Revisiting Early Detection of Oral Cancer: A Review on Methods, Impact on Survival Rates, and Recurrence Prevention

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ABSTRACT

Oral cancer, particularly oral squamous cell carcinoma, represents a significant global health concern, with approximately 377,000 new cases diagnosed annually. Early detection is crucial, as the prognosis is heavily influenced by disease stage. Localized oral cancers can have a five-year survival rate exceeding 80%, compared to only 38% for metastatic cases. This literature review emphasizes the importance of early detection as a means of improving patient outcomes and quality of life. Major risk factors, including tobacco use, excessive alcohol consumption, human papillomavirus infection, and poor oral hygiene contribute to the disease's prevalence. While symptoms such as persistent ulcers and lumps may be overlooked, advancements in diagnostic techniques -such as visual examinations, fluorescence imaging, and molecular diagnostics- offer promising avenues for early identification. Public health initiatives focusing on awareness campaigns, regular dental check-ups, and comprehensive screening programs are essential for identifying at-risk populations. This review analyzes various methodologies, including salivary biomarkers, advanced imaging technologies, and tumor markers, which contribute to early detection strategies. As advancements in research and technology continue, the integration of these innovative approaches may enhance early intervention efforts. Ultimately, a collaborative approach involving education, research, and healthcare innovation is vital for combating oral cancer. Prioritizing early detection can significantly reduce the societal burden of oral cancer and improve the overall quality of life for affected individuals.

Keywords: Cancer diagnosis and treatments; early detection; health; oncology; oral cancer; oral squamous cell carcinoma; public health initiatives; survival rates

INTRODUCTION

Oral cancer remains a significant global health issue, with approximately 377,000 new cases diagnosed each year worldwide, according to the Global Cancer Observatory (2020).[1] The most common type of oral cancer is oral squamous cell carcinoma (OSCC), which accounts for over 90% of all oral cancers. The prognosis for patients with oral cancer is largely determined by the stage at which the disease is identified. If diagnosed early, the five-year survival rate for localized cases can exceed 80%, whereas advanced stage diagnoses are associated with much lower survival rates.[2,3]

Early detection plays a vital role in improving patient outcomes and enhancing quality of life. Major risk factors for oral cancer include tobacco use, excessive alcohol consumption, human papillomavirus (HPV) infection, and poor oral hygiene.[4] The subtle onset of oral cancer often leads to late-stage diagnoses, as individuals may not recognize the signs or symptoms. Common symptoms include persistent

ulcers, lumps, and changes in the oral mucosa, which are often overlooked or misinterpreted.[5]

Recent advances in dentistry and oncology have led to improvements in the early detection of oral cancer. Techniques such as visual examinations, adjunctive technologies like fluorescence imaging, and molecular diagnostics have shown potential in enhancing screening effectiveness.[6] Increasing public awareness, promoting regular dental check-ups, and implementing comprehensive screening programs are key strategies for identifying at-risk individuals early.[7]

To improve outcomes for those with oral cancer, it is essential to focus on education, research, and technological innovation in the ongoing effort to combat this disease. In this review, we highlight the importance of early detection of oral cancer by comparing different stages of oral cancer with overall survival (OS) rates and disease-specific survival (DSS) rates.

METHODOLOGY

A literature review was performed on the PUBMED database using the search terms "OSCC," "TNM staging," and "Prognosis" for a duration of ten years between 2015 and 2024. Qualifying literature included full-text articles pertaining to case reports, clinical studies, clinical trials, multicenter studies, and observational studies. Applying the search strategies yielded a total of 470 articles, of which 21 were selected after initial screening. Further screening was performed to select articles that described the staging of oral cancers, that included OS rates or DSS rates as prognostic factors. Finally, a total of 11 articles were included for qualitative analysis. The results are tabulated in Table 1. Additionally, a literature review was performed using the search terms "OSCC", "TNM staging" and "Recurrence" for a duration of ten years with qualifying literature as specified in the previous literature search. A total of 167 articles were screened initially, resulting in 29 articles being screened further, leading to a final yield of 9 articles, the findings of which are summarized in Table 2.

