Original article

MedInform

DOI: 10.18044/MEDINFORM.2026132.2423

ISSUE 2, 2026

Oral leukoplakia classification and staging system: A literature review and evaluation of its prognostic value

Samuil Dzhenkov, Konstantin Stamatov, Pavel Stanimirov

Department of Dental, Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Medical University of Sofia, Sofia, Bulgaria.

Department of Maxillofacial Surgery, University Hospital "Alexandrovska", Sofia, Bulgaria.

Abstract

The classification and staging system of oral leukoplakia (OL) is a useful tool for standardizing the staging of oral leukoplakia cases. Studies investigating its prognostic value have shown promising results. In the present study, we investigated the prognostic value of the oral leukoplakia staging system, staging 58 cases of OL out of a total of 221 cases with oral potentially malignant disorders (OPMDs). The results found a trend towards an increasing risk of OL malignancy with higher stages of OL, confirming the statistical significance of the association between stage IV and a higher risk of malignancy. The study confirms the negative influence of the higher stage of OL on the occurrence of malignant transformation, confirming the clinical usefulness within the diagnostic algorithm of OL cases.

Keywords: Leukoplakia, Staging, Classification, Prognostic value, Malignant transformation

Introduction

Oral leukoplakia (OL) is defined as “a predominantly white plaque of questionable risk having excluded other known diseases or disorders that carry no increased risk for cancer” [1]. OL is the most common entity within the group of oral potentially malignant disorders (OPMD), with a reported global prevalence of 4.11%, with the highest rates observed in Asia (7.77%) [2], and with an increasing trend worldwide [3]. OL is characterized by unpredictable biological behavior, with reported annual malignant transformation rates ranging between 0.5% and 1% [4].

The first classification and staging system of OL was introduced in 1994 at a conference in Uppsala, Sweden, with the aim of improving standardization and comparability [5]. The system defines two types of diagnoses:

DOI: 10.18044/MEDINFORM.2026132.2423 ISSUE 2, 2026

- Provisional diagnosis – established on clinical examination, when a white lesion that cannot be attributed to any other disease or condition is observed;
- Definitive diagnosis – established following histopathological examination and confirmation of the diagnosis of OL.

The system includes two clinical criteria - size (L) and clinical appearance (C), and one histological criterion - epithelial dysplasia (P).

According to the clinical size, the following categories are defined:

- L1 – lesion up to 2 cm;
- L2 – lesion between 2 and 4 cm;
- L3 – lesion larger than 4 cm;
- Lx – unspecified size.

Based on the clinical appearance the lesions are categorized as homogeneous or non-homogeneous.

According to the presence and the degree of epithelial dysplasia, the following categories are defined:

- P1 – no epithelial dysplasia;
- P2 – mild epithelial dysplasia;
- P3 – moderate epithelial dysplasia;
- P4 – severe epithelial dysplasia;
- Px – unspecified degree of epithelial dysplasia.

Based on these clinical and histological parameters, the following OL stages are defined:

- Stage 1: any L, C1, P1–P2;
- Stage 2: any L, C2, P1–P2;
- Stage 3: any L, any C, P3–P4 [5].

When applying the staging system, the following principles are observed:

- In cases of uncertainty between two stages of any of the parameters (L, C, or P), the lower stage is assigned.
- In cases of multiple OL lesions, the size of the largest lesion is considered.
- When lesions exhibit different features, the lesion with the highest stage is considered dominant.
- In cases of multiple incisional biopsies, the highest degree of epithelial dysplasia is recorded.
- Anatomical location is reported according to the ICD-DA classification system [5].

In 2002, van der Waal et al. introduced an updated version of the staging system of OL [6]. This version incorporated a C-factor (certainty factor), assessing the level of diagnostic certainty. The C-factor takes into account the clinical and histopathological circumstances, based on which a diagnosis is made. According to the C-factor, four levels of diagnostic certainty are defined:

- C1 – clinical findings from initial examination and palpation, suggesting OL (provisional clinical diagnosis);
- C2 – a lesion, persisting at the follow-up visit 2–4 weeks after elimination of the suspected etiological factors, including mechanical and local dental factors (definitive clinical diagnosis);
- C3 – corresponds to C2, with additionally performed incisional biopsy, which excludes other lesions (histologically confirmed diagnosis);

DOI: 10.18044/MEDINFORM.2026132.2423 ISSUE 2, 2026

- C4 – confirmation of diagnosis of OL following complete excision and histological examination of the whole lesion [6].

