REVIEW

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Surveillance Strategies for Oral Potentially Malignant Disorders: A Comprehensive Review and Clinical Decision Tree

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Abstract

Objective: Oral potentially malignant disorders are a group of oral mucosal conditions with a significant risk of transforming into oral squamous cell carcinoma. Early detection and proper follow-up are crucial in improving patient outcomes. This review consolidates evidence on the clinical features, malignant potential, treatment, and follow-up strategies for the four most common oral potentially malignant disorders: oral leukoplakia, proliferative verrucous leukoplakia, erythroplakia, and oral lichen planus. It also proposes a clinical decision tree for structured surveillance of these lesions. **Methods:** This review consolidates evidence on the clinical features, malignant potential, treatment, and follow-up strategies for the four most common oral potentially malignant disorders. **Results:** This review highlights the variability in follow-up recommendations and emphasizes the need for individualized, evidence-informed monitoring strategies. **Conclusion:** To the best of our knowledge, this is among the first structured attempts to present a comprehensive clinical decision tree to guide practitioners in the surveillance of OPMDs. The proposed model provides clinicians with a practical tool to minimize the risk of malignant progression. Nevertheless, despite a growing body of literature, standardized surveillance protocols are still lacking, and further longitudinal research is required.

Keywords: Oral potentially malignant disorders- leukoplakia- proliferative verrucous leukoplakia-erythroplakia

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Introduction

Oral potentially malignant disorders (OPMDs) comprise a diverse group of oral mucosal lesions that carry an increased risk of malignant transformation. These disorders present with distinct clinical and histopathological features and are associated with various risk factors and etiologies. Prominent examples of OPMDs include leukoplakia, erythroplakia, proliferative verrucous leukoplakia (PVL), and oral lichen planus [1]. According to the World Health Organization (WHO), oral potentially malignant disorders (OPMDs) are defined as "clinical presentations that carry a risk of cancer development in the oral cavity, whether in clinically definable precursor lesions or in clinically normal oral mucosa" [2]. The oral cavity is the primary site for head and neck squamous cell carcinoma (HNSCC), with approximately 350,000 new cases of oral cavity squamous cell carcinoma (OCSCC) diagnosed globally each year. This leads to around 175,000 deaths annually, and the overall five-year survival rate remains approximately 50% [2].

Diagnoses of oral cavity squamous cell carcinoma (OCSCC) are often made at advanced stages, contributing to poor patient outcomes and significantly affecting quality of life [2, 3]. Timely identification and intervention during the early stages of oral squamous cell carcinoma (OSCC) are critical, as the five-year survival rate markedly decreases from approximately 80% for early-stage diagnoses to 30% for advanced-stage cases [3]. Early detection not only improves survival rates but also enhances quality of life and reduces treatment costs [2, 3].Although extensive literature exists regarding the etiology, clinical features, and histopathological characteristics of dysplasia associated with OPMDs, there remains a lack of universally accepted clinical management guidelines [2].

The importance of regular follow-up in patients with oral potentially malignant disorders (OPMDs) has been emphasized in the literature, as it significantly improves survival outcomes and enables early detection of malignant transformation [3]. Although several reviews have addressed OPMDs, few have provided a unified clinical decision-making algorithm. This review aims to fill this gap by presenting a practical decision tree that integrates current evidence for clinical surveillance. The proposed decision tree is designed to guide the follow-up of patients with oral potentially malignant disorders (OPMDs), recognizing that early detection and appropriate management are critical for reducing the risk of malignant transformation and improving

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patient outcomes. Building upon previous applications of decision trees for diagnosing peripheral exophytic oral lesions [4], this study emphasizes the role of structured algorithms in optimizing OPMD management. The most common OPMDs including leukoplakia, erythroplakia, proliferative verrucous leukoplakia (PVL), and oral lichen planus are comprehensively reviewed in terms of their definition, epidemiology, clinical presentation, malignant potential, therapeutic approaches, and recommended surveillance protocols. Furthermore, to consolidate the currently scattered information in the literature, a novel clinical decision-making algorithm is proposed to standardize the follow-up and management strategies for each disorder.

Leukoplakia

Definition and terminology

The term "leukoplakia" was initially introduced by Schwimmer in 1877. In 1978, the World Health Organization (WHO) defined leukoplakia as a persistent white patch that cannot be characterized clinically or histopathologically as any other specific disorder. This definition was updated in 1994 to state that "oral leukoplakia is not linked to any physical or chemical cause, except for smoking, and has the potential to progress to cancer." In 2012, the most recent WHO definition described leukoplakia as "a predominantly white lesion or plaque with uncertain behavior, after excluding clinically and histopathologically any other identifiable white disease or disorder" [5].

Epidemiology and etiology

The estimated global prevalence of oral leukoplakia is approximately 2% [6]. Moreover, variations in gender distribution have been observed across different geographical regions. Smokers are approximately six times more likely to develop leukoplakia compared to non-smokers, and alcohol consumption represents an independent risk factor, regardless of the type of beverage or drinking pattern. However, studies investigating the potential role of human papillomavirus (HPV) infection in the development of leukoplakia have yielded conflicting results [6].