DISCUSSION

The Importance of Early Detection of Oral Cancer

Early detection of oral cancer, particularly OSCC, is crucial for improving patient prognosis and reducing the disease's impact on individuals and healthcare systems.[8] Factors such as clinical staging, OS rates, and DSS rates guide prognostic assessments.[9] The American Joint Committee on Cancer categorizes oral cancer into early stages (I and II), stage III (which includes cases with regional metastases and larger tumors), and late stages (IV), indicating advanced or metastatic disease.[10] Oral cancer is often asymptomatic in its early stages,

leading to late-stage diagnoses when treatment options become limited. Early detection improves survival rates, extends treatment options, minimizes complications, lowers treatment costs, and helps prevent disease progression.[8] Key survival estimates for clinical prognosis include OS and DSS rates.[11] A review of eleven studies (Table 1), which included multicenter retrospective, single institution retrospective, and one prospective study, demonstrated decreased survival rates with increased cancer staging.[10,12-21] Given the rising global incidence of oral cancer, public health initiatives must emphasize early detection through regular screenings, awareness campaigns, and advancements in diagnostic technologies. Prioritizing early detection can significantly enhance patient outcomes and mitigate the societal burden of oral cancer.

Early detection of oral cancer significantly enhances survival rates. The primary advantage of early detection is its positive impact on survival rates; cancers diagnosed at stages I and II have significantly higher 5-year survival rates compared to those diagnosed at stages III and IV. For instance, the American Cancer Society notes that the five-year survival rate for localized oral cancer is approximately 84%, declining to about 38% for cancers that have metastasized.[8] Additionally, early detection allows for less invasive treatment options, such as surgery or laser therapy, which can preserve surrounding healthy tissues. As the disease advances, treatments often become more complicated, necessitating combinations of therapies that could affect both function and aesthetics.[22]

Furthermore, diagnosing cancer at an early stage helps minimize both immediate and long-term treatment complications. Advanced oral cancer treatments may lead to significant functional impairments, affecting essential daily activities. Early intervention allows for less invasive procedures, preserving normal function and enhancing quality of life.[23] Tumour recurrences are one of the most important complications affecting the overall prognosis of oral cancer patients. Recurrent cases have shown lower 2-year and 5-year survival rates when compared to non-recurrent cases.[24] The clinical staging of the tumour shows a correlation with the rate of recurrence.[25] It has been found that 25-30% of early stage (stage I & II) cases of OSCC show recurrences, whereas for advanced cases (stage III & IV), the recurrence rate is doubled, ranging from 50-60% in advanced cases. The pattern of recurrence also varies and may show local, regional, or locoregional disease failure.[26] A review of nine studies (Table 2) indicates that recurrences are dependent on a number of clinicopathological factors, with early detection being a key factor in improving the survival rates and prognosis.[25,27-34]

SN	Authors	Year	Type of study	Sample size	TNM staging	OS	DSS	Conclusion
1	Amit et al.[12]	2015	Multicenter retrospective study	1815	Stage I - 268 (15%)	T1N1 - 71% (5 years)	-	Reclassification of T3N1 as stage IVa
					Stage II - 333 (18%)	T2N1 - 67% (5 years)		
					Stage III - 236 (13%)	T3N0 - 73% (5 years)		T3N1 represents patients at high risk of treatment failure similar to stage IVa.
					Stage IV - 973 (54%)	T3N1 - 52% (5 years)		
					T3/T4 - 81	T3/T4 - 81		
2	López-Ce-drún and Andrés de Llano[13]	2015	Retrospective observational study	64	Stage III - 28	(5 years) 34.4%	(5 years) 35.9%	Long-term overall & specific survival is influenced by age & comorbidities. Prognosis was influenced by ganglionar status and histopathological characteristics of the primary tumour.
					Stage IV - 36	(22 years) - 6.3%	(22 years) - 7.2%	
3	Nandaku-mar et al.[14]	2016	Multicenter retrospective study	4773	Tongue cancer- Stage I & II: 449	(3 years) - 79.5% (5 years) - 75.3%	-	Separating out individual anatomical sites of head and neck squamous cell carcinoma is important. surgical treatment in locally advanced cancers of the anterior tongue and mouth is the mainstay of an effective therapeutics though additional RT and/or CT do have their benefit.
					Tongue cancer- Stage III & IV: 424	(3 years) - 48.5% (5 years) - 42.8%		
					Cancer mouth- Stage I & II: 414	(3 years) - 76.7% (5 years) - 70.3%		
					Cancer mouth- Stage III & IV: 1390	(3 years) - 53.2% (5 years) - 46.1%		
4	Mroueh et al.[15]	2017	Multicenter retrospective study	360	Stage I - 77 (33%)	5 years – 61%	Stage I - 87% (5 years)	Histologic prognostic models could be used to detect high risk patients.
					Stage II - 75 (32%)		Stage II - 73% (5 years)	
					Stage III - 51 (22%)		Stage III - 69% (5 years)	Multimodality treatment advocated - patients with advanced disease.
					Stage IV - 32 (14%)		Stage IV - 51% (5 years)	
5	Ebrahimi et al.[10]	2020	Multicenter retrospective study	1146	Stage III - 108 (9.4%)	-	(5 years) 86.1% (stage III)	There was a wide variation in DSS noted in pN2a, pN3b, and TNM stage IV disease based on the well-established prognostic factors im-munosuppression, size, and number of nodal metastases and PNI.
					Stage IV - 1038 (90.6%)		76.1% (stage IV)	
6	Otsuru et al.[16]	2019	Multicenter retrospective study	1234	T12N0M0	(10 years) 87.1% (END)	(10 years) 89.1% (END)	Elective neck dissection (END) for tumours with tumour depth of 4-5 mm or more is beneficial.
						76.2% (observation)	82.2% (observation)	

