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Oral Leukoplakia: Modern Diagnostic Techniques and Therapeutic Strategies

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Abstract

Oral leukoplakia is a potentially malignant disorder of the oral mucosa associated with an increased risk of squamous cell carcinoma. Because of its potential for malignant transformation, it requires appropriate diagnosis, treatment, and long-term follow-up. The aim of this review was to present contemporary diagnostic and therapeutic methods for oral leukoplakia, with particular emphasis on advanced imaging techniques, artificial intelligence-based tools, and laser therapies. A narrative review of the literature published between 2015 and 2026 was conducted using the PubMed/MEDLINE, Scopus, and Web of Science databases. Studies addressing diagnostic methods, surgical treatment, laser therapy, photodynamic therapy, and factors influencing recurrence and malignant transformation were analyzed. The findings indicate that modern imaging techniques, such as autofluorescence, narrow band imaging, and optical coherence tomography, may support the early detection of lesions with an increased risk of malignancy. Laser treatment, particularly with CO_2 and Er:YAG lasers, shows efficacy comparable to or greater than conventional methods, with a favorable healing profile and reduced postoperative symptoms. Photodynamic therapy also provides promising results. Despite technological progress, no method completely eliminates the risk of malignant transformation. Early diagnosis, individualized treatment, and long-term patient monitoring remain essential.

Keywords: oral leukoplakia; oral potentially malignant disorders; laser therapy; artificial intelligence; oral cancer; diagnostic imaging; photodynamic therapy

Introduction

Oral leukoplakia (OL) is one of the most common oral potentially malignant disorders (OPMDs) and represents an important diagnostic and therapeutic problem in contemporary dentistry, maxillofacial surgery, and oral medicine. The particular clinical importance of leukoplakia results from its potential for malignant transformation into oral squamous cell carcinoma (OSCC); therefore, this lesion requires appropriate diagnosis, treatment, and long-term clinical follow-up (Warnakulasuriya et al. 2021; Pimenta-Barros et al. 2025).

According to the World Health Organization definition, leukoplakia is a white plaque of the mucosa that cannot be clinically or histopathologically classified as any other disease entity and is associated with an increased risk of malignant neoplasia (Warnakulasuriya et al. 2021). These lesions are most frequently located on the buccal mucosa, tongue, floor of the mouth, and alveolar ridges. Clinically, leukoplakia is divided into homogeneous and non-homogeneous forms. Particular attention is given to non-homogeneous variants, including erythroleukoplakia and proliferative verrucous leukoplakia (PVL), which are considered to have a higher potential for malignant transformation (Pimenta-Barros et al. 2025).

Oral leukoplakia is a globally prevalent disorder, with an estimated prevalence ranging from 1% to 4% in the general population, although considerable geographic variation exists depending on exposure to risk factors and differences in diagnostic criteria. The highest prevalence rates are observed in populations with widespread tobacco use, alcohol consumption, and betel quid chewing. The clinical significance of oral leukoplakia stems not only from its potential for malignant transformation but also from the difficulty in predicting the biological behavior of individual lesions. While some lesions remain stable for many years, others may progress to oral squamous cell carcinoma despite an initially innocuous clinical appearance (Warnakulasuriya et al. 2021; Villa and Woo 2021).

The histopathological presentation of leukoplakia is heterogeneous and may include hyperkeratosis, acanthosis, and epithelial dysplasia of varying severity. In some cases, features of carcinoma in situ or invasive carcinoma may also be present. Because there is no unequivocal relationship between the clinical appearance and the severity of histopathological alterations, biopsy and histopathological examination remain the basis for the diagnosis of leukoplakia and other potentially malignant oral lesions (Warnakulasuriya et al. 2021).

The etiopathogenesis of leukoplakia is multifactorial. The main risk factors include tobacco smoking, alcohol consumption, betel quid chewing, and chronic mechanical irritation of the oral mucosa. A particularly important role is attributed to tobacco, which is regarded as the most important factor associated with the development of leukoplakia and other oral precancerous lesions (Zhou et al. 2023). Increasing attention is also being paid to the contribution of molecular and genetic factors to malignant transformation, which supports the development of new diagnostic and therapeutic methods (Villa and Woo 2021).

In recent years, increasing attention has been directed toward identifying markers that enable more accurate assessment of malignant transformation risk. In addition to established clinical predictors, such as lesion size, anatomical location, and the presence of epithelial dysplasia, numerous molecular and genetic alterations have been investigated. These include genomic instability, dysregulation of cell-cycle control mechanisms, and alterations in tumor suppressor genes. Current evidence suggests that malignant transformation is a complex multistep process involving a series of biological events that occur long before invasive carcinoma becomes clinically evident (Villa and Woo 2021; Pimenta-Barros et al. 2025).