Clinical Features

Oral leukoplakia can be categorized into two primary subtypes based on macroscopic features: homogeneous and non-homogeneous [2,6]. Homogeneous leukoplakia appears as predominantly white plaques with a uniform, flat, and thin surface, often showing shallow keratin cracks. These plaques typically exhibit a smooth, wrinkled, or corrugated texture. In contrast, non-homogeneous leukoplakia presents a mixture of white and red areas, such as in erosive leukoplakia or erythroleukoplakia, and may display irregular flatness, nodularity (speckled appearance), or verrucous growth patterns. Proliferative verrucous leukoplakia (PVL), a distinct variant of verrucous leukoplakia, is characterized by multifocal presentation, resistance to conventional therapies, and a markedly high risk of malignant transformation [7].

Malignant Transformation

The annual transformation rate (ATR) of oral leukoplakia (OL) is commonly used as a reference point for assessing malignant potential. ATR is calculated by dividing the number of patients who experience malignant transformation by the total number of patients followed in a specific study over a one-year period. Not all relevant studies provide time-specific data to enable an accurate estimation of ATR. However, based on the available evidence, the annual transformation rate of OL is estimated to be approximately 2–3% [8].

Management and Treatment

Surgical excision remains the standard and most widely recommended approach for treating oral leukoplakia, as it also provides tissue for histopathological evaluation [9]. Wide local excision using a cold knife or electrocautery is typically employed, with the general recommendation to include a margin of clinically normal mucosa to achieve negative surgical margins. In cases of recurrence, re-resection with an additional 2–3 mm margin has been proposed [9]. Well-demarcated leukoplakias <2cm with no dysplasia may be observed instead of excision [10].

Alternative treatment modalities include photodynamic therapy (PDT), cryoablation, and laser ablation, although these are generally considered secondary options to surgical management [9].

Follow-up and Surveillance

In light of the absence of a standardized protocol for the follow-up of oral leukoplakia, multiple studies have proposed a variety of recommendations:

• Isaäc van der Waal proposed lifelong follow-up at six-month intervals for non-dysplastic lesions, and every three months for dysplastic leukoplakia, with excision of lesions smaller than 2–3 cm [6].

• Bedi and Scully recommended excision of dysplastic lesions, followed by regular follow-up at 3–6 month intervals. They also noted that recurrence occurs in more than one-third of cases [11].

• Isaäc van der Waal suggested that semiannual (twice yearly) follow-up visits may be beneficial in managing leukoplakia [12].

• Villa and Woo recommended that poorly demarcated leukoplakias (e.g., frictional keratosis) should undergo re-biopsy and continued follow-up [26]. For well-demarcated large lesions (>3 cm), follow-up every three months with annual re-biopsy was advised, shifting to every 3–6 months if no recurrence occurs. Small lesions (<3 cm) should be excised or ablated with narrow margins, followed by three-monthly follow-ups, and excision with a 2–3 mm margin in case of recurrence.

• Staines and Rogers noted the absence of specific guidelines but indicated that follow-up every 3–6 months is a widely accepted practice based on individual risk assessment and patient preference [8].

• Awadallah et al. emphasized that long-term follow-up is mandatory for any patient with a history of dysplasia or malignancy, due to the risk of second primary tumor development [13]. Ideally, follow-up should be lifelong, adjusted based on patient risk stratification and lesion

severity.

• Chaturvedi et al. [14] recommended at least annual follow-up for all patients with oral leukoplakia, with more frequent surveillance for those with dysplastic changes.

• Chen et al. [15] strongly advocated for regular follow-up of all patients diagnosed with oral leukoplakia, regardless of risk factors or treatment. They advised follow-up every three months for low-risk patients, and every 1–3 months for high-risk individuals (including older patients, females, lesions exceeding 200 mm², non-homogeneous leukoplakia, and high-grade dysplasia).

• Archibald et al. [9] emphasized that, given the low but persistent risk of malignant transformation, leukoplakia requires constant observation regardless of its duration or clinical appearance. They proposed a follow-up protocol stratified by histological grade:

Hyperkeratosis or no dysplasia

Clinical follow-up every six months for 1–2 years, with biopsy only upon noticeable changes.

Mild dysplasia

Follow-up every six months for five years, with re-biopsy every two years.

Moderate dysplasia

Follow-up every three months for five years, with re-biopsy within 12–18 months.

Severe dysplasia or carcinoma in situ (CIS)

Follow-up every three months for five years, with re-biopsy every 3–9 months, or earlier if changes occur. They also recommend confirming the histology on referral biopsy and distinguishing between CIS and severe dysplasia using standardized criteria.

• Baharvand et al. reported that the interval between follow-up sessions for leukoplakia varies widely across studies, ranging from a few months to one year. They recommend close monitoring every 3 to 6 months, accompanied by tobacco and alcohol cessation and a diet rich in vegetables and fresh fruits. It was also stated that patients who remain disease-free for up to three years after treatment may not require further follow-up [16].

• Jena et al. suggested that leukoplakia without dysplasia should be followed every six months for life, regardless of treatment status. In cases with dysplasia, they recommended follow-up every three months for life, with excision of lesions smaller than 2–3 cm [5].

• Kumar et al. stated that close monitoring (every 3–6 months) is advisable after incisional biopsy, independent of the presence of epithelial dysplasia. They noted that no strict guidelines exist regarding the duration and frequency of follow-up, but lifelong surveillance at intervals of 6–12 months is commonly suggested. In untreated dysplastic lesions, three-monthly follow-up may sometimes be warranted [7].

