

# Malignant potential of oral lichen planus: A meta-analysis

## Potencial de transformação maligna do líquen plano bucal: uma meta-análise

### Abstract

**Purpose:** Several studies have pointed out the malignant transformation potential of oral lichen planus, yet the findings are controversial. The aim of this study was to evaluate the malignant transformation rate of oral lichen planus.

**Methods:** An electronic search of the literature was performed in the PubMed MEDLINE database using the descriptors "oral lichen planus" and "malignant transformation" from January 1988 to September 2008. Ninety-five articles were retrieved and assessed for inclusion. Only prospective and retrospective studies that reported the oral lichen planus malignant transformation rates were considered, as well as studies that included the number of cases with clear criteria for diagnosis of the disease. From the 24 selected studies, information on clinical presentation and location of the lesions, and subjects' gender and age were recorded.

**Results:** From a total of 11,225 cases of oral lichen planus, 183 (1.63%) developed malignant transformation approximately 6 years after the initial diagnosis. The reticular form was the most common clinical presentation, and the jugal mucosa and tongue were the most frequent locations. However, only the clinical presentation of the disease (atypical forms: atrophic, erosive, "in plaque") and the location of the lesion (tongue) were associated with a higher malignant transformation risk.

**Conclusion:** Epidemiological studies from the last 20 years revealed a malignant transformation rate of 0.27% per year, emphasizing the importance of the clinical follow-up of oral lichen planus patients.

**Key words:** Lichen planus; oral cancer; meta-analysis

### Resumo

**Objetivo:** Diversos estudos relatam o potencial de transformação maligna do líquen plano bucal, mas os achados são controversos. O objetivo deste estudo foi avaliar a taxa de transformação maligna do líquen plano bucal.

**Metodologia:** Realizou-se uma busca eletrônica da literatura na base de dados PubMed MEDLINE usando os descritores "oral lichen planus" e "malignant transformation", de janeiro de 1988 a setembro de 2008. Um total de 95 artigos foi obtido, os quais foram avaliados para inclusão. Foram incluídos somente estudos prospectivos e retrospectivos com relato de taxa de transformação maligna de líquen plano bucal, bem como estudos com o número de casos com critérios de diagnóstico para a doença. Dos 24 estudos selecionados, os dados coletados incluíram apresentação clínica e localização anatômica das lesões e idade e gênero dos sujeitos.

**Resultados:** De um total de 11.225 casos de líquen plano bucal, 183 (1,63%) desenvolveram transformação maligna aproximadamente seis anos após o diagnóstico inicial. A forma reticular foi a apresentação clínica mais frequente e a mucosa jugal e lingual as localizações mais frequentes das lesões. Entretanto, somente a apresentação clínica (formas atípicas: atrófica, erosiva, "em placa") e a localização da lesão (língua) foram associados a maior risco de transformação maligna.

**Conclusão:** Estudos epidemiológicos realizados nos últimos 20 anos revelaram uma taxa de transformação maligna de 0,27% ao ano para o líquen plano bucal, o que enfatiza a importância do acompanhamento clínicos destes pacientes.

**Palavras-chave:** Líquen plano; câncer bucal; meta-análise

**Fernando Augusto C. Garcia de Sousa<sup>a</sup>**  
**Thaís Cachutê Paradella<sup>a</sup>**

<sup>a</sup> Department of Bioscience and Oral Diagnosis, São José dos Campos Dental School, São Paulo State University, São José dos Campos, SP, Brazil

### Correspondence:

Fernando Augusto Cervantes Garcia de Sousa  
Rua Irmã Maria Demétria Kfuri, 196  
Jardim Esplanada II  
São José dos Campos, SP – Brazil  
12.242-500  
E-mail: facgs@uol.com.br

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## Introduction

Lichen planus is a *mucocutaneous* disease, characterized by an unspecific chronic inflammatory process, which leads to an intense destruction of the basal layer of the epithelium. Lichen planus affects from 1% to 2% of the population, being the most frequent dermatological disease that involves the oral cavity. Although relatively common, studies on oral lichen planus are controversial, especially regarding its malignant transformation potential (1).