Despite advances in diagnosis and treatment, leukoplakia remains an important clinical challenge. In recent years, modern diagnostic methods supporting conventional clinical examination and histopathological assessment have developed rapidly. Non-invasive techniques, such as autofluorescence, narrow band imaging (NBI), optical coherence tomography (OCT), and analysis of molecular and salivary biomarkers, are gaining increasing importance (Aubreville et al. 2017). In parallel, diagnostic tools based on artificial intelligence and machine-learning algorithms are being developed to support the analysis of clinical images and histopathological specimens (Li et al. 2024; Yang et al. 2024b).

Simultaneously, advances in digital technologies have led to the emergence of novel diagnostic approaches. Artificial intelligence-based tools are increasingly being applied to the analysis of clinical photographs, endoscopic images, and histopathological specimens. These technologies facilitate the automated detection of suspicious areas associated with epithelial dysplasia or malignant transformation and may improve both diagnostic accuracy and reproducibility. Recent systematic reviews and meta-analyses have demonstrated promising diagnostic performance of machine-learning algorithms in the detection of oral potentially malignant disorders, suggesting that artificial intelligence may become an important component of future clinical workflows (Li et al. 2024; Yang et al. 2024b).

The development of modern diagnostic methods is also associated with the search for more effective and less invasive approaches to the treatment of oral leukoplakia. In addition to conventional surgical treatment, laser techniques are increasingly used, particularly CO_2 and Er:YAG lasers, as well as photodynamic therapy and other minimally invasive methods (Liu et al. 2020; Luo et al. 2024). Contemporary therapeutic management focuses not only on lesion removal, but also on reducing the risk of recurrence and monitoring patients for malignant transformation (Dipalma et al. 2026).

Despite significant progress in both diagnosis and treatment, no therapeutic strategy has yet been shown to completely eliminate the risk of recurrence or malignant transformation. Consequently, contemporary management of oral leukoplakia should extend beyond local treatment and include comprehensive risk assessment, elimination of etiological factors, patient education, and long-term clinical surveillance.

The aim of this article is to present contemporary methods for the diagnosis and treatment of oral leukoplakia, with particular emphasis on modern imaging techniques, artificial intelligence-based methods, and innovative therapies used in the management of potentially malignant oral lesions.

Methodology

This study was designed as a narrative review of the literature on contemporary diagnostic and therapeutic methods for oral leukoplakia (OL), with particular emphasis on laser techniques, photodynamic therapy, imaging methods, and artificial intelligence-based tools. The analysis was conducted using the PubMed/MEDLINE, Scopus, and Web of Science databases and included publications published between 2015 and 2026.

The search strategy was based on combinations of the following keywords: “oral leukoplakia”, “oral potentially malignant disorders”, “laser therapy”, “CO_2 laser”, “diode laser”, “Er:YAG laser”, “photodynamic therapy”, “artificial intelligence”, “diagnostic imaging”, “autofluorescence”, “optical coherence tomography”, “narrow band imaging”, “recurrence”, “malignant transformation”, and “oral squamous cell carcinoma”. In addition, references cited in the included publications were screened to identify further potentially relevant studies. Because of the narrative nature of the review, no formal quality assessment or protocol typical of systematic reviews was applied.

A narrative literature review was performed, including original research articles, randomized clinical trials, prospective and retrospective studies, cohort studies, meta-analyses, and systematic reviews published in English and concerning the diagnosis, treatment, and monitoring of oral leukoplakia. Studies evaluating the efficacy of surgical treatment, laser therapy, photodynamic therapy, and modern diagnostic methods were included, as were papers analyzing the risk of recurrence and malignant transformation. Because of the narrative nature of the review, no formal quality assessment or protocol typical of systematic reviews was applied.

Publications that did not meet the thematic criteria, case reports, commentaries, letters to the editor, conference abstracts, and studies concerning other potentially malignant disorders of the oral mucosa without a separate analysis of leukoplakia were excluded. Publications without full-text availability and papers of limited informational value were also excluded.

After duplicate removal, publications were initially screened on the basis of titles and abstracts, followed by full-text analysis of eligible articles. Ultimately, publications meeting the adopted criteria concerning modern diagnostic and therapeutic methods used in oral leukoplakia were included in the review. A narrative synthesis of the literature was performed, with particular attention paid to the type of therapy used, treatment efficacy, recurrence rate, risk of malignant transformation, adverse effects, and potential benefits associated with modern diagnostic and therapeutic technologies.

Results

Surgical excision versus laser therapy

Studies comparing conventional scalpel surgery with laser therapy reported comparable outcomes. In a controlled clinical trial including 64 patients, participants were assigned to treatment with a diode laser (33 patients) or scalpel surgery (31 patients) (de Pauli Paglioni et al. 2025). No significant differences in postoperative pain intensity were found between the groups at any time point (24 h, 48 h, and 7 days). Although statistically significantly better wound-healing parameters (edges, shape, and texture) were observed in the laser group on postoperative day 7, no clinically significant differences were present after 1 and 3 months. The authors concluded that both methods provide comparable long-term outcomes, without significant differences in perceived pain or final healing.

