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# *Artificial intelligence in early diagnosis and prevention of oral cancer*

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***Abstract: The global occurrence of oral cancer (OC) has increased in recent years. OC that is diagnosed in its advanced stages results in morbidity and mortality. The use of technology may be beneficial for early detection and diagnosis and thus help the clinician with better patient management. The advent of artificial intelligence (AI) has the potential to improve OC screening. AI can precisely analyze an enormous dataset from various imaging modalities and provide assistance in the field of oncology. This review focused on the applications of AI in the early diagnosis and prevention of OC. A literature search was conducted in the PubMed and Scopus databases using the search terminology "oral cancer" and "artificial intelligence." Further information regarding the topic was collected by scrutinizing the reference lists of selected articles. Based on the information obtained, this article reviews and discusses the applications and advantages of AI in OC screening, early diagnosis, disease prediction, treatment planning, and prognosis. Limitations and the future scope of AI in OC research are also highlighted..***

***Keywords: Oral cancer, Artificial intelligence; Screening; Early diagnosis.***

## I. INTRODUCTION

The global occurrence of oral cancer (OC) has increased in recent years, with oral squamous cell carcinomas (OSCCs) counting for more than 90% of these cancers. OSCCs are also the sixth most common malignancy in the world. In 2012, The World Health Organization reported 529,000 new cases of OC and 300,000 deaths due to OC each year. OC that is diagnosed in its advanced stage results in morbidity and mortality. A crucial factor in providing successful treatment is the early detection of cancerous lesions. Inaccessible lesions and the late detection of cancers are associated with low survival, increased symptoms, and a higher treatment cost. Early diagnosis can increase the survival rate to 75%–90%.

Early detection includes the diagnosis of oral potentially malignant disorders (OPMDs) and regular follow-ups. OPMDs have been defined as "any oral mucosal abnormality that is associated with a statistically increased risk of developing OC." OPMDs include oral leukoplakia, proliferative verrucous leukoplakia, erythroplakia, oral lichen planus, oral submucous fibrosis, palatal lesions in reverse smokers, oral lupus erythematosus, actinic keratosis, and dyskeratosis congenita. Newly included lesions in the recent classification are oral lichenoid lesion and oral chronic graft-versus-host disease.

Initial detection of OC requires self-examination of the oral cavity as well as professional consultation. Screening of high-risk populations is needed to avoid the late diagnosis, but these populations are often located in remote regions with limited access to healthcare facilities. Poor knowledge regarding OC symptoms is a major hindrance. The use of technology may be beneficial for the early detection of OC. The advent of artificial intelligence (AI) has the potential to improve OC screening. The increase in research based on AI technology for medical imaging and diagnosis has been promising. AI technologies have been found to be effective in detecting breast, lung, and oral cancers. The potential of AI to improve the efficiency of OC screening is the reason for its implementation in oncology.

AI can be divided into traditional machine learning (ML) and deep learning. Traditional ML uses algorithms and computer processes to calculate information and recognize input data patterns to offer a quantified diagnostic result. ML methods are divided into supervised and unsupervised. Deep learning or neural networks are techniques comprising of nonlinear processing units with multiple layers to learn and understand input and associate output with the relevant input.

Presently, these techniques are being assessed for more effective methods for diagnosis, especially for the screening of diseases, where fewer doctors and trained experts are available. AI can be used in many ways in the prevention of OC and its early diagnosis. AI can precisely analyze a vast dataset of various imaging modalities, such as fluorescent, hyperspectral, cytological, histological, radiological, endoscopic, clinical, and infrared thermal modalities. Recently, vision-based adjunctive technologies were developed to detect OPMDs that carry the risk of cancer development. This review discusses the applications of AI in OC screening, early diagnosis, disease prediction, treatment planning, and prognosis.

## II. Methods

This review was done in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

## III. Literature Survey

A data search was carried out in two databases, namely PubMed and Scopus. The search string (“oral cancer” AND “Artificial intelligence”) was used to search both databases for articles published between 2012 and 2022. Further research was conducted to extract information regarding the topic based on the reference lists of the selected articles and pertinent reviews. Details about AI in OC screening, early diagnosis, prediction, and management were obtained from the articles that met the selection criteria for the present review.

