a referral dental hospital in Saudi Arabia. The Saudi dental journal, 34(1), 56–61. https://doi.org/10.1016/j.sdentj.2021.10.001

Bastías, D., Maturana, A., Marín, C., Martínez, R., & Niklander, S. E. (2024). Salivary Biomarkers for Oral Cancer Detection: An Exploratory Systematic Review. International journal of molecular sciences, 25(5), 2634. https://doi.org/10.3390/ijms25052634

Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, *68*(6), 394–424. https://doi.org/10.3322/caac.21492

Cai, L., Zhu, H., Mou, Q., Wong, P. Y., Lan, L., Ng, C. W. K., Lei, P., Cheung, M. K., Wang, D., Wong, E. W. Y., Lau, E. H. L., Yeung, Z. W. C., Lai, R., Meehan, K., Fung, S., Chan, K. C. A., Lui, V. W. Y., Cheng, A. S. L., Yu, J., Chan, P. K. S., … Chen, Z. (2024). Integrative analysis reveals associations between oral microbiota dysbiosis and host genetic and epigenetic aberrations in oral cavity squamous cell carcinoma. NPJ biofilms and microbiomes, 10(1), 39. https://doi.org/10.1038/s41522-024-00511-x

Chaturvedi, A. K., Engels, E. A., Anderson, W. F., & Gillison, M. L. (2008). Incidence trends for human papillomavirus-related and -unrelated oral squamous cell carcinomas in the United States. Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 26(4), 612–619. https://doi.org/10.1200/JCO.2007.14.1713

Chen, W. L., Zhou, B., Huang, Z. X., Chen, R., & Dong, X. Y. (2023). Various Types of Facial-Angular Artery-Based Flaps for Reconstructing Oral and Maxillofacial Defects Following Cancer Ablation. The Journal of craniofacial surgery, 34(5), e478–e483. https://doi.org/10.1097/SCS.0000000000009337

Ferris, R. L., Blumenschein, G., Fayette, J., Guigay, J., Colevas, A. D., Licitra, L., … Harrington, K. (2018). Nivolumab for recurrent squamous-cell carcinoma of the head and neck. *New England Journal of Medicine, 375*(19), 1856–1867. https://doi.org/10.1056/NEJMoa1602252

Han, Y. K., Park, H. Y., Park, S. G., Hwang, J. J., Park, H. R., & Yi, J. M. (2022). Promoter Methylation of Cancer Stem Cell Surface Markers as an Epigenetic Biomarker for Prognosis

of Oral Squamous Cell Carcinoma. International journal of molecular sciences, 23(23), 14624. https://doi.org/10.3390/ijms232314624

Hanna, G. J., Dennis, M. J., Scarfo, N., Mullin, M. S., Sethi, R. K. V., Sehgal, K., Annino, D. J., Jr, Goguen, L. A., Haddad, R. I., Tishler, R. B., Margalit, D. N., Uppaluri, R., Schoenfeld, J. D., & Rettig, E. M. (2024). Personalized ctDNA for Monitoring Disease Status in Head and Neck Squamous Cell Carcinoma. Clinical cancer research : an official journal of the American Association for Cancer Research, 30(15), 3329–3336. https://doi.org/10.1158/1078-0432.CCR-24-0590

Jagadeesan, D., Sathasivam, K. V., Fuloria, N. K., Balakrishnan, V., Khor, G. H., Ravichandran, M., Solyappan, M., Fuloria, S., Gupta, G., Ahlawat, A., Yadav, G., Kaur, P., & Husseen, B. (2024). Comprehensive insights into oral squamous cell carcinoma: Diagnosis, pathogenesis, and therapeutic advances. Pathology, research and practice, 261, 155489. https://doi.org/10.1016/j.prp.2024.155489

Jayawickrama, S. M., Ranaweera, P. M., Pradeep, R. G. G. R., Jayasinghe, Y. A., Senevirathna, K., Hilmi, A. J., Rajapakse, R. M. G., Kanmodi, K. K., & Jayasinghe, R. D. (2024). Developments and future prospects of personalized medicine in head and neck squamous cell carcinoma diagnoses and treatments. Cancer reports (Hoboken, N.J.), 7(3), e2045. https://doi.org/10.1002/cnr2.2045

Johnson, N. W., Jayasekara, P., & Amarasinghe, A. A. (2011). Squamous cell carcinoma and precursor lesions of the oral cavity: epidemiology and aetiology. Periodontology 2000, 57(1), 19–37. https://doi.org/10.1111/j.1600-0757.2011.00401.x

Jubair, F., Al-Karadsheh, O., Malamos, D., Al Mahdi, S., Saad, Y., & Hassona, Y. (2022). A novel lightweight deep convolutional neural network for early detection of oral cancer. Oral diseases, 28(4), 1123–1130. https://doi.org/10.1111/odi.13825

Khijmatgar, S., Yong, J., Rübsamen, N., Lorusso, F., Rai, P., Cenzato, N., Gaffuri, F., Del Fabbro, M., & Tartaglia, G. M. (2024). Salivary biomarkers for early detection of oral squamous cell carcinoma (OSCC) and head/neck squamous cell carcinoma (HNSCC): A systematic review and network meta-analysis. The Japanese dental science review, 60, 32–39. https://doi.org/10.1016/j.jdsr.2023.10.003