A retrospective analysis included 60 patients with 87 leukoplakia lesions treated using various surgical techniques: scalpel surgery and Nd:YAG, Er:YAG, CO_2, and QMR laser systems (Monteiro et al. 2017). The mean follow-up period was 21.6 months. Absence of recurrence (complete remission) was achieved in 72.4% of cases, while the recurrence rate was 27.6%. The lowest recurrence rate was observed after Er:YAG laser treatment, which was significantly more effective than scalpel excision. The overall analysis did not reveal significant differences among all methods; however, the authors emphasized a trend toward better outcomes after laser therapy, especially Er:YAG. In one case (1.1%), malignant transformation to squamous cell carcinoma was diagnosed after 35 months of follow-up in a patient from the QMR group.

In an observational study, laser treatment (type not specified) was used in patients with homogeneous oral leukoplakia (OL) and reticular oral lichen planus (OLP) (Arora et al. 2018).

The OL group was predominated by men (21 patients), whereas the OLP group was predominated by women (18 patients). Most lesions were located on the buccal mucosa. A biopsy was performed before treatment; in most patients, dysplasia was either absent or mild. During and after the procedure, patients rarely reported pain or bleeding, and pain and swelling almost completely resolved over the following days. After approximately 2 weeks, all wounds healed properly without complications; after 4 weeks, the authors assessed the results as satisfactory. No recurrence occurred during the observation period in either OL or OLP patients. Thus, in this small study, laser treatment resulted in complete remission of lesions (100% of patients) and 0% recurrence during 1 month of follow-up; no long-term results were reported in the publication.

In a retrospective study, 56 patients with 77 OL lesions were treated with a diode laser (Shivhare et al. 2022). Ablation (lesion vaporization) was used in 66.2% of lesions, and laser excision in 33.8%. Complete initial resolution of the lesion was achieved in all patients. During the 4- to 6-month follow-up period, recurrence was identified in 19.5% of patients, more often after ablation (25.5%) than after laser excision (7.6%). Recurrences most commonly involved gingival lesions. After treatment, all patients experienced mild or moderate pain. Swelling and wound granulomas were more frequent in the laser excision group, although the differences were not statistically significant; only higher pain intensity on the visual analogue scale (VAS) on postoperative day 3 after laser excision was significant ($p = 0.047$). No infection or malignant transformation was recorded in any case.

Outcomes after CO_2 laser treatment

Several studies analyzed the outcomes of CO_2 laser treatment in detail. In a prospective study including 34 patients with 48 OL lesions, a CO_2 laser was used (Rodriguez-Lujan et al. 2022). The mean age was approximately 61 years. Non-homogeneous lesions accounted for 62.5%, and most lesions were <2 cm in size. Histological examination showed no dysplasia in 77.1% of lesions; the remaining lesions had low- or high-grade dysplasia. Postoperative complications were rare and mild, and pain after 1 week was usually limited. After 18 months, treatment efficacy, defined as absence of recurrence, was 43.8%; recurrence occurred in 54.2% of cases. Transformation to OSCC was recorded in 2.1% of lesions (one case). The mean time to recurrence was approximately 10 months. Clinical features and patient habits did not significantly affect recurrence risk.

In a study of 37 patients, outcomes after CO_2 laser treatment (10,600 nm) were assessed with a mean follow-up of 36 months (Campos et al. 2022). Non-homogeneous lesions accounted for 59.5%, and 70.3% had an area >200 mm^2; the most common sites were the lateral border of the tongue and buccal mucosa. Epithelial dysplasia was found in 78.4% of patients, including high-grade dysplasia in 11 patients. Treatment was safe: no complications were observed, and complete wound healing occurred after approximately 4-5 weeks. Recurrence occurred in 35.1% of patients, and malignant transformation was diagnosed in 21.6%, on average 50.6 months after treatment. After 50 months, the probability of recurrence was estimated at approximately 76%, whereas the probability of remaining cancer-free was 87%. Cox regression analysis did not identify significant factors (age, sex, smoking, alcohol, lesion type, or dysplasia grade) affecting recurrence or malignant transformation.

A study including 58 patients with 78 OL lesions, mainly located on the buccal mucosa and gingiva, analyzed the effect of safety vaporization margins during CO_2 laser treatment (Vilar-Villanueva et al. 2023). Complete lesion resolution without recurrence was observed in 47.4% of patients treated with margins, corresponding to a recurrence rate of 52.6%. Squamous cell carcinoma developed at the treatment site in 2 patients (2.6%). The mean time to recurrence was 11.6 months. The use of a safety margin significantly reduced the risk of recurrence and improved disease-free survival (DFS). Postoperative pain or granulation tissue was observed in some patients, but most patients had no complications.