Compared to the previous classification system, where an incisional biopsy was sufficient for a definitive diagnosis, the updated version introduces an additional fourth level with a higher level of diagnostic certainty, requiring an excisional biopsy and a complete histopathological assessment of the lesion. The clinical appearance criterion is excluded, leaving only one clinical criterion – size (L) and one histological criterion – epithelial dysplasia (P). A significant change is observed in epithelial dysplasia subdivisions:

- P0 – absence of epithelial dysplasia or uncertain data for mild epithelial dysplasia;
- P1 – presence of epithelial dysplasia;
- Px – lack of data for presence and/or severity of epithelial dysplasia [6].

Additionally, another classification of the severity of epithelial dysplasia has been incorporated using the OIN-oral intraepithelial neoplasia system:

OIN0 – no dysplasia; OIN1 – mild to moderate dysplasia; OIN2 – moderate to severe dysplasia; OIN3 – severe dysplasia/carcinoma in situ [6].

In the updated version, a more detailed stratification into four stages has been proposed:

- Stage I - L1P0;
- Stage II - L2P0;
- Stage III - L3P0 or L1L2P1;
- Stage IV - L3P1 [10].

When analyzing the changes, concerning epithelial dysplasia, several aspects are striking:

1. All lesions with epithelial dysplasia, regardless of their severity, are combined into one category – P1, combining lesions with a different malignant potential in one group.
2. Although it offers an additional distinction through the OIN system, it does not directly participate in the staging of lesions, which limits its clinical application.

In the 2009 modification, the staging system's modifications primarily concerned epithelial dysplasia [4]:

- P0 – no epithelial dysplasia;
- P1 – mild or moderate epithelial dysplasia;
- P2 – severe epithelial dysplasia;
- Px – lack of data regarding presence and/or severity.

The staging system included four stages:

- Stage I – L1P0;
- Stage II – L2P0;
- Stage III – L3P0 or L1–L2P1;
- Stage IV – L3P1, any L with P2.

The latest modification of the staging system was presented in 2022 [7]. It mainly presents modifications, regarding the definition of the L3 category. In addition to lesions with a size > 4 cm, this category also includes multiple lesions with a total size > 4 cm. Increasing evidence supporting the prognostic significance of differentiated dysplasia has led to its incorporation into the staging system [8], [7]. Cases with histologically confirmed differentiated dysplasia are categorized as P2, despite the lack of classical criteria for conventional epithelial dysplasia [7].

DOI: 10.18044/MEDINFORM.2026132.2423 ISSUE 2, 2026

A limited number of studies have been presented in the scientific literature investigating the prognostic value of the staging system in relation to the risk of malignant transformation [7], [9]. The reported data indicates that the severe epithelial dysplasia, the presence of differentiated dysplasia and stage IV cases have a predictive value for higher risk for malignant transformation [7], [9].

Aim

Based on the currently reported data, and in order to evaluate the prognostic value of the staging OL system, we conducted a clinical study on a cohort of patients with histologically confirmed OL, followed up with clinical examinations over time.

Materials And Methods

The study included 221 patients with OPMDs, diagnosed and treated at the Clinic of Maxillofacial Surgery "Alexandrovska" hospital between 2020-2025. The patients underwent a clinical examination, metric measurement of the clinical size of the lesions on the surface, and a biopsy - incisional, punch- or excisional biopsy for the needs of histopathological examination. The histopathological examination was performed at the Clinic of General and Clinical Pathology "Alexandrovska" hospital by experienced specialists at oral and maxillofacial pathology. The study was designed as retrospective, non-experimental, conducted in accordance with ethical and deontological principles. The treatment performed was carried out according to the clinical guidelines for management of patients with OPMDs and without any influence of the study performed on the therapeutic decision-making. Cases with a histologically confirmed malignant transformation at the initial incisional biopsy were excluded from the study. Statistical processing was performed with IBM SPSS 19.0. The inclusion criteria for further OL stage evaluation were as follows:

- Patients diagnosed with OL with a C-factor score 3 or 4;
- Patients with OL for whom sufficient information regarding lesion size and epithelial dysplasia (ED) status was available;
- Patients who attended regular follow-up visits for re-evaluation of OL.

The exclusion criteria were as follows:

- Patients with histological evidence of malignant transformation of OL at the initial visit;
- Patients presenting with white or white–red lesions that were not histologically confirmed as OL after histopathological examination;
- Patients with histologically confirmed OL who did not attend the recommended follow-up visits and for whom lesion re-evaluation was not possible.

DOI: 10.18044/MEDINFORM.2026132.2423 ISSUE 2, 2026

Results

After applying of the inclusion and exclusion criteria, 56 of the 221 patients (26.2%) were eligible for staging according to the Van der Waal OL classification system [10], based on the clinical size and severity of epithelial dysplasia. Stage I cases were 12 (21.40%), Stage II cases – 8 (14.30%), Stage III cases – 22 (39.30%), Stage IV cases – 14 (25.00%).