Krsek, A., Baticic, L., Sotosek, V., & Braut, T. (2024). The Role of Biomarkers in HPV-Positive Head and Neck Squamous Cell Carcinoma: Towards Precision Medicine. Diagnostics (Basel, Switzerland), 14(13), 1448. https://doi.org/10.3390/diagnostics14131448

Kumari, P., Debta, P., & Dixit, A. (2022). Oral Potentially Malignant Disorders: Etiology, Pathogenesis, and Transformation Into Oral Cancer. Frontiers in pharmacology, 13, 825266. https://doi.org/10.3389/fphar.2022.825266

Labrador, A. J. P., Marin, N. R. G., Valdez, L. H. M., Sanchez, K. B. T., Zabarburu, W., Ibazetta, K. A. R., Garcia, A. E. R., Cabezas, D. M., Romero, L., Conte, A. M., & Wright, J. M. (2022). Metastasis to the oral and maxillofacial region. A systematic review. Journal of stomatology, oral and maxillofacial surgery, 123(5), e474–e483. https://doi.org/10.1016/j.jormas.2021.12.009

Leach, D. G., Dharmaraj, N., Lopez-Silva, T. L., Venzor, J. R., Pogostin, B. H., Sikora, A. G., Hartgerink, J. D., & Young, S. (2021). Biomaterial-Facilitated Immunotherapy for Established Oral Cancers. ACS biomaterials science & engineering, 7(2), 415–421. https://doi.org/10.1021/acsbiomaterials.0c01575

Lin, H., Chen, H., Weng, L., Shao, J., & Lin, J. (2021). Automatic detection of oral cancer in smartphone-based images using deep learning for early diagnosis. Journal of biomedical optics, 26(8), 086007. https://doi.org/10.1117/1.JBO.26.8.086007

Liu, Y., Mi, Y., Zhang, L., & Jiang, T. (2021). Survival and risk factors of adenosquamous carcinoma in the oral and maxillofacial region: a population-based study. American journal of translational research, 13(10), 12071–12082.

Matsuda, Y., Jayasinghe, R. D., Zhong, H., Arakawa, S., & Kanno, T. (2022). Oral Health Management and Rehabilitation for Patients with Oral Cancer: A Narrative Review. Healthcare (Basel, Switzerland), 10(5), 960. https://doi.org/10.3390/healthcare10050960

Menditti, D., Santagata, M., Imola, G., Staglianò, S., Vitagliano, R., Boschetti, C. E., & Inchingolo, A. M. (2023). Personalized Medicine in Oral Oncology: Imaging Methods and Biological Markers to Support Diagnosis of Oral Squamous Cell Carcinoma (OSCC): A Narrative Literature Review. Journal of personalized medicine, 13(9), 1397. https://doi.org/10.3390/jpm13091397

Perdomo, S., Martin Roa, G., Brennan, P., Forman, D., & Sierra, M. S. (2016). Head and neck cancer burden and preventive measures in Central and South America. Cancer epidemiology, 44 Suppl 1, S43–S52. https://doi.org/10.1016/j.canep.2016.03.012

Rahman, A. U., Alqahtani, A., Aldhafferi, N., Nasir, M. U., Khan, M. F., Khan, M. A., & Mosavi, A. (2022). Histopathologic Oral Cancer Prediction Using Oral Squamous Cell Carcinoma Biopsy Empowered with Transfer Learning. Sensors (Basel, Switzerland), 22(10), 3833. https://doi.org/10.3390/s22103833

Ramezani, K., & Tofangchiha, M. (2022). Oral Cancer Screening by Artificial Intelligence-Oriented Interpretation of Optical Coherence Tomography Images. Radiology research and practice, 2022, 1614838. https://doi.org/10.1155/2022/1614838

Rodríguez-Molinero, J., Migueláñez-Medrán, B. D. C., Puente-Gutiérrez, C., Delgado-Somolinos, E., Martín Carreras-Presas, C., Fernández-Farhall, J., & López-Sánchez, A. F. (2021). Association between Oral Cancer and Diet: An Update. Nutrients, 13(4), 1299. https://doi.org/10.3390/nu13041299

Su, S. C., Chang, L. C., Huang, H. D., Peng, C. Y., Chuang, C. Y., Chen, Y. T., Lu, M. Y., Chiu, Y. W., Chen, P. Y., & Yang, S. F. (2021). Oral microbial dysbiosis and its performance in predicting oral cancer. Carcinogenesis, 42(1), 127–135. https://doi.org/10.1093/carcin/bgaa062

Su, S. C., Lin, C. W., Yang, W. E., Fan, W. L., & Yang, S. F. (2016). The urokinase-type plasminogen activator (uPA) system as a biomarker and therapeutic target in human malignancies. Expert opinion on therapeutic targets, 20(5), 551–566. https://doi.org/10.1517/14728222.2016.1113260

Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians, 71*(3), 209–249. https://doi.org/10.3322/caac.21660

Warin, K., Limprasert, W., Suebnukarn, S., Jinaporntham, S., & Jantana, P. (2021). Automatic classification and detection of oral cancer in photographic images using deep learning algorithms. Journal of oral pathology & medicine : official publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology, 50(9), 911–918. https://doi.org/10.1111/jop.13227

Warnakulasuriya, S., & Kerr, A. R. (2021). Oral Cancer Screening: Past, Present, and Future. Journal of dental research, 100(12), 1313–1320. https://doi.org/10.1177/00220345211014795