Photodynamic therapy and nanotechnology

Photodynamic therapy (PDT) represents a minimally invasive alternative. In a retrospective evaluation of 50 patients (26 men, 24 women; mean age 55.5 years) with OL, local PDT was used (Wang et al. 2024). Most patients smoked or consumed alcohol; lesions were more often located in the floor of the mouth and buccal mucosa, and homogeneous leukoplakia, often with dysplasia, predominated. After PDT, a therapeutic response was achieved in 68% of patients (12% complete response, CR; 56% partial response, PR). Homogeneous lesions responded better than non-homogeneous lesions. DNA ploidy analysis showed a reduction in aneuploidy among patients with dysplasia after PDT. Common adverse effects included oral pain and local ulceration (52% of patients), usually resolving within 2 weeks. During 2 years of follow-up, recurrence occurred in 32% of patients, and malignant transformation was observed in 4%. Buccal location was identified as a protective factor against recurrence.

Experimental studies reported results of therapy using multifunctional nanoparticles (ITIC-Th) activated by a 660-nm laser (Lin et al. 2022). In vitro studies and a rat model showed that the nanoparticles had a stable structure, favorable near-infrared fluorescence properties, and strong photothermal and photodynamic activity, including generation of reactive oxygen species (ROS). Treatment with ITIC-Th plus laser inhibited the progression of precancerous lesions and reduced the expression of cancer-related markers (ALDH1, p53, cyclin D1, and PDPN). In the rat model, this therapy was more effective in limiting dysplasia and carcinogenesis than standard ALA-PDT, while maintaining low toxicity and good biocompatibility.

Prognostic factors for recurrence and malignant transformation

Retrospective analyses indicate that important risk factors for recurrence and malignant transformation include the clinical type of lesion (non-homogeneous form), large lesion size, the presence of intraepithelial dysplasia, and a previous history of head and neck cancer. In a study including 144 patients treated with CO_2 laser for tongue lesions between 2002 and 2019, the mean follow-up period was 54.9 months (Yang et al. 2021a). Recurrence occurred in 20.8% of patients (annual rate 5.76%), and the mean time to recurrence was approximately 3.6 years. Independent factors associated with recurrence were a previous history of head and neck cancer and larger lesion area. Malignant transformation was found in 8.3% of patients (annual rate 2.28%), most commonly on the tongue, and was associated with high-grade dysplasia, non-homogeneous leukoplakia, and recurrence. In multivariate analysis, oncological history alone was an independent prognostic factor for both recurrence and malignant transformation.

Similar observations were obtained in an analysis of 124 patients (224 OL lesions) after treatment for head and neck cancer, including surgery, radiotherapy, or chemoradiotherapy (Yang et al. 2024a). The mean follow-up period was approximately 6 years. Recurrence occurred in 30 patients; in 17 cases, transformation to OSCC occurred, on average after 3.3 years. Leukoplakia located in a non-irradiated area of the oral cavity was associated with a higher risk of malignant transformation: carcinoma developed in 15 lesions on non-irradiated mucosa and in 2 lesions on irradiated mucosa. In multivariate analysis, previous radiotherapy was a clinical prognostic factor associated with a reduced risk of transformation among irradiated patients.

In a prospective study combining Er:YAG laser therapy with post-treatment mucosal image texture analysis, reconstruction of the mucosal microstructure to a state similar to healthy tissue was observed (Jurczyszyn and Kozakiewicz 2020). This was confirmed by texture-analysis parameters, such as a reduction in the number of bright fields, restoration of regularity, and an increase in fractal dimension. The authors identified these methods (texture analysis and fractal analysis) as promising tools for evaluating treatment effectiveness.

Table 1. Summary of studies on the treatment of oral leukoplakia (efficacy, recurrence, malignant transformation, complications).

Table 1. Summary of studies on the treatment of oral leukoplakia (efficacy, recurrence, malignant transformation, complications)

Author (year)	Study characteristics	n (patients/ lesions)	Intervention	Follow-up period	Remission (%)	Recurrence (%)	Malignant transformation (%)	Main complications
de Pauli Paglioni et al. (2025)	RCT (controlled clinical trial)	64 (33 diode laser, 31 scalpel)	diode laser vs scalpel	24 h-3 months	not reported	not reported	not reported	comparable postoperative pain; bette healing in th laser group o day 7, n differences after 1- months
Monteiro et al. (2017)	retrospective	60 (87 lesions)	scalpel + lasers (Nd:YAG, Er:YAG, CO_2, QMR)	21.6 months (mean)	72.4%	27.6%	1.1% (1/87; after 35 months, QMR group)	lowest recurrence after Er:YAG no significan overall differences
Arora et al. (2018)	observational	not precisely reported (OL and OLP groups)	laser (type not specified)	~4 weeks	100%	0%	not assessed (0% during follow-up)	rare pain/bleeding healing without complications after ~ weeks
Shivhare et al. (2022)	retrospective	56 (77 lesions)	diode laser (ablation 66.2% vs excision 33.8%)	4-6 months	100% (initially)	19.5% (ablation 25.5%; excision 7.6%)	0%	mild/moderate pain (VAS) swelling, granulomas; no infection
Rodriguez-Lujan et al. (2022)	prospective	34 (48 lesions)	CO_2 laser	18 months	43.8%	54.2% (mean time to recurrenc	2.1% (1/48)	rare and mild slight pai after 1 week