TABLE 1: Comparison of various clinical stages of oral cancer with the overall survival rate (OS) and disease specific survival rate (DSS).

SN	Authors	Year	Type of study	Sample size	TNM staging		OS	DSS	Conclusion

TABLE 1: Continued.

SN	Authors	Year	Type of study	Sample size	TNM staging	OS	DSS	Conclusion
7	Kavabata et al.[17]	2019	Multicenter retrospective study	193	Stage I - 140 (72.5%)	(5 years) 55% without lymph node metastasis	(5 years) 100% without lymph node metastasis	Patients with stage I and II SCC of the lip with tumour size greater than 18 mm and more aggressive pattern of invasion must be considered a high-risk group for LNM and an END should be performed.
					Stage II - 53 (27.5%)	42% with late lymph node metastasis	68% with late lymph node metastasis	
8	Zanoni et al.[18]	2019	Retrospective observational study	2082	Stage I - 562	pT1 - 81% (5 years)	pT1 - 92.8% (5 years)	Pathological nodal staging (American Joint Committee on Cancer 8th edition) was the single most powerful & consistent predictor of outcomes in patients with oral squamous cell carcinoma.
					Stage II - 583	pT2 - 64.3% (5 years)	pT2 - 79.6% (5 years)	
					Stage III - 261	pT3 - 51.8% (5 years)	pT3 - 67.3% (5 years)	
					Stage IV - 354	pT4 - 39.1% (5 years)	pT4 - 54.3% (5 years)	
9	Hakim et al.[19]	2020	Prospective observational study	77	Stage I - 22	T1 & T2 tumours: (2 years) - 83.3%; (5 years) - 77.2%	-	Tumor size had the highest impact on local control, disease-free and overall survival.
					Stage II - 13	T3 & T4 tumours: (2 years) - 47.6%; (5 years) - 38.9%		
					Stage III - 11	N0 tumours: (2 years) - 80.0%; (5 years) - 72.4%		A tumor size > T2, the presence of distant metastasis and positive resection margins were all associated with poor prognosis.
					Stage IV - 31	N+ tumours: (2 years) - 41.5%; (5 years) - 35.6%		
10	Liu et al.[20]	2021	Multicenter retrospective study	773	Stage I & II - 279	Overall 5 years survival - 62%	5 years - 78%	Disease-free survival was found to be improved in patients who received a referral for adjuvant radiotherapy for stage III or IV disease.
					Stage III & IV - 494			
11	Shinohara et al.[21]	2021	Multicenter retrospective study	1055	Stage III - 108	Stage I & II: (2 years) - 94.5%; (5 years) 92.2%		Post-operative radiotherapy or chemotherapy improved survival outcomes specially in advanced cases of oral cancer.
					Stage IV - 1038	Stage III & IV: (2 years) - 76.8%; (5 years) 56.1%		