Proliferative verrucous leukoplakia (PVL)

Definition and terminology

Proliferative verrucous leukoplakia (PVL) is recognized as a particularly aggressive and distinct subtype of leukoplakia. It was first described by Hansen et al. in 1985 [17]. PVL typically begins as a non-dysplastic keratotic lesion and, over a prolonged period- sometimes exceeding two decades- progresses into confluent, multifocal oral keratoses [18]. According to the World Health Organization (WHO), PVL is defined as a "progressive, persistent, and irreversible disorder characterized by the presence of multiple leukoplakias that frequently become warty" [19].

Epidemiology and etiology

Proliferative verrucous leukoplakia (PVL) exhibits a higher prevalence in women compared to men, with a reported female-to-male ratio of approximately 4:1 [20]. The most commonly affected sites include the lower gingiva, buccal mucosa, and tongue [21]. Although the exact etiology of PVL remains unclear, tobacco use has been largely ruled out as a major contributing factor, given that PVL has been observed in both smokers and non-smokers [20]. Human papillomavirus (HPV) has been detected in PVL lesions, with 89% of cases testing positive, predominantly for HPV-16 [22]. Moreover, Epstein-Barr virus (EBV) has been identified in approximately 60% of PVL samples [19, 23].

Clinical Features

Proliferative verrucous leukoplakia (PVL) commonly presents as diffuse hyperkeratosis, characterized by a slow, irreversible, and persistent progression. Exophytic, wart-like manifestations of leukoplakia are hallmark features of PVL and tend to be highly resistant to most treatment modalities. Clinically, PVL may exhibit a spectrum of appearances, including epithelial hyperkeratosis, verrucous carcinoma, and squamous cell carcinoma [19, 24, 25].

Malignant Transformation

The malignant transformation rate in proliferative verrucous leukoplakia (PVL) varies among different case series. A systematic review conducted in 2014, which pooled data from 12 studies, reported an overall transformation rate of 56.2%. When considering an average follow-up duration of 7.4 years, the rate increased to 60.7%. Moreover, a more recent systematic review published in 2015 reported a malignant transformation rate of 63.9% in a subgroup analysis of 277 PVL patients, with approximately 40% of the patients ultimately succumbing to the disease [8]. PVL is recognized as having one of the highest rates of malignant transformation among all oral potentially malignant disorders (OPMDs) [19].

Management and Treatment

Despite the use of various treatment modalities, management of PVL remains challenging due to its high recurrence rates. Wide surgical excision with histologically clear margins is considered the most effective approach; however, high recurrence rates have been reported [25]. Non-surgical interventions, such as laser ablation and cryosurgery, may be effective for localized lesions but are generally less successful for multifocal disease. Regardless of the treatment modality, long-term and

close follow-up is mandatory given the persistent risk of malignant transformation [19].

Follow-up and Surveillance

Various follow-up recommendations have been proposed in the literature for proliferative verrucous leukoplakia (PVL):

• Villa and Woo recommended that PVL patients be followed up every three months. In cases where verrucous or nodular areas are identified, excision is advised, and if no recurrence is observed, follow-up can be extended to every 3–6 months [26].

• Speight et al. emphasized that close follow-up and repeat biopsies are essential to ensure early detection and appropriate management in patients with PVL [27].

• Lorini et al. stated that PVL lesions often display varying degrees of dysplasia and can progress to oral squamous cell carcinoma (OSCC), thereby mandating close and continuous surveillance [1].

• Kumari et al. highlighted the progressive nature of PVL, noting that the evolution from early hyperkeratosis to epithelial hyperplasia, atypia, verrucous carcinoma, and ultimately squamous cell carcinoma necessitates multiple and repeat biopsies alongside close follow-up [7].

• Jena et al. suggested that patients with PVL should undergo clinical follow-up every 3–6 months, with the length of follow-up extending to at least five years [5].

Oral Erythroplakia

Definition and terminology

The term erythroplakia is widely used to describe fiery red patches in the oral mucosa that cannot be characterized clinically or pathologically as any other specific lesion. While a definition based on exclusion is considered less ideal than a positive diagnostic description, erythroplakia remains primarily a diagnosis of exclusion. Given the frequent association of erythroplakia with lichenoid lesions, a novel approach has been proposed to define erythroplakia based on its clinical features: fiery red appearance, sharp demarcation, and a slight depression relative to the surrounding mucosa. Such a definition could potentially aid clinicians in distinguishing erythroplakia from other red lesions in the oral cavity [28].

Epidemiology and etiology

Typically, oral erythroplakia (OE) is considered a red variation of a premalignant lesion that shares similar etiology and pathogenesis with oral leukoplakia. While consuming fruits and vegetables may offer some protection, various studies have indicated that factors such as tobacco chewing, tobacco smoking, betel quid chewing (with or without tobacco), and alcohol usage contribute to the development of erythroplakia.

Human papillomavirus (HPV) infections have also been identified as an etiologic cofactor for erythroplakia. In one study, 5 out of 10 erythroplakias were found to be HPV-positive, and all lesions that progressed to cancer were also positive for HPV. However, due to the limited number of cases examined, it is challenging to draw definitive conclusions regarding the role of HPV.