Author (year)	Study characteristics	n (patients/ lesions)	Intervention	Follow-up period	Remission (%)	Recurrence (%)	Malignant transformation (%)	Main complications
						e ~10 months)		
Campos et al. (2022)	retrospective	37 patients	CO_2 laser (10,600 nm)	36 months (mean)	not directly reported	35.1%	21.6% (mean 50.6 months)	no complications; healing ~4- weeks
Vilar-Villanueva et al. (2023)	retrospective	58 (78 lesions)	CO_2 laser (+ vaporization margins)	not reported (mean time to recurrence 11.6 months)	47.4%	52.6%	2.6% (2/78)	postoperative pain, granulation tissue in som patients; mos without complication
Wang et al. (2024)	retrospective	50 patients	photodynamic therapy (PDT)	24 months	response 68% (CR 12%, PR 56%)	32%	4%	oral pain ulcerations (52%), resolving after ~ weeks
Yang et al. (2021, Clin Oral Investig)	retrospective	144 patients	CO_2 laser (tongue)	54.9 months (mean)	not directly reported	20.8% (annual 5.76%; mean ~3.6 years)	8.3% (annual 2.28%)	not reported
Yang et al. (2024, BMC Oral Health)	retrospective	124 patients (224 lesions)	surgical treatment (patients after treatment for head and neck cancer, after RT/CHRT)	~6 years (~72 months)	not directly reported	30 patients (~24%)	13.7% (17/124; mean 3.3 years)	not reported

RCT - randomized clinical trial; OL - oral leukoplakia; OLP - oral lichen planus; CR - complete response; PR - partial response; RT - radiotherapy; CHRT - chemoradiotherapy; VAS - visual analogue scale. "Not reported / not provided" - data not presented in the study.

The Lin et al. (2022) study, which was preclinical (in vitro / rat model, ITIC-Th nanoparticles), and the study by Jurczyszyn and Kozakiewicz (2020), which evaluated healing *using image texture analysis, were not included in the summary because they did not report clinical rates of remission, recurrence, or malignant transformation.*

Discussion

Oral leukoplakia remains the most common potentially malignant disorder of the oral mucosa, and its diagnosis and treatment continue to pose a substantial clinical challenge. Contemporary diagnostic methods, including advanced imaging techniques, optically guided biopsy, and molecular biomarker analysis, allow earlier detection of lesions at high risk of malignant transformation. However, despite diagnostic progress, effective prevention of leukoplakia progression remains limited by its heterogeneous biological course.

The malignant transformation rate of leukoplakia remains approximately 6.64% (Pimenta-Barros et al. 2025). Risk factors that significantly influence transformation include lesion non-homogeneity, larger lesion size, location on the lateral surface of the tongue, tobacco smoking, and epithelial dysplasia. The authors emphasize that the presence of dysplasia is the most important clinical determinant of progression toward cancer; therefore, individualized therapeutic management and monitoring of patients with risk factors are essential.

Despite various attempts at both conservative and surgical treatment of leukoplakia, there is no clear evidence supporting the efficacy of pharmacological therapy in preventing malignant transformation (Lodi et al. 2016). Cancer development was assessed in trials of systemic vitamin A, systemic bleomycin, and systemic beta-carotene. Although some individual studies of vitamin A and beta-carotene suggested that these methods may be effective in improving or treating oral lesions, leading to partial regression, their long-term effect on reducing the risk of oral cancer has not been demonstrated. These findings indicate that no pharmacological therapy can currently be regarded as a standard approach for the prevention of malignant transformation.

Surgical treatment is attracting increasing interest, particularly for lesions with high-grade dysplasia. Available randomized clinical trials are scarce, but cohort studies suggest a potential benefit from surgical removal of precancerous lesions (Zhou et al. 2023). However, the authors point to the heterogeneity of available studies, differences in patient selection criteria, and the lack of long-term follow-up, which limit the possibility of clearly determining the impact of surgical procedures on reducing the risk of carcinogenesis. This means that the decision to perform surgical treatment should take into account lesion location, degree of dysplasia, and individual patient risk. Therefore, treatment should be supplemented with regular clinical follow-up and patient education regarding lifestyle modification.

Particularly promising results have been reported for laser technologies. Laser procedures provide comparable or even higher clinical efficacy than conventional methods, while reducing postoperative discomfort and shortening healing time (Dipalma et al. 2026). The authors also note reduced intraoperative bleeding and improved postoperative patient comfort, which is important for patients' quality of life. Similar conclusions arise from a meta-analysis indicating that laser therapy may be an effective and less burdensome alternative to conventional surgical treatment of oral leukoplakia (Luo et al. 2024).