Table 1 - Distribution of Oral Leukoplakia Cases According to Stage and Malignant Transformation Status (p=0.014)

OL Stage	Parameter	Leukoplakia with malignant transformation during follow-up	Leukoplakia without malignant transformation during follow-up	Total
Stage I	Number	1	11	12
	% of malignant transformation	8.30%	25.00%	21.40%
Stage II	Number	0	8	8
	% of malignant transformation	0.00%	18.20%	14.30%
Stage III	Number	4	18	22
	% of malignant transformation	33.3%	40.90%	39.30%
Stage IV	Number	7	7	14
	% of malignant transformation	58.30%	15.90%	25.00%
Total	Number	12	44	56
	% of malignant transformation	100.00%	100.00%	100.00%

DOI: 10.18044/MEDINFORM.2026132.2423 ISSUE 2, 2026

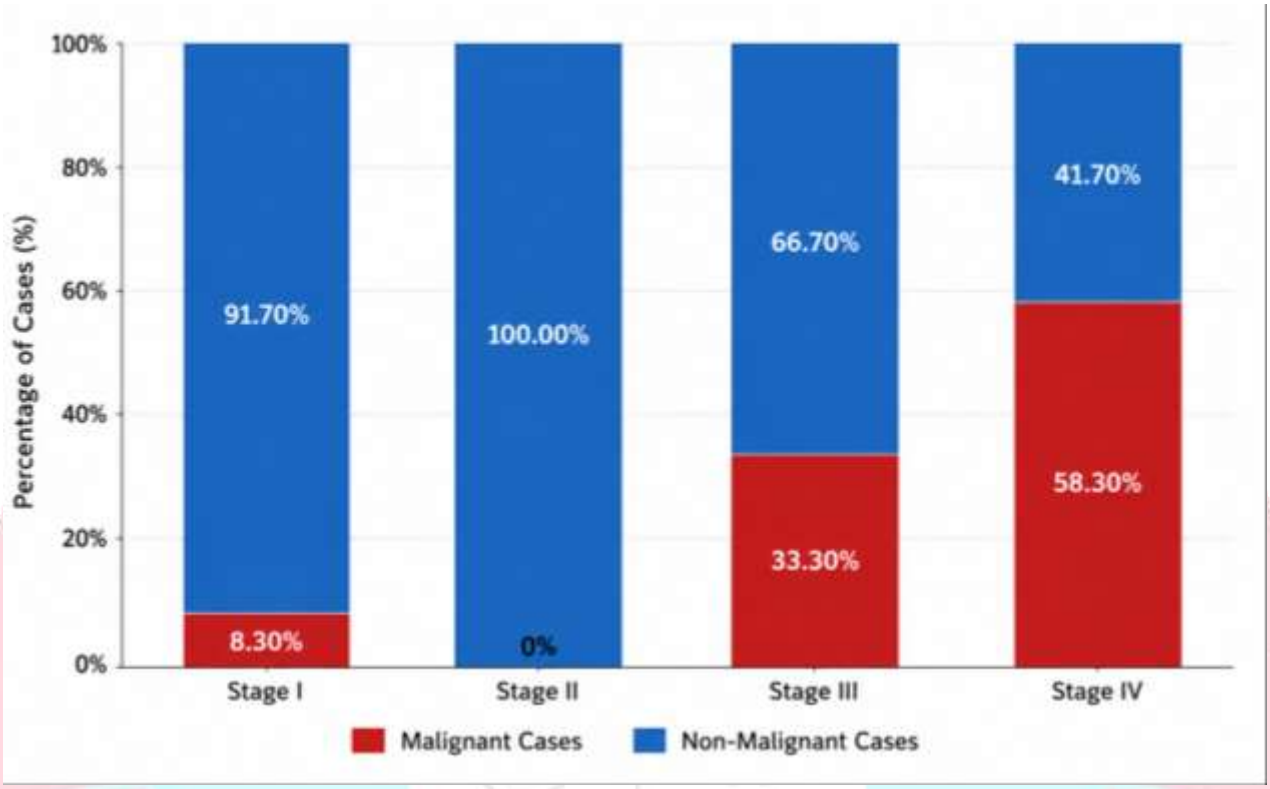

Figure 1 – Distribution of malignant vs non-malignant cases by Stage

In Stage I, malignant transformation was observed in 8.30% of cases; in Stage II – 0%; in Stage III – 33.30%; and in Stage IV – 58.30%. The results found a clear trend towards an increase in the risk of malignant transformation with increasing stage, confirming a statistically significant relationship for stage IV (p=0.014).