There is a scarcity of data regarding the prevalence of oral erythroplakia, with most available information derived from specific groups such as hospital-associated populations and individuals with particular habits. For instance, a clinical hospital-based study of 500 consecutive patients (with only one woman) who were habitual psychoactive substance users reported a prevalence of 0.6%. Similarly, the prevalence was nearly identical (0.7%) among 559 tobacco users (25% women) in Saudi Arabia. However, among 210 residents of addiction treatment centers (30% women) in southern Ireland, four lesions suggestive of erythroplakia were identified, indicating a higher estimated prevalence of 1.9% within this cohort. In general population samples outside of hospital settings, the prevalence tends to be lower. For example, among 1241 individuals (47.1% women) in India, the prevalence of erythroplakia was 0.24%, and a similar prevalence of 0.3% was found among 1385 rural Brazilian workers, of which 53.2% were females.[7]

Clinical Features

The clinical features of oral erythroplakia have been comprehensively reviewed by several authors. Typically, lesions present as smooth, velvety, or granular surfaced red patches. Different sites of predilection have been observed across populations. For instance, a Scandinavian study reported the buccal mucosa as the most frequently affected site, whereas a Thai population study indicated a higher prevalence on the palatal mucosa [7].

Malignant Transformation

Erythroplakia and erythroplakic lesions demonstrate a wide spectrum of clinical outcomes upon follow-up. While some lesions may regress spontaneously, others exhibit a significant potential for malignant progression, with reported transformation rates ranging from 14% to 50%. Oral erythroplakia (OE) is traditionally regarded as the oral potentially malignant disorder (OPMD) with the highest incidence of malignant transformation [7].

Management and Treatment

The standard treatment for oral lesions at high risk of malignant transformation, such as those exhibiting severe epithelial dysplasia or carcinoma in situ, is surgical excision [29].

CO_2 laser excision techniques have also been demonstrated to be safe and effective, offering advantages such as minimal postoperative complications, including the absence of wound bleeding, trismus, and difficulties with chewing, swallowing, and articulation [19].

Follow-up and Surveillance

Various follow-up recommendations have been proposed in the literature regarding oral erythroplakia (OE):

• Holmstrup et al. stated that patients with OE should be followed intensively at short intervals, irrespective of any possible association with other diseases or local irritants [28].

• Lorenzo-Pouso et al. recommended that patients diagnosed with OE should undergo lifelong active follow-

up, considering the high risk of malignant transformation associated with this lesion [30].

• Kumari et al. emphasized that excisional biopsy is advised for cases exhibiting severe dysplasia or carcinoma in situ. For lesions with moderate dysplasia or no dysplasia, they suggested a strategy of close and timely clinical follow-up [19].

Oral Lichen Planus

Definition and terminology

Lichen planus (LP) is a relatively common chronic inflammatory disorder of the oral cavity. It is a chronic, immune-mediated disease of unknown etiology that may affect not only the oral mucosa (oral LP), but also the skin and its adnexal structures (cutaneous LP), as well as the mucosal surfaces of the external genitalia (genital LP) [31].

Epidemiology and etiology

The exact etiology of oral lichen planus (OLP) remains unknown; however, several potential triggers have been proposed, including local and systemic inducers of cell-mediated hypersensitivity, viral infections, and psychological stress.

According to a recent systematic review and meta-analysis, the global prevalence of OLP is estimated at approximately 1.01%. Significant regional differences have been observed, with higher prevalence rates reported in South America, Africa, and Europe compared to Asia and North America.

Women are disproportionately affected, exhibiting a prevalence three to four times higher than that observed in men. The typical age of onset ranges between 30 and 70 years, with men generally developing the condition at an earlier age. Furthermore, the prevalence of OLP demonstrates a gradual and significant increase after the age of 40. Pediatric cases are rare, with only a few reported instances documented in the literature [32].

Clinical Features

Various clinical classifications of oral lichen planus (OLP) have been described in the literature. Andreasen proposed a system comprising six clinical types: reticular, erosive, atrophic, plaque, papular, and bullous.

Silverman, in contrast, categorized OLP into three major forms: reticular, atrophic, and erosive, with the atrophic and erosive variants characterized by ulceration and atrophic changes. Similarly, Eisen proposed a three-type classification: reticular, atrophic, and erosive.

OLP can affect any site within the oral mucosa; however, the buccal mucosa is the most commonly involved site, accounting for over one-third of cases, followed by the gingiva and tongue. Moreover, more than half of OLP cases exhibit bilateral lesions [32].

Malignant Transformation

A recent comprehensive analysis of multiple systematic reviews reported that the malignant transformation rate of oral lichen planus (OLP) varies between 0.44% and 2.28% [32].

Although the overall risk is relatively low compared to other oral potentially malignant disorders, the possibility of delayed malignant transformation underscores the importance of long-term clinical follow-up and careful monitoring of OLP patients.

Management and Treatment

Currently, there is no definitive cure for oral lichen planus (OLP). The primary objective of treatment is to alleviate symptoms such as pain and burning sensation, thereby improving the patient's overall quality of life. Given the immune-mediated nature of OLP, therapeutic approaches primarily focus on the use of anti-inflammatory, immunomodulatory, and immunosuppressive agents [32].

Follow-up and Surveillance

Various follow-up recommendations have been proposed in the literature regarding oral lichen planus (OLP):

• Mortazavi et al. emphasized that patients with OLP should be followed over a long period, due to the chronic nature of the disease and the risk of malignant transformation [33].

• Isaäc van der Waal pointed out that although the long-term efficacy of continuous follow-up remains debated, structured and regular follow-up has been proposed as beneficial. A follow-up interval of 6–12 months, lifelong, appears to be a reasonable approach [12].

• Chiang et al. noted that OLP patients should be referred to medical doctors for regular and close follow-up, not only for oral monitoring but also to evaluate associated systemic conditions such as gastric disorders and thyroid dysfunction [29].