## IV. Inclusion and Exclusion Criteria

The inclusion criteria for the articles were as follows:

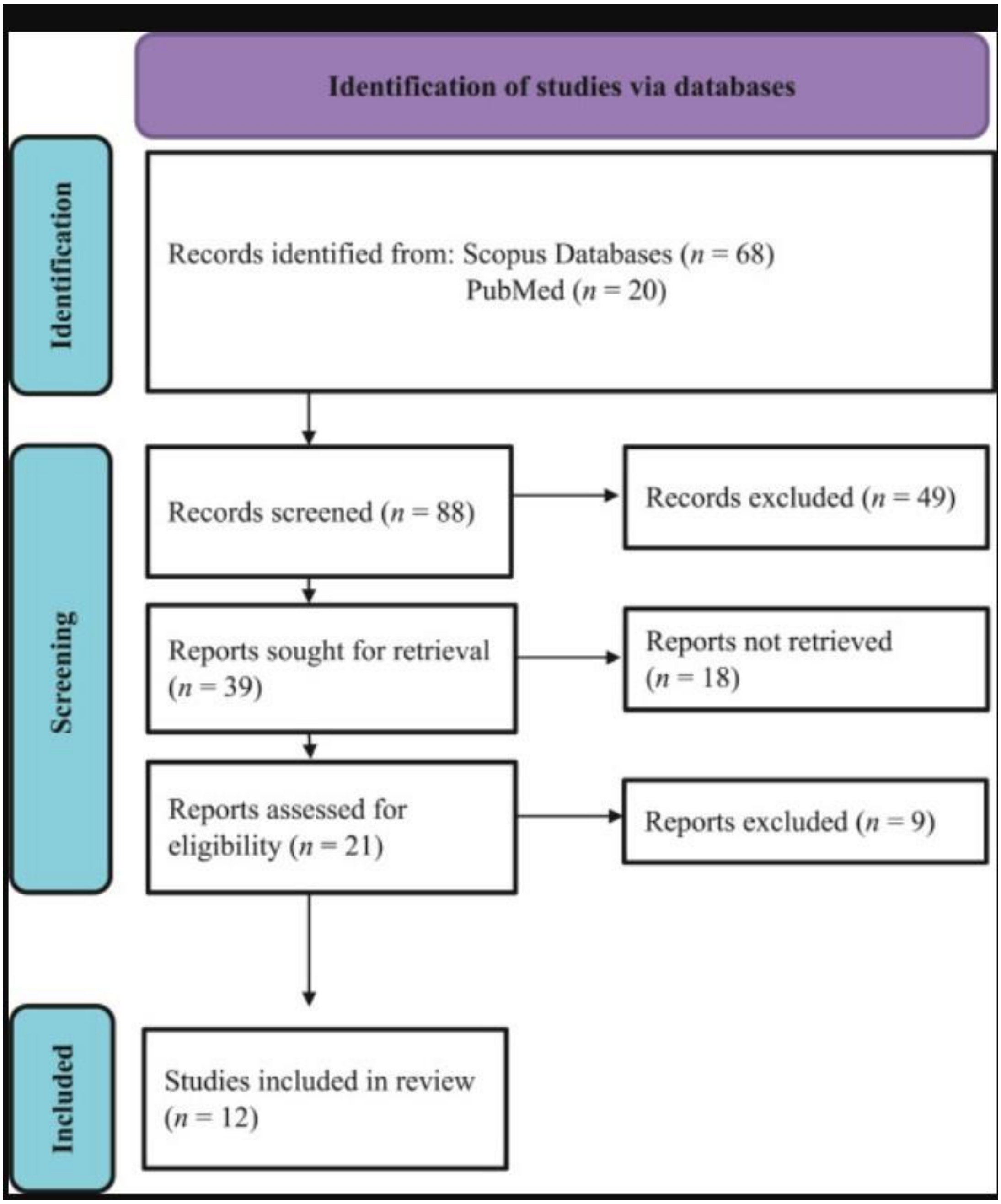
- Published between 2012 and 2022.
- Original research articles.
- Full text available in the institutional digital library.
- Written in English or Chinese.

The exclusion criteria were as follows:

- Animal studies.
- Types of study: Case reports, short communications, personal viewpoints, letters to editors, conference abstracts, and literature reviews.
- Not written in English or Chinese.

## V. Results

The article selection process followed is documented in the PRISMA flowchart. The literature search in the databases resulted in a total of 88 potential records. The title and abstracts of these records were evaluated in terms of the selection criteria, resulting in 49 exclusions. Reports were sought for retrieval from the remaining articles, of which the full text of 21 articles was read by the reviewers for potential inclusion.