Discussion

The classification and staging system proposed in 1994 by Axell et al. is the first attempt to systematize cases of OL [5]. The system includes clinical (size, clinical appearance) and histological (epithelial dysplasia) criteria, thus creating a scale for easy comparability and categorization of OL lesions according to their individual characteristics. The modified version of the system proposed by Van der Waal et al. in 2002 [6] incorporated significant changes. The criterion "clinical appearance" was excluded from the system, while the clinical size and the presence and severity of epithelial dysplasia remained. A C-factor was also implemented in order to increase the diagnostic certainty and created a clear and reproducible approach for the diagnosis, treatment and follow-up of patients with OL. The revised system from 2009 optimized some of the limitations of its previous version, improving the stratification of lesions according to epithelial dysplasia and providing a more precise distribution of cases according to their risk of malignant transformation [4]. The latest modification was presented in 2022 [7]. The system offers further simplification by eliminating some of the elements of previous versions, and facilitates its clinical application. The concept of

DOI: 10.18044/MEDINFORM.2026132.2423 ISSUE 2, 2026

differentiated dysplasia has also been introduced, which helps to more accurately determine the risk of malignant transformation at different stages. However, some issues remain unresolved. Combining lesions with different severity of epithelial dysplasia into a common category may hinder the real biological potential of individual lesions. The concept of differentiated dysplasia is relatively new, its application is not still yet widely recognized in the clinical practice and its predictive value may need further investigation.

The results of our study are consistent with those reported in the literature [7], [9]. The study confirms the predictive value of the staging system, showing a statistically significant association between stage IV OL and an increased risk of malignant transformation (p=0.014). Thus, the staging system is not only a useful statistical and systematizing tool, but also supports the individualized approach in the diagnosis, treatment and follow-up of cases with OL.

Conclusion

The classification and staging system is a useful tool for statistical processing and unified presentation of cases with OL. The assessment of the clinical size of the lesion and epithelial dysplasia, indicated as risk factors for malignancy, helps identifying cases at risk for malignant transformation [10], [11]. The results of our study confirm the literature data on the predictive value of the staging system, confirming a statistically significant association between stage IV and malignant transformation. The introduction of the staging system as a tool in daily clinical practice would help identifying high risk cases and would facilitate the diagnostic and therapeutic approach in the individual clinical case.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

References

1. Warnakulasuriya S., Lodi G. Oral potentially malignant disorders: Proceedings from an expert symposium. Oral Diseases, 2021, 27.8.
2. Mello F., et al. Prevalence of oral potentially malignant disorders: a systematic review and meta-analysis. Journal of Oral Pathology & Medicine, 2018, 47.7: 633-640.
3. Petti S. Pooled estimate of world leukoplakia prevalence: a systematic review. Oral oncology, 2003, 39.8: 770-780
4. Van der Waal I. Potentially malignant disorders of the oral and oropharyngeal mucosa; terminology, classification and present concepts of management. Oral oncology, 2009, 45.4-5: 317-323.
5. Axell T., et al. Oral white lesions with special reference to precancerous and tobacco-related lesions: conclusions of an international symposium held in Uppsala, Sweden, May 18–21 1994. Journal of oral pathology & medicine, 1996, 25.2: 49-54.

DOI: 10.18044/MEDINFORM.2026132.2423 ISSUE 2, 2026

6. Van der Waal I., Axell T. Oral leukoplakia: a proposal for uniform reporting. Oral Oncology, 2002, 38.6: 521-526.
7. Brouns E., et al. Oral leukoplakia classification and staging system with incorporation of differentiated dysplasia. Oral Diseases, 2023, 29.7: 2667-2676.
8. Evren I, et al. Annual malignant transformation rate of oral leukoplakia remains consistent: A long-term follow-up study. Oral Oncology, 2020, 110: 105014.
9. Sun Z.; Gong Y. Huang J. Analysis of relationship between risk factors of malignant transformation of oral leukoplakia and the LSCP system. Chinese Journal of Stomatology, 2001, 36.5: 364-366.
10. Iocca O., et al. Potentially malignant disorders of the oral cavity and oral dysplasia: A systematic review and meta-analysis of malignant transformation rate by subtype. Head & neck, 2020, 42.3: 539-555.
11. Kierce J., et al. Identification of specific clinical risk factors associated with the malignant transformation of oral epithelial dysplasia. Head & Neck, 2021, 43.11: 3552-3561.

Corresponding author:

Samuil Dzhenkov
Department of Dental, Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Medical University of Sofia, Sofia, Bulgaria.
Department of Maxillofacial Surgery, University Hospital "Alexandrovska", Sofia, Bulgaria.
E-mail: s.dzhenkov@fdm.mu-sofia.bg

Dzhenkov S, Stamatov K, Stanimirov P, Oral leukoplakia classification and staging system: A literature review and evaluation of its prognostic value. J. Med. Dent. Pract, 2026; 13(2):2423-2430.