• Campana et al. advocated for close monitoring, recommending monthly visits for patients with severe symptoms, poorly controlled erosive disease, or those receiving systemic therapy. Once disease activity is better controlled, follow-up intervals of 6–12 months are considered appropriate, with adjustments based on symptom severity [34].

• Lajolo et al. emphasized the need for strict follow-up and control biopsies, particularly in cases with atypical clinical features or persistent symptoms. They highlighted the absence of standardized guidelines, noting that clinicians often prefer tighter follow-up schedules. In line with this, Mignogna et al. recommended follow-up visits at least three times a year, with shorter intervals (every two months) if disease progression is suspected [31].

• Louisy et al. (2024) suggested that due to the chronic relapsing course of OLP and its association with oral squamous cell carcinoma (OSCC), clinical follow-up is recommended. Although no specific frequency has been firmly established, it is customary to perform at least an annual clinical evaluation, with more frequent monitoring (every 2–6 months) for erythematous, erosive, or atrophic forms at higher risk for malignant change [32].

• Jena et al. stated that patients with erosive lichen planus or poorly controlled disease, especially those with a history of dysplasia, should undergo clinical follow-up every 3–6 months, with a recommended follow-up duration of five years [5].

Discussion on General Follow-up Strategies for Oral Potentially Malignant Disorders (OPMDs)

In addition to specific follow-up recommendations for individual lesions, several studies have generally addressed the surveillance of patients with oral potentially malignant disorders (OPMDs):

• Diajil et al. recommended mandatory long-term follow-up and active surveillance for all patients with potentially malignant disorders [35].

• Dionne et al. noted that due to persistent malignant potential, regular surveillance should be maintained, although follow-up protocols remain subjective and based largely on clinical judgment and histopathological findings [36].

• Holmstrup stressed the importance of initiating follow-up from the time of diagnosis. They advocated for surveillance intervals of 3–6 months regardless of dysplasia presence, given the possibility of malignant transformation over a prolonged period, recommending at least 20 years of follow-up, or lifelong monitoring when possible [28].

• Goodson et al. suggested that long-term follow-up in specialized clinics is necessary for patients with clinically suspicious lesions, irrespective of histopathological diagnosis [37].

• Chiang et al. proposed a classification system based on clinical and histopathological evaluation. They categorized patients into three groups: (1) patients with clinical suspicion of OPMD without biopsy, (2) patients with biopsy-confirmed dysplasia, and (3) patients with no histopathological evidence of dysplasia. They also emphasized management variations according to the severity of oral epithelial dysplasia (OED) [29].

• Bedi et al. highlighted the absence of evidence-based guidelines for OPMD surveillance. They emphasized that given the unpredictable nature of malignant transformation (MT), lifelong follow-up is generally recommended, with intervals tailored to the patient's clinical evolution [11].

• Awadallah et al. pointed out that despite the lack of concrete guidelines, regular and frequent follow-up is critical, particularly for lesions with moderate to severe dysplasia. Follow-up strategies should be individualized based on patient-specific and lesion-specific factors such as age, gender, substance use, anatomical location, and dysplasia grade [13].

• Warnakulasuriya emphasized that follow-up intervals should be individualized based on patient risk assessment and compliance, as cancer can arise at any stage during the natural history of OPMDs [2].

• Wetzel and Wollenberg advocated for surgical excision of high-risk dysplastic lesions with close and long-term follow-up thereafter [38].

• Jäwert et al. noted that lifelong monitoring is necessary for all patients who have undergone excision or ablation of OPMDs, although standardized protocols are lacking. They suggested reassessment every 3–6 months for high-risk lesions, while low-risk OPMDs may be followed every 6–12 months [3].

• Pritzker et al. highlighted that oral squamous cell carcinoma (OSCC) may arise even in clinically concerning lesions without histopathological evidence of dysplasia, reinforcing the importance of vigilant follow-up [39].

• Virgone and Badreh underscored the necessity for systematic biopsy and appropriate follow-up of precancerous lesions to ensure early detection of malignant changes [40].

• Kudva et al. emphasized that, due to the unpredictability of malignant transformation timelines, which may vary from months to years, strict and long-term follow-up is essential. They noted the absence of standardized protocols, encouraging individualized surveillance based on patient-specific risk stratification [41].

After reviewing the various follow-up strategies for oral potentially malignant disorders (OPMDs) presented in the literature, this paper proposes a new model in the form of a clinical decision tree (Figure 1). This decision tree aims to guide the follow-up of each premalignant lesion based on its distinct clinical and pathological features. The development of such decision-making tools can help address inconsistencies observed in current follow-up protocols and provide a standardized framework to improve the long-term management of patients with OPMDs. Our proposed model consolidates heterogeneous recommendations from the literature into a single, structured approach that may enhance consistency in clinical practice. However, the absence of prospective validation underscores the need for multicenter clinical studies to confirm its applicability and reliability. The proposed clinical decision tree for the follow-up of OPMDs is presented in Figure 1.

Limitations and Future Directions

Despite the extensive literature on oral potentially malignant disorders (OPMDs), several limitations persist.

For oral leukoplakia, there is no consensus regarding optimal follow-up intervals, with various studies recommending intervals ranging from three months to yearly evaluations.