Summary of studies using AI in oral cancer early detection, diagnosis, and treatment outcome.

| Author (Year) | Aims | Sample | Methods | Main findings |
|---|---|---|---|---|
| Adeoye (2021)[24] | To compare and validate supervised deep and conventional learning algorithms for the risk-probability prediction of malignant transformation in OPMDs | A total of 716 patients with a clinical diagnosis of oral leukoplakia, oral lichen planus, or oral lichenoid lesions who underwent biopsy | Twenty-six features available from electronic health records were used to train four learning algorithms—Cox-Time, DeepHit, Deep Surv, and random survival forest | Time-to-event models are successful in predicting the malignant transformation of oral leukoplakia and oral lichenoid lesions. |
| Alhazmi (2021)[22] | To develop an artificial neural network model that helps to predict the individuals' risk of | Seventy-three cases with confirmed diagnosis and pathologic reports | A popular data mining algorithm artificial neural network was used for developing the | Machine learning technique has the potential to help in oral cancer screening and diagnosis |

| Author (Year) | Aims | Sample | Methods | Main findings |
|---|---|---|---|---|
| | developing oral cancer based on data on risk factors, systematic medical condition, and clinic-pathological features | were included in this study | artificial intelligence-based prediction model. A total of 29 variables that were associated with the patients were used for developing the model. The dataset was randomly split into the training dataset 54 (75%) cases and testing dataset 19 (25%) cases | based on the datasets. The results demonstrate that the artificial neural network could perform well in estimating the probability of malignancy and improve the positive predictive value that could help to predict the individuals' risk of developing OC based on knowledge of their risk factors, systemic medical conditions, and clinic-pathological data. |
| Chu (2021)[23] | To revisit this well-characterized patient cohort to evaluate the ability of supervised machine learning models to predict disease outcome | Retrospective review of 467 OSCC patients treated over a 19-year period facilitated the construction of a detailed clinicopathological database | Overall survival was determined from the date of primary diagnosis until death or most recent clinic follow-up. Thirty-four prognostic features from the database were used to populate four machine learning algorithms, such as LR, DT, SVM, and KNN models, to attempt progressive disease outcome prediction | Machine learning models assist clinicians in accessing digitized health information and appear promising in predicting progressive disease outcomes. |
| James et al. (2021)[21] | To integrate OCT imaging with automated image processing and deep learning to reduce the subjectivity in image interpretation, and it is large-scale, in-vivo, validation in the delineation of OSCC, and dysplastic lesions from normal/benign lesions in both community and tertiary care settings. | Validation of a portable, robust OCT device in 232 patients (lesions: 347) in different clinical settings | OCT imaging was followed by incisional or excisional biopsy. The captured images were classified by a simple algorithm. The image features were extracted using multiple ANN and the SVM model. Both the methods were compared with histological or clinical diagnosis depending on whether biopsy was indicated or not | The study provides evidence toward the utility of the robust and low-cost OCT instrument as a point-of-care device in resource-constrained settings and the potential clinical application of device in screening and surveillance of oral cancer |

## VI. Datasets used in AI and oral cancer research

- Clinical images and photographic images
- Patients' geographic data and habits history
- Auto fluorescence image and white light image
- Optical coherence tomography

- Raman spectroscopy
- Spectroscopy probe
- Confocal laser endomicroscopy images
- Multidimensional hyperspectral images
- Gene expression data
- Radiographic images such as computed tomography (CT) images and magnetic resonance imaging (MRI)
- Saliva metabolites
- Histopathologic images and P 53 immune stained tissue section

## VII. Applications and Advantages of AI in Oral Oncology

- Screening of high-risk populations
- Helps in early diagnosis of oral cancer in populations residing at remote regions with limited access to healthcare facility
- Ability to precisely analyze an enormous dataset
- Detection and classification of cancerous lesions
- Interpretation of images as normal oral mucosa/precancerous/cancerous lesions
- Ease of use in multicentre study
- AI allows automated learning without human arbitration
- Automate processes and combine variables at different levels and provide outcome
- Ability to constantly train on further data
- Guide clinician in decision-making
- AI system assists expert pathologist to deliver superior results with minimum diagnostic errors
- Potential for combination of history, geographical data, risk factors, clinicopathologic features, imaging features, and omics data to generate risk assessments
- Prediction of the malignant transformation of OPMDs
- Detecting accurate biomarkers
- Lymph node metastasis prediction
- Support clinician in treatment planning

## VIII. Discussion

### AI in oral cancer screening and detection

Recent systematic reviews reported that Asia had the highest incidence of lip and OC globally. Thus, this region was the focus of the majority of the studies. Various imaging modalities using AI have been used for OC screening and detection. For example, clinical photographs were used in various studies to demonstrate that suspected OSCC lesions could be differentiated automatically and easily by the application of algorithms. Al-Rawi et al. analyzed AI usage in the diagnosis of OC in 17 studies. They reported that ML was used in six studies and deep learning in the remainder. They concluded that deep learning was more precise than supervised ML for OC early diagnosis.