SN	Authors	Year	Type of study	Sample size	TNM staging	No. of recurrence	Average time of recurrence	Conclusion
					TABLE 2: Comparison of various clinical stages of oral cancer with number of recurrences and average recurrence time.			
1	Ebrahimi et al.[27]	2016	Multicenter retrospective study	739	Stage III - 387 / Stage IV - 342	177	-	The overall prognosis of pN2a nodal disease was comparable to that of pN1 disease in patients with oral squamous cell carcinoma.
2	Deneuve et al.[28]	2017	Retrospective observational study	72	T1/T2 - 25 (34.7%) / T3/T4 - 47 (65.3%)	16 patients (22.2%) (3 cases showed nodal involvement) / 20 patients showed isolated nodal recurrence.	-	Lymph node dissection should be considered for N0 patients as nodal recurrence worsens the prognosis of such patients.
3	Liu et al.[29]	2018	Retrospective observational study	109	T1 - 52 / T2 - 30 / T3 - 15 / T4 - 12	24	Within 24 months	Invasion depth & differentiation degree have reliable value for predicting regional metastasis.
4	Zukauskaite et al.[30]	2018	Multicenter retrospective study	1576	-	102	-	There was no relation between the distribution of recurrences as functions of the tumour margins.
5	Sun et al.[31]	2019	Multicenter retrospective study	Immunosuppressed-40	T1/T2 - 28 / T3/T4- 9	Locoregional - 31 / Distant - 4 / Combined - 5	9.1 months	Patients with recurrent head & neck squamous cell carcinoma have poor survival irrespective of their survival status.
				Immunocompetent - 32	T1/T2 - 11 / T3/T4- 13	Locoregional - 21 / Distant - 7 / Combined - 4	10.1 months	
6	Zenga et al.[32]	2019	Multicenter retrospective study	102	T1/T2 - 60 / T3/T4 - 38 / N0 - 50 / N+ - 52	Local - 56 / Regional - 28 / Locoregional - 18	6.1 months	A negative resection margin was a significant predictor of overall survival in patients with oral squamous cell carcinoma.
7	Spoerl et al.[33]	2020	Multicenter retrospective study	745	Stage I - 231 / Stage II - 123 / Stage III - 120 / Stage IV - 271	157 (21.25)	-	Lymphatic & vascular invasion are independent risk factors in survival and recurrence of oral squamous cell carcinoma patients.
8	Liu et al.[34]	2021	Retrospective observational study	65	T1N0 - 65	5 years - 29.2% / 10 years - 33.8%	35 months	Understanding clinicopathological factors associated with recurrent disease may lead to improved treatment and follow-up protocols.
9	Kim and Ahn[25]	2024	Retrospective observational study	168	Stage I, II - 64 / Stage III, IV - 104	81	-	pTNM stage and recurrence were significant prognostic factors in oral squamous cell carcinoma.

Moreover, early detection can result in substantial cost savings since treating advanced-stage oral cancer is often more costly. Patients diagnosed early typically experience lower healthcare expenses compared to those diagnosed at later stages, highlighting the economic advantages of early intervention.[35]

It is acknowledged that oral cancer often evolves from precancerous lesions like leukoplakia and erythroplakia. Early detection enables healthcare providers to identify and manage these precursors, preventing their advancement to invasive cancer.[36] Furthermore, focusing on early detection raises public awareness about oral cancer. Educating individuals about risk factors, symptoms, and the significance of regular dental check-ups promotes timely evaluations for suspicious lesions. Targeted educational campaigns are essential for reducing the burden of oral cancer, especially among at-risk populations.[37]

Advancements in Research and Technology

Innovative diagnostic technologies, including molecular profiling, digital imaging, and artificial intelligence, are enhancing early detection capabilities. Ongoing research aims to develop more precise tools for identifying oral cancer and its precursors at earlier stages, reinforcing early detection as a vital strategy in combating oral cancer.[38]