Both Er:YAG and CO_2 lasers are effective tools in the treatment of neoplastic and precancerous oral lesions, but they differ in selected clinical parameters (Liu et al. 2020). Er:YAG laser use was associated with higher efficacy of complete lesion removal compared with CO_2 laser use; however, there were no significant differences between the two methods in terms of lesion recurrence. This suggests that, despite different mechanisms of action, both Er:YAG and CO_2 lasers provide comparable long-term efficacy. The choice of laser type should depend on operator experience and lesion characteristics.

Analysis of the current literature indicates that, despite the rapid development of diagnostic and therapeutic methods, there is currently no single treatment strategy that guarantees complete elimination of the risk of malignant transformation of leukoplakia. Therefore, a multidirectional approach is essential, including elimination of risk factors, accurate histopathological assessment, appropriately selected treatment, and long-term patient follow-up.

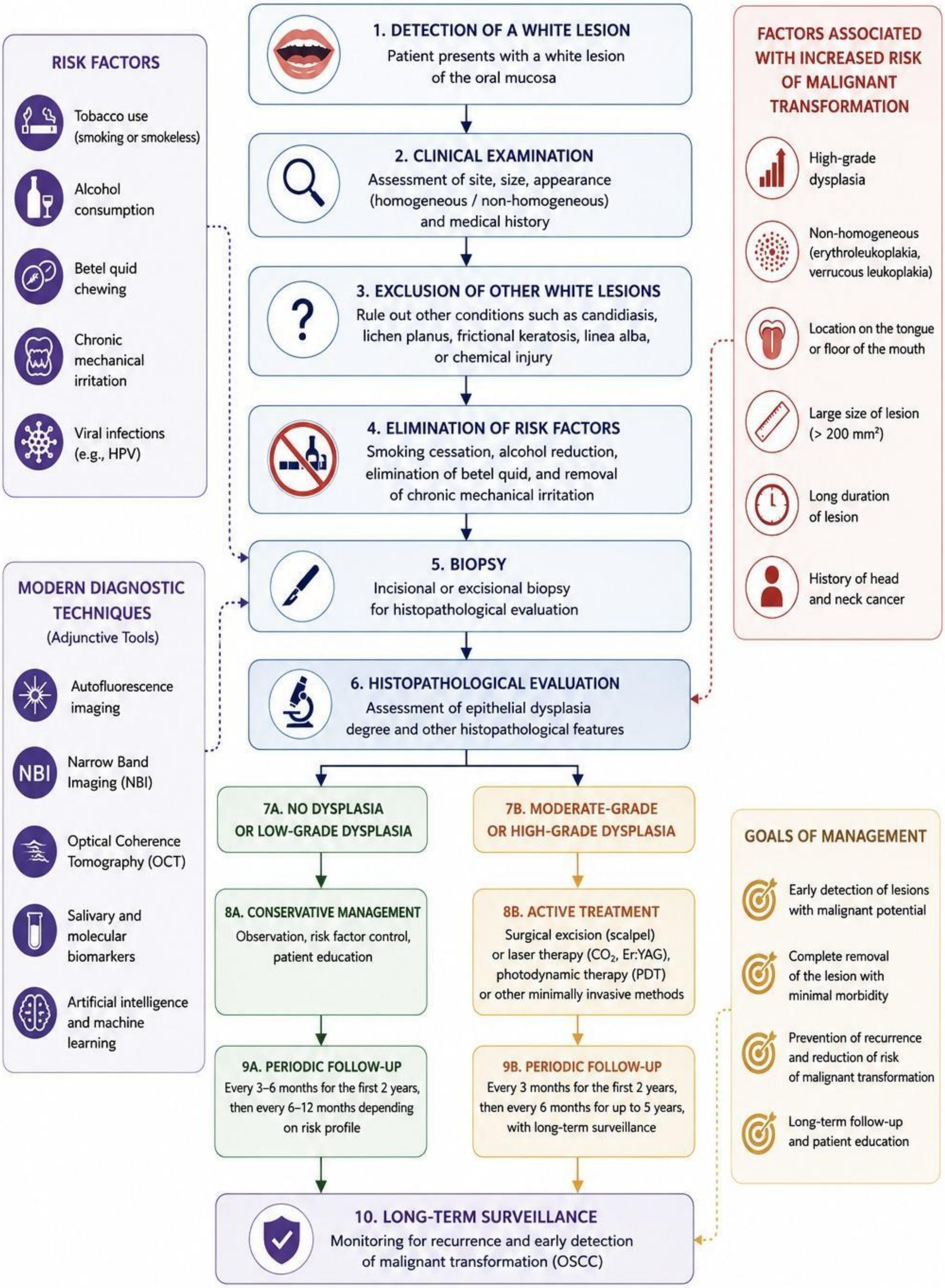
Conclusions

Advances in the diagnosis and management of oral leukoplakia have created new opportunities for earlier detection and more effective therapeutic intervention. The integration of conventional diagnostic methods with advanced imaging techniques, molecular biomarkers, and artificial intelligence-based technologies may enhance the identification of lesions at increased risk of malignant transformation and contribute to improved patient outcomes.