In the case of proliferative verrucous leukoplakia (PVL), although its high malignant potential is well recognized, standardized treatment protocols and long-term management strategies are lacking. Epidemiological data regarding oral erythroplakia are particularly scarce and show considerable variability depending on the characteristics of the studied populations.

Regarding oral lichen planus (OLP), while the risk of malignant transformation is relatively low, uncertainties persist concerning appropriate follow-up intervals, the necessity of repeat biopsies in atypical clinical presentations, and the overall duration of surveillance. These gaps underscore the need for well-designed, multicenter, longitudinal studies to develop evidence-based guidelines for the management and follow-up of OPMDs.

Although this review proposes a clinical decision tree to address variability in current follow-up recommendations, it should be acknowledged that no universally accepted, evidence-based protocols for OPMDs are available to date. Future studies should therefore validate this model across diverse populations and healthcare settings to establish its generalizability and clinical utility.

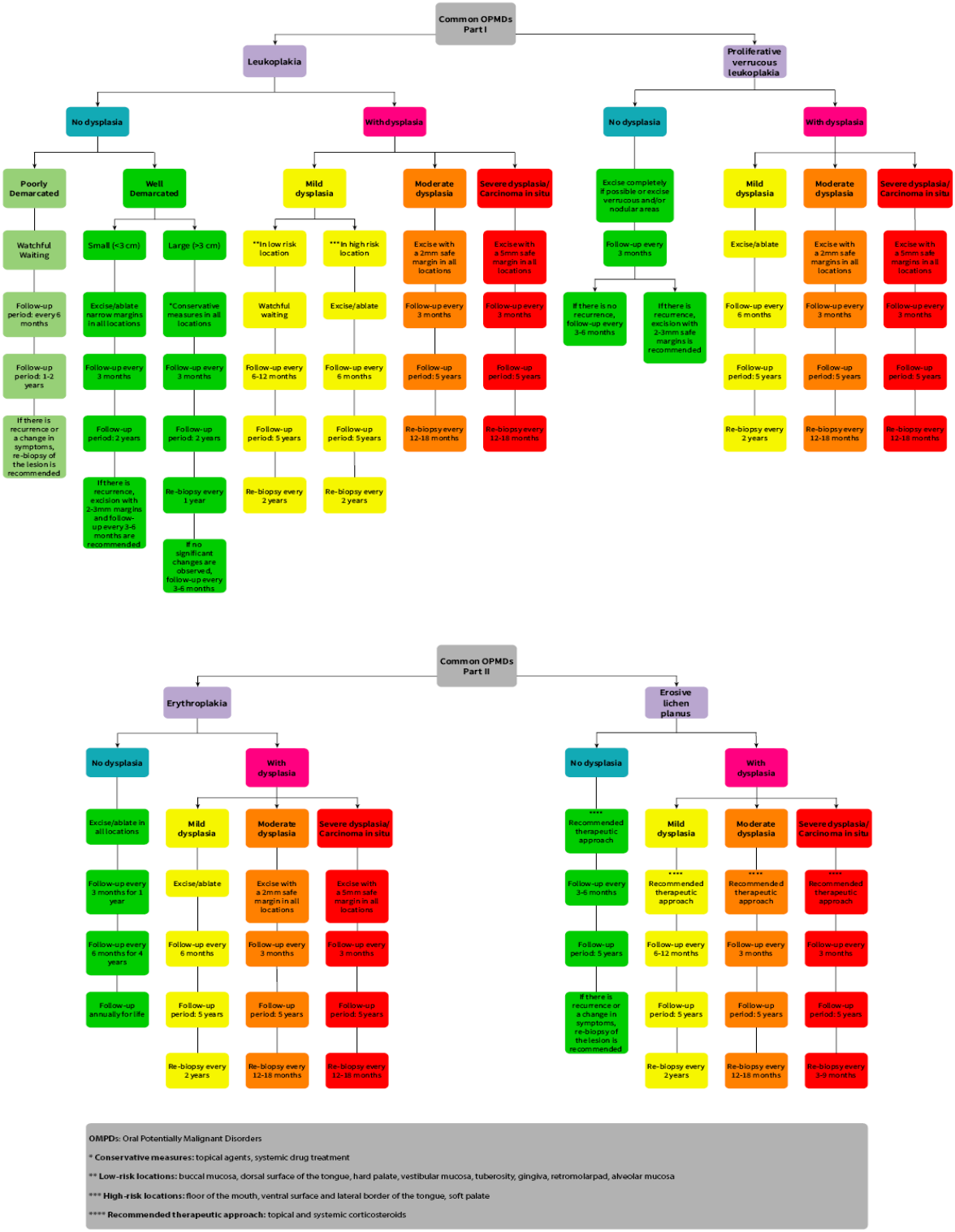

Figure 1. OMPDs Diagram

Author Contribution Statement

Hamed Mortazavi: Responsible for the writing of the manuscript, reviewing the literature, and developing the clinical decision tree. Abolfazl Beigzadeh Jalali: Responsible for the critical review of the manuscript, editing, and final approval of the article.