Methods of Early Detection of Oral Cancer

Key clinical signs and symptoms to monitor for oral cancer include persistent sores or ulcers lasting more than two weeks, which may indicate malignancy.[39] Changes in oral mucosa, such as white patches (leukoplakia) or red patches (erythroplakia), require evaluation.[40] Additionally, the presence of lumps or thickened areas in the mouth or neck could suggest malignancy.[41] Symptoms such as difficulty in swallowing (dysphagia) or chewing may indicate oral cancer affecting the throat or tongue,[42] while sudden numbness in the mouth or face necessitates further examination.[43] A chronic sore throat or persistent hoarseness may signal throat-related lesions,[44] and changes in denture fit can indicate underlying health problems.[45] Unexplained, persistent bad breath (halitosis) that does not improve with hygiene should also raise concern about oral cancer.[46]

Salivary biomarkers offer a promising non-invasive method for the early detection of oral cancer. Numerous studies have identified specific markers that could enhance early identification, which is crucial for improving patient survival and treatment outcomes. Research should focus on validating these biomarkers and incorporating them into clinical practices. Notably, certain microRNAs (miRNAs) in saliva, such as elevated levels of miR-21 and miR-148a, have been linked to OSCC.[47] Additionally, proteomic analysis has revealed specific proteins, including increased levels of aspergillin and cystatin S, that differentiate healthy individuals from those with OSCC.[48]

Tumor markers have been utilized for the purpose of early detection. Various tumor markers have been investigated for the diagnosis and monitoring of oral cancer. Carcinoembryonic antigen, although primarily associated with other cancers, has shown elevated levels in OSCC patients, indicating its potential as a supplementary diagnostic tool.[49] Another key marker is squamous cell carcinoma antigen (SCC-Ag), which specifically correlates with SCC elevated SCC-Ag levels are associated with disease progression, making it valuable for early detection and monitoring of OSCC.[50] Additionally, genetic and epigenetic changes, such as tumor protein p53 mutations and hypermethylation of tumor suppressor genes like cyclin dependent kinase inhibitor p16INK4a, are important in cancer progression. Detecting these alterations in saliva or tissue biopsies can help identify individuals at increased risk for oral cancer.[51] Furthermore, analyzing deoxyribonucleic acid (DNA) methylation patterns in oral rinse samples may facilitate early diagnosis.[52]

Advanced Imaging Techniques

Advanced imaging methods, while not traditional biomarkers, can significantly improve the early detection of oral cancer. Techniques such as fluorescence imaging and narrowband imaging (NBI) have improved the identification of dysplastic changes in mucosal tissues.[53] Oral cancer, particularly OSCC, poses a major global health challenge due to its high incidence and mortality rates. Timely diagnosis is essential for better patient outcomes, prompting innovations in detection techniques.

Emerging tools like optical coherence tomography (OCT), autofluorescence imaging (AFI), optical spectroscopy, genomic analysis, liquid biopsy, and machine learning are reshaping early detection strategies. OCT offers high-resolution images of the oral mucosa, aiding in differentiating benign from malignant lesions.[54] NBI enhances the visibility of blood vessels, aiding in identifying early-stage malignancies.[55] AFI detects lesions earlier than conventional methods,[56] while optical spectroscopy analyzes changes in tissue optical properties, assisting in cancer detection.[57]

Genomic analysis through next generation sequencing enhances the detection of genetic mutations relevant to cancer,[58] and liquid biopsy offers a non-invasive approach to analyze circulating tumor DNA for early diagnosis.[59] Finally, machine learning can process large datasets for pattern recognition in imaging and genomic data, thereby enhancing screening accuracy.[60] The integration of these

advanced diagnostic technologies provides a transformative opportunity for improving early oral cancer detection and highlights the need for ongoing research and clinical application to enhance patient care and outcomes.

Advanced Methods of Treatment for Oral Cancer

Oral cancer, primarily OSCC, poses significant treatment challenges due to its aggressive nature and complications associated with traditional therapies such as surgery, radiation, and chemotherapy. Recent advancements focus on improving efficacy, reducing side effects, and enhancing patient quality of life.