Current evidence indicates that laser-based therapies, particularly those employing CO_2 and Er:YAG lasers, represent effective alternatives to conventional surgical approaches, offering favorable wound healing characteristics and improved postoperative comfort. Photodynamic therapy has also demonstrated promising results and may serve as a valuable minimally invasive treatment option in selected patients.

Nevertheless, none of the currently available therapeutic modalities completely eliminates the risk of lesion recurrence or progression to oral squamous cell carcinoma. Therefore, individualized treatment planning remains essential and should take into account clinical presentation, lesion size, anatomical location, histopathological findings, degree of epithelial dysplasia, and patient-specific risk factors.

Long-term follow-up remains a cornerstone of successful management, as malignant transformation may occur several years after treatment. Future research should focus on the identification of reliable prognostic biomarkers, the standardization of emerging diagnostic technologies, and the long-term evaluation of laser therapies, photodynamic approaches, and artificial intelligence-assisted diagnostic systems. Such efforts may contribute to the development of more precise and personalized management strategies and ultimately reduce the burden of oral cancer among patients with oral leukoplakia.



OSCC – oral squamous cell carcinoma; CO_2 – carbon dioxide laser; Er:YAG – erbium, yttrium-aluminum-garnet laser; PDT – photodynamic therapy; HPV – human papillomavirus.

Figure 1. Diagnostic and Therapeutic Algorithm for Oral Leukoplakia.

Disclosure
Author Contributions:

Conceptualization: WP

Methodology: WZ

Formal analysis: WC

Investigation: WP

Data curation: KB

Writing – original draft preparation: WP, AJ, WZ, GC, KK

Writing – review and editing: KG, KB, WC, GC, KK

Supervision: AJ

Project administration: GC

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During the preparation of this manuscript, the authors used ChatGPT (OpenAI) exclusively for language editing, grammar correction, and translation support. Following the use of this tool, the authors carefully reviewed and edited the manuscript and take full responsibility for the final content of the publication.

References

Arora KS, Bansal R, Mohapatra S, Verma A, Sharma S, and Pareek S. 2018. Prevention of malignant transformation of oral leukoplakia and oral lichen planus using laser: An observational study. Asian Pacific Journal of Cancer Prevention 19(12):3635–3641. doi: 10.31557/APJCP.2018.19.12.3635

Aubreville M, Knipfer C, Oetter N, Jaremenko C, Rodner E, Denzler J, Bohr C, Neumann H, Stelzle F, and Maier A. 2017. Automatic classification of cancerous tissue in laserendomicroscopy images of the oral cavity using deep learning. Scientific Reports 7:11979. doi: 10.1038/s41598-017-12320-8

Campos WG, Esteves CV, Gallo CB, Domaneschi C, Aranha ACC, and Lemos CA. 2022. Treatment of oral leukoplakia with CO_2 laser (10,600 nm): Analysis of 37 cases. Brazilian Oral Research 36:e014. doi: 10.1590/1807-3107bor-2022.vol36.0014

de Pauli Paglioni M, Pedroso CM, Faustino ISP, Vargas PA, de Goes MF, Martins MD, Lopes MA, and Santos-Silva AR. 2025. Wound healing and pain evaluation following diode laser surgery vs. conventional scalpel surgery in the surgical treatment of oral leukoplakia: A randomized controlled trial. Frontiers in Oral Health 6:1568425. doi: 10.3389/froh.2025.1568425

Dipalma G, Inchingolo AM, Lauria P, et al. 2026. Laser therapy versus conventional treatments in oral leukoplakia: A systematic review of efficacy, recurrence, and postoperative outcomes. International Journal of Dentistry 2026:2130179. doi: 10.1155/ijod/2130179

Jurczyszyn K and Kozakiewicz M. 2020. Application of texture and fractal dimension analysis to estimate effectiveness of oral leukoplakia treatment using an Er:YAG laser: A prospective study. Materials 13(16):3614. doi: 10.3390/ma13163614

Li W, Chen Y, Zhao H, et al. 2024. Diagnostic accuracy of artificial intelligence-assisted clinical detection of oral potentially malignant disorders: A systematic review and meta-analysis. Frontiers in Oncology 14:1357921. doi: 10.3389/fonc.2024.1357921

Lin L, Song C, Wei Z, Zou H, Han S, Cao Z, Zhang X, Zhang G, Ran J, Cai Y, and Han W. 2022. Multifunctional photodynamic/photothermal nano-agents for the treatment of oral leukoplakia. Journal of Nanobiotechnology 20(1):106. doi: 10.1186/s12951-022-01310-2