A scoping review highlighted the effect that the variabilities of photographic images could have on the identification process of OC or OPMDs. Warin et al. conducted a study to develop an automated classification and detection system for OC screening. This study included 700 clinical oral photographs, consisting of 350 images of OSCCs and 350 images of normal oral mucosa. DenseNet121 was used for the classification model and faster R-CNN for the detection model. The study concluded that the DenseNet121 and faster R-CNN algorithm had the potential for the detection and classification of cancerous lesions.

A multicentre study used simple smartphone probes with deep learning algorithms for OC screening. The screening was done in high-risk populations in inaccessible regions with limited infrastructure facilities, with a probe designed to access all parts of the oral cavity. The autofluorescence and polarization images from the probe were combined with a tabulation of risk factors, such as habits. The information was analyzed by deep learning-based algorithms, which then generated outputs for screening guidance.

Optical coherence tomography (OCT) has been used in a few studies for diagnosis with AI. Studies indicated that the addition of a diagnostic algorithm to an OCT system would overcome the training requirements of the users concerning the reading of the OCT images. A low-cost OCT prototype was used to develop and evaluate an automated diagnostic algorithm linked to an image-processing application and user interface. Ilhan et al. reported that the automated cancer screening platform could differentiate between healthy and dysplastic/malignant tissues with 87% sensitivity and 83% specificity. Similarly, Ramezani et al. reported that AI algorithms rendered positive outcomes in the interpretation of OCT images of normal oral mucosa and precancerous and cancerous lesions. Automated OC screening by OCT requires the progression of AI algorithms

for their interpretation; hence, a continuous data feed is needed to function as ground information.

Tissue sections of head and neck cancers from different sites, such as the tongue, floor of the mouth, gingivae, alveolar ridge, mandible, soft palate, supraglottis, nose, maxillary sinus, parotid gland, and thyroid were evaluated in various studies. The role of ML techniques as a diagnostic tool for histology images in recognizing OSCC and a few OPMDs was highlighted in recent systematic reviews. García-Pola et al. reported that a few studies used exfoliative, liquid, scraped, and brush biopsies for cytological diagnosis.[3] Mahmood et al. evaluated studies that used various ML approaches to differentiate specific histological features and compare alterations in the spatial architectural patterns to statistically distinguish benign and malignant lesions. They stated that unicentric small datasets could lead to a high risk of bias due to limited evidence. Therefore, they recommended that prospective studies with large samples and in multiple centres would best support the medical practice.

According to Mahmood et al., algorithm training mainly included histology whole-slide and radiological imaging. The increasing use of digital slide scanners in pathology laboratories and the advent of radiomics have widened the scope. Sultan et al. reported that AI had achieved admirable results compared to pathologists. Studies on OSCC digital histopathologic images demonstrated potential when the predictive models included both clinical and genomic data. When the skills of

expert pathologists were combined with AI systems, superior results could be delivered with fewer diagnostic errors. A Cochrane review stated that none of the early diagnostic tests available at that time could replace a biopsy for an OC diagnosis. Chiesa-Estomba et al. analyzed eight studies and concluded that ML had the potential to considerably advance the field of OC research due to the ability of ML models to constantly learn with additional data.

## IX. Limitations

The research information used in this review was limited to data retrieved from articles published in PubMed and Scopus databases only. As a result, the limitations inherent in those articles affected the detail of this review. These limitations included a limited amount of data available, the retrospective collection of data, image quality, the comparison of images taking into consideration that healthy tissue could be present with mucosal alterations, imbalances in the data used to train, the risk of missing data, the lack of studies collaborating with clinical diagnosis and biopsy findings, the task of automation, infrastructure requirements for data storage, building and training AI models, and patient privacy and ethical issues.

## X. Implications for Future Research

Future studies in the field of AI and OC may be helpful in overcoming the present limitations. Radiomics is an emerging field of research using radiographic images and data characterization algorithms. Radiomics has helped extract features, such as intensity, shape, and surface texture from CT and MRI images of malignancy, which might go unnoticed by the human eye. Radiomics could become a valuable tool for oncologists to evaluate tumor metastatic potential, oncogene expression, and treatment response.

## XI. Conclusion

In recent years, the use of AI for the diagnosis and prognosis of diseases has evolved. Previous studies have proved that ML produces accurate results for OC detection. It assists clinicians in diagnostic processes and minimizes inadvertent errors. However, previous studies based on deep learning (neural network) provided more accuracy with the early detection of OC as compared to ML. AI presents the opportunity to develop new techniques combined with traditional approaches to improve the accuracy of detection of OC and OPMDs, as well as to predict the course of the precancerous/cancerous lesions from retrospective data. Future research could consider the innovation of data fusion algorithms combining various modalities, such as clinical, radiological, histological, and molecular assessments, to support the early diagnosis and outcome estimation of the disease.

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