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Data Availability Statement:

Data sharing is not applicable to this article as no new data were created or analyzed in this study. All data used in this review are publicly available from previously published studies.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Lorini L, Bescós Atín C, Thavaraj S, Müller-Richter U, Alberola Ferranti M, Pamias Romero J, et al. Overview of oral potentially malignant disorders: From risk factors to specific therapies. Cancers (Basel). 2021;13(15):3696. https://doi.org/10.3390/cancers13153696.
2. Warnakulasuriya S. Oral potentially malignant disorders: A comprehensive review on clinical aspects and management. Oral Oncol. 2020;102:104550. https://doi.org/10.1016/j.oraloncology.2019.104550.
3. Jäwert F, Nyman J, Olsson E, Adok C, Helmersson M, Öhman J. Regular clinical follow-up of oral potentially malignant disorders results in improved survival for patients who develop oral cancer. Oral Oncol. 2021;121:105469. https://doi.org/10.1016/j.oraloncology.2021.105469.
4. Mortazavi H, Safi Y, Baharvand M, Rahmani S, Jafari S. Peripheral exophytic oral lesions: a clinical decision tree. Int J Dent. 2017;2017(1):9193831.https://doi.org/10.1155/2017/9193831.
5. Jena A, Sharan J, Ghodke S, Venkatachalapathy A, Barhate U. Oral leukoplakia: Management protocol for primary health-care providers and family physicians. Indian J Community Fam Med. 2019;5:19. https://doi.org/10.4103/IJCFM.IJCFM_9_19.
6. van der Waal I. Potentially malignant disorders of the oral and oropharyngeal mucosa; terminology, classification and present concepts of management. Oral Oncol. 2009;45(4-5):317-23. https://doi.org/10.1016/j.oraloncology.2008.05.016.
7. Kumar A, Cascarini L, McCaul JA, Kerawala CJ, Coombes D, Godden D, et al. How should we manage oral leukoplakia? Br J Oral Maxillofac Surg. 2013;51(5):377-83. https://doi.org/10.1016/j.bjoms.2012.10.018.
8. Staines K, Rogers H. Oral leukoplakia and proliferative verrucous leukoplakia: A review for dental practitioners. Br Dent J. 2017;223(9):655-61. https://doi.org/10.1038/sj.bdj.2017.881.
9. Archibald H, Buryska S, Ondrey FG. An active surveillance program in oral preneoplasia and translational oncology benefit. Laryngoscope Investig Otolaryngol. 2021;6(4):764-72. https://doi.org/10.1002/lio2.612.
10. Mortazavi H, Safi Y, Baharvand M, Jafari S, Anbari F, Rahmani S. Oral White Lesions: An Updated Clinical Diagnostic Decision Tree. Dent J (Basel). 2019;7:15.https://doi.org/ 10.3390/dj7010015.
11. Bedi R, Scully C. Oral potentially malignant disorders. In: Scully C, editor. Tropical oral health. London: BDJ Books; 2018. P. 73–8.
12. van der Waal I. Oral potentially malignant disorders: Is malignant transformation predictable and preventable? Med Oral Patol Oral Cir Bucal. 2014;19(4):e386-90. https://doi.org/10.4317/medoral.20205.
13. Awadallah M, Idle M, Patel K, Kademani D. Management update of potentially premalignant oral epithelial lesions. Oral Surg Oral Med Oral Pathol Oral Radiol. 2018;125(6):628-36. https://doi.org/10.1016/j.oooo.2018.03.010.
14. Chaturvedi AK, Udaltsova N, Engels EA, Katzel JA, Yanik EL, Katki HA, et al. Oral leukoplakia and risk of progression to oral cancer: A population-based cohort study. J Natl Cancer Inst. 2020;112(10):1047-54. https://doi.org/10.1093/jnci/djz238.
15. Chen Q, Dan H, Pan W, Jiang L, Zhou Y, Luo X, et al. Management of oral leukoplakia: A position paper of the society of oral medicine, Chinese stomatological association. Oral Surg Oral Med Oral Pathol Oral Radiol. 2021;132(1):32-43. https://doi.org/10.1016/j.oooo.2021.03.009.
16. Baharvand M, Tehranchi A, Taghavi N, Rahmani S, Sadeghi H, Tabatabaei Tabrizi A, et al. Setting up a registry for oral potentially malignant disorders (opmd). Int J Cancer Manag. 2022;15(3):e115640. https://doi.org/10.5812/ijcm-115640.
17. Hansen LS, Olson JA, Silverman S, Jr. Proliferative verrucous leukoplakia. A long-term study of thirty patients. Oral Surg Oral Med Oral Pathol. 1985;60(3):285-98. https://doi.org/10.1016/0030-4220(85)90313-5.
18. Batsakis JG, Suarez P, El-Naggar AK. Proliferative verrucous leukoplakia and its related lesions. Oral Oncol. 1999 Jul 1;35(4):354-9.https://doi.org/ 10.1016/S1368-8375(99)00007-X.
19. Kumari P, Debta P, Dixit A. Oral potentially malignant disorders: Etiology, pathogenesis, and transformation into oral cancer. Front Pharmacol. 2022;13:825266. https://doi.org/10.3389/fphar.2022.825266.
20. Abadie WM, Partington EJ, Fowler CB, Schmalbach CE. Optimal Management of Proliferative Verrucous Leukoplakia: A Systematic Review of the Literature. Otolaryngol Head Neck Surg. 2015;153(4):504–511. doi:10.1177/0194599815586779.
21. Bagan JV, Jimenez Y, Sanchis JM, Poveda R, Milian MA, Murillo J, Scully C. Proliferative verrucous leukoplakia: high incidence of gingival squamous cell carcinoma. J Oral Pathol Med. 2003;32(7):379-82.https://doi.org/ 10.1034/j.1600-0714.2003.00167.x.
22. JM, Silverman S Jr, Abdel-Salaam M, Daniels TE, Greenspan JS. Association between proliferative verrucous leukoplakia and infection with human papillomavirus type 16. J Oral Pathol Med. 1995;24(5):193–197. doi:10.1111/j.1600-0714.1995.tb01165.x.
23. Bagan JV, Jiménez Y, Murillo J, Poveda R, Díaz JM, Gavaldá C, et al. Epstein-Barr virus in oral proliferative verrucous leukoplakia and squamous cell carcinoma: A preliminary study. Med Oral Patol Oral Cir Bucal. 2008;13(2):E110–E113.
24. RJ, Morton TH Jr, Epstein JB. Proliferative verrucous leukoplakia and its progression to oral carcinoma: a review of the literature. J Oral Pathol Med. 2007;36(5):255–261. doi:10.1111/j.1600-0714.2007.00506.x.
25. DL, Gonçalves JM, Abrantes AA, Grando LJ, Daniel FI. Proliferative verrucous leukoplakia: diagnosis, management and current advances. Braz J Otorhinolaryngol. 2017;83(5):585–593. doi:10.1016/j.bjorl.2016.12.005.
26. Villa A, Woo SB. Leukoplakia-a diagnostic and management algorithm. J Oral Maxillofac Surg. 2017;75(4):723-34. https://doi.org/10.1016/j.joms.2016.10.012.
27. Speight PM, Khurram SA, Kujan O. Oral potentially malignant disorders: Risk of progression to malignancy. Oral Surg Oral Med Oral Pathol Oral Radiol. 2018;125(6):612-27. https://doi.org/10.1016/j.oooo.2017.12.011.
28. Holmstrup P. Oral erythroplakia-what is it? Oral Dis. 2018;24(1-2):138-43. https://doi.org/10.1111/odi.12709.
29. Chiang CP, Yu-Fong Chang J, Wang YP, Wu YH, Lu SY, Sun A. Oral lichen planus - differential diagnoses, serum autoantibodies, hematinic deficiencies, and management. J Formos Med Assoc. 2018;117(9):756-65. https://doi.org/10.1016/j.jfma.2018.01.021.
30. Lorenzo-Pouso AI, Lafuente-Ibáñez de Mendoza I, Pérez-Sayáns M, Pérez-Jardón A, Chamorro-Petronacci CM, Blanco-Carrión A, et al. Critical update, systematic review, and meta-analysis of oral erythroplakia as an oral potentially malignant disorder. J Oral Pathol Med. 2022;51(7):585-93. https://doi.org/10.1111/jop.13304.