Liu R, Sun K, Wang Y, Jiang Y, Kang J, and Ma H. 2020. Clinical comparison between Er:YAG and CO_2 laser in treatment of oral tumorous lesions: A meta-analysis. Medicine 99(30):e20942. doi: 10.1097/MD.0000000000020942

Lodi G, Franchini R, Warnakulasuriya S, Varoni EM, Sardella A, Kerr AR, Carrassi A, MacDonald LCI, and Worthington HV. 2016. Interventions for treating oral leukoplakia to prevent oral cancer. Cochrane Database of Systematic Reviews 7:CD001829. doi: 10.1002/14651858.CD001829.pub4

Luo R, Wang Y, Li R, et al. 2024. Laser therapy decreases oral leukoplakia recurrence and boosts patient comfort: A network meta-analysis and systematic review. BMC Oral Health 24(1):469. doi: 10.1186/s12903-024-04179-9

Monteiro L, Barbieri C, Warnakulasuriya S, Martins M, Salazar F, Pacheco JJ, Vescovi P, and Meleti M. 2017. Type of surgical treatment and recurrence of oral leukoplakia: A retrospective clinical study. Medicina Oral, Patología Oral y Cirugía Bucal 22(5):e520–e526. doi: 10.4317/medoral.21645

Pimenta-Barros LA, Ramos-García P, González-Moles MÁ, Aguirre-Urizar JM, and Warnakulasuriya S. 2025. Malignant transformation of oral leukoplakia: Systematic review and comprehensive meta-analysis. Oral Diseases 31(1):69–80. doi: 10.1111/odi.15140

Rodriguez-Lujan A, López-Jornet P, and Pons-Fuster López E. 2022. Recurrence of oral leukoplakia after CO_2 laser resection: A prospective longitudinal study. Cancers 14(21):5455. doi: 10.3390/cancers14215455

Shivhare P, Haidry N, Kumar A, Parihar A, Singh A, and Subramanyam S. 2022. Diode laser in the management of leukoplakia: A retrospective study. Annals of Maxillofacial Surgery 12(2):178–184. doi: 10.4103/ams.ams_117_22

Vilar-Villanueva M, Somoza-Martín JM, Blanco-Carrión A, García-García A, García-Carnicero T, Marichalar-Mendía X, Gallas-Torreira M, and Gándara-Vila P. 2023. Importance of vaporization margins during CO_2 laser treatment of oral leukoplakia: A survival study. Oral Diseases 29:2689–2695. doi: 10.1111/odi.14345

Villa A and Woo SB. 2021. Leukoplakia—A diagnostic and management algorithm. Journal of Oral and Maxillofacial Surgery 79(4):831–843. doi: 10.1016/j.joms.2020.10.025

Wang Y, Tang H, Wang K, Zhao Y, Xu J, and Fan Y. 2024. Clinical evaluation of photodynamic therapy for oral leukoplakia: A retrospective study of 50 patients. BMC Oral Health 24(1):9. doi: 10.1186/s12903-023-03791-5

Warnakulasuriya S, Kujan O, Aguirre-Urizar JM, et al. 2021. Oral potentially malignant disorders: A consensus report from an international seminar on nomenclature and classification. Oral Diseases 27(8):1862–1880. doi: 10.1111/odi.13704

Yang SW, Lee YS, Chang LC, Hwang CC, and Chen TA. 2020. Clinicopathological characteristics and treatment outcomes of oral leukoplakia by carbon dioxide laser excision in elderly patients. Head & Neck 42(5):1014–1023. doi: 10.1002/hed.26074

Yang SW, Lee YS, Chang LC, Yang CH, Luo CM, and Wu PW. 2021a. Oral tongue leukoplakia: Analysis of clinicopathological characteristics, treatment outcomes, and factors related to recurrence and malignant transformation. Clinical Oral Investigations 25(6):4045–4058. doi: 10.1007/s00784-020-03735-1

Yang SW, Lee YS, Wu PW, Chang LC, and Hwang CC. 2021b. A retrospective cohort study of oral leukoplakia in female patients: Analysis of risk factors related to treatment outcomes. International Journal of Environmental Research and Public Health 18(16):8319. doi: 10.3390/ijerph18168319

Yang SW, Lin CY, Lee YS, and Huang SM. 2024a. Treatment outcomes of oral leukoplakia on the irradiated or nonirradiated mucosa among survivors of head and neck cancer in the population where practice of betel nut chewing and cigarette smoking are widespread. BMC Oral Health 24(1):851. doi: 10.1186/s12903-024-04628-5

Yang Y, Tomita N, Yeo JY, et al. 2024b. Artificial intelligence in oral cancer and oral potentially malignant disorders: Current status and future perspectives. Cancers 16(3):512. doi: 10.3390/cancers16030512

Zhou S, Zhang X, Liu W, and Chen W. 2023. Evaluating surgical excision to prevent progression of oral precancerous lesions: Highlighting randomized controlled trials and cohort studies. Journal of Dental Sciences 18(4):1876–1882. doi: 10.1016/j.jds.2023.05.033