Targeted therapy is a pivotal approach that aims to disrupt specific molecular pathways involved in cancer cell growth. Notably, epidermal growth factor receptor inhibitors, such as cetuximab, have shown efficacy in treating advanced oral cancer, especially when combined with chemotherapy and radiation.[61] Additionally, inhibitors targeting the phosphoinositide 3 kinase (PI3K/Akt/mTOR) signaling pathway, such as everolimus, have produced promising results in phase II clinical trials for OSCC.[62]

Immunotherapy is increasingly used to engage the body's immune system against cancer cells. Checkpoint inhibitors such as pembrolizumab and nivolumab, which block the programmed cell death protein 1 receptor, have shown success in treating recurrent or metastatic OSCC by enhancing T-cell activation.[63] Furthermore, therapeutic vaccines targeting HPV-related oncoproteins E6 and E7 are under development, with early trials yielding promising results.[64]

Surgery remains a foundational treatment for oral cancer, with newer techniques enhancing precision and recovery. Transoral robotic surgery, a minimally invasive method, allows for tumor removal with reduced postoperative pain and quicker recovery.[65] Additionally, laser-assisted surgery, particularly using carbon dioxide lasers, offers high precision, minimizing damage to surrounding tissues and promoting faster healing.[66]

Radiotherapy innovations have also improved outcomes for oral cancer patients. Intensity modulated radiation therapy enables precise targeting of tumors while sparing healthy tissues, thereby reducing acute and chronic side effects.[67] Stereotactic body radiotherapy provides high doses of radiation to localized tumors in fewer treatment sessions, increasing patient convenience.[68]

Finally, the emergence of personalized medicine, driven by advances in genomics, allows for tailored treatment plans based on the genetic characteristics of individual tumors. Identifying biomarkers helps in customizing therapies, particularly, since HPV positive OSCC patients may respond differently than patients with HPV negative tumors.[69] This personalization extends to selecting post-surgical adjuvant therapies, enhancing treatment effectiveness and minimizing unnecessary side effects.

Overall, the evolving landscape of oral cancer treatment, driven by targeted therapies, immunotherapy, advanced surgical techniques, radiotherapy innovations, and personalized medicine, holds great promise for improving patient survival and quality of life.

Maintenance and Follow-up Care After Treatment and Cure of Oral Cancer

Oral cancer, specifically OSCC, poses significant challenges not only during treatment but also in the long-term care of survivors. A comprehensive maintenance and follow-up plan is vital post-treatment, focusing on detecting recurrence, managing long-term side effects, and enhancing quality of life. Regular check-ups and vigilant monitoring for recurrence are essential, as research indicates the highest risk of recurrence occurs within the first few years after treatment.[70] Managing long-term co-morbidities is another critical aspect; many patients face persistent side effects such as xerostomia (dry mouth), dysphagia (difficulty swallowing), and alterations in taste. Regular follow-up visits allow healthcare providers to effectively track and manage these complications.[71] Additionally, psychosocial support is crucial. Survivors may encounter challenges such as anxiety, depression, and changes in self-image. Ongoing follow care provides opportunities to address these emotional and mental health issues, ensuring comprehensive patient care.[72] By adopting a comprehensive, interdisciplinary approach, healthcare providers can significantly enhance the quality of life for individuals recovering from oral cancer.

CONCLUSION

Early detection of oral cancer, particularly OSCC, is vital for improving patient outcomes and survival rates. With the alarming rise in global incidence and mortality, healthcare systems must prioritize early diagnostic practices. Research shows that early-stage detection correlates with higher five-year survival rates and enables less invasive treatments, reducing complications associated with advanced disease. Public awareness campaigns, regular dental check-ups, and comprehensive screening programs are crucial for reaching at-risk populations and ensuring timely evaluations. Advancements in diagnostic technologies, such as molecular profiling, fluorescence imaging, and novel imaging techniques, enhance early identification of oral cancer. Innovations like salivary biomarkers and genetic analyses, are transforming detection methodologies and require further

research to confirm their clinical applicability. Education plays a key role in combating oral cancer by raising awareness of risk factors and symptoms, empowering individuals to seek timely medical advice. This can help detect precancerous lesions early, allowing for intervention before progression to invasive disease.

In conclusion, early detection is the best defense against oral cancer. Collaborative efforts among researchers, clinicians, and public health advocates can improve diagnosis and treatment, thereby enhancing the quality of life for affected individuals. Investing in education, research, and technological advancements offers hope in the fight against oral cancer.

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