31. Lajolo C, Rupe C, Gioco G, Giuliani M, Contaldo M, Salo T, et al. Cost of illness of oral lichen planus: A multicenter university hospital-based outpatient observational study. Clin Oral Investig. 2022;26(5):3865-73. https://doi.org/10.1007/s00784-021-04353-1.
32. Louisy A, Humbert E, Samimi M. Oral lichen planus: an update on diagnosis and management. Am J Clin Dermatol. 2024;25(1):35-53. https://doi.org/10.1007/s40257-023-00814-3.
33. Mortazavi H, Baharvand M, Mehdipour M. Oral potentially malignant disorders: An overview of more than 20 entities. J Dent Res Dent Clin Dent Prospects. 2014;8(1):6-14. https://doi.org/10.5681/joddd.2014.002.
34. Campana F, Lan R, Girard C, Rochefort J, Le Pelletier F, Leroux-Villet C, et al. French guidelines for the management of oral lichen planus (excluding pharmacological therapy). Ann Dermatol Venereol. 2022;149(1):14-27. https://doi.org/10.1016/j.annder.2021.04.003.
35. Diajil A, Robinson CM, Sloan P, Thomson PJ. Clinical outcome following oral potentially malignant disorder treatment: A 100 patient cohort study. Int J Dent. 2013;2013:809248. https://doi.org/10.1155/2013/809248.
36. Dionne KR, Warnakulasuriya S, Zain RB, Cheong SC. Potentially malignant disorders of the oral cavity: Current practice and future directions in the clinic and laboratory. Int J Cancer. 2015;136(3):503-15. https://doi.org/10.1002/ijc.28754.
37. Goodson ML, Sloan P, Robinson CM, Cocks K, Thomson PJ. Oral precursor lesions and malignant transformation–who, where, what, and when?. Br J Oral Maxillofac Surg. 2015;53(9):831-5. https://doi.org/10.1016/j.bjoms.2015.08.268.
38. Wetzel SL, Wollenberg J. Oral potentially malignant disorders. Dent Clin North Am. 2020;64(1):25-37. https://doi.org/10.1016/j.cden.2019.08.004.
39. Pritzker KPH, Darling MR, Hwang JT, Mock D. Oral potentially malignant disorders (OPMD): What is the clinical utility of dysplasia grade? Expert Rev Mol Diagn. 2021;21(3):289-98. https://doi.org/10.1080/14737159.2021.1898949.
40. Virgone A, Badreh S. The 4P: Preventing preneoplasia through patients partnership. Cancers (Basel). 2021;13(17). https://doi.org/10.3390/cancers13174408.
41. Kudva A, Kumar M, John ER, Dhara V. Occurrence of second oral potentially malignant disorder following excision of primary lesion: A prospective study of cases from a tertiary care centre. J Maxillofac Oral Surg. 2023;22(1):252-7. https://doi.org/10.1007/s12663-022-01764-9.