Currently, the World Health Organization (WHO) classifies oral lichen planus, leukoplakia, and erythroplakia as potentially malignant disorders (2). However, the risk of progression of oral lichen planus to oral carcinoma is lower than the risk of leukoplakia and erythroplakia (2). Nonetheless, the malignant transformation rate of oral lichen planus and the factors that influence this rate are still questionable. For instance, Van der Meij et al. (3) reviewed the literature from 1977 to 1999 and found that only one third of the related cases presented sufficient documented evidences of malignant transformation.

Thus, the purpose of this study was to perform a meta-analysis of the potential of malignant transformation of oral lichen planus, including most prospective and retrospective epidemiological studies published in the last 20 years. The outcome measures included the malignant transformation rate and possible risk factors that influenced this rate.

## Methods

An electronic search of the literature was performed in the PubMed MEDLINE database using the descriptors “oral lichen planus” and “malignant transformation” from January

1988 to September 2008. Ninety-five articles were retrieved and preliminary checked for inclusion and exclusion criteria. Only prospective and retrospective studies that reported the oral lichen planus malignant transformation rate were considered, as well as studies that included the number of cases with clear criteria for diagnosis of oral lichen planus as defined by Eisenberg (4) (Fig. 1). Studies with methodological flaws were excluded. A total of 24 articles were selected for assessment.

The outcome measures were: number of cases, malignant transformation rate, clinical presentation of the disease (reticular, atrophic, erosive, and “in plaque”), localization of the lesions, subjects’ gender and age. Data were analyzed comparatively.

## Results

The 24 selected studies yielded a total of 11,225 oral lichen planus cases, from which 183 (1.63%) had malignant transformation approximately six years after the initial diagnosis (Table 1). The computed mean rate was 0.27% per year.

The most common clinical presentation of oral lichen planus was the reticular form, and the jugal mucosa and tongue were the most frequent locations of the disease, representing more than 70% of the cases. Oral lichen planus also showed strong predisposition for occurrence in females, with a proportion of 5:1 in comparison with males. Regardless gender, most oral lichen planus cases occurred between the 4<sup>th</sup> and 6<sup>th</sup> decades of life. However, only the clinical presentation of the disease (atypical forms: atrophic, erosive, “in plaque”) and the location of the lesions (tongue) were associated with a higher malignant transformation risk.

<p><b>Essential features</b></p> <ul style="list-style-type: none"> <li>• Basal cell liquefaction</li> <li>• Band-like lymphocytic infiltrate at epithelial-stromal junction with obfuscation of basal cell region</li> <li>• Normal epithelial maturation pattern</li> </ul>
<p><b>Other features</b></p> <ul style="list-style-type: none"> <li>• “Candle-dripping”, spindly rete ridges</li> <li>• Parakeratosis</li> <li>• Civatte bodies</li> <li>• Ragged separation of epithelium from lamina propria due to basal cell destruction</li> </ul>
<p><b>Exclusion features</b></p> <ul style="list-style-type: none"> <li>• Nuclear enlargement or hyperchromasia</li> <li>• Prevalent dyskeratosis</li> <li>• Increased numbers of mitotic figures; aberrant mitoses</li> <li>• Blunted, droplet-shaped rete ridges</li> <li>• Absence of basal cell liquefaction</li> <li>• Stratification disarray</li> <li>• Heterogeneous lichenoid infiltrate</li> <li>• Deeper submucosal extension of infiltrate beyond superficial stroma</li> <li>• Perivascular infiltration</li> </ul>

Fig. 1. Histological criteria for oral lichen planus diagnosis according to Eisenberg, 2000 (4).

**Table 1.** Prospective and retrospective articles on the malignant potential transformation of oral lichen planus selected for this study (from January 1988 to September 2008).

Author	Year	Country	Cases of Oral Lichen Planus	Malignant Transformation Rate (%)	Follow-up (years)
Holmstrup et al. (6)	1988	Denmark	611	1.5	7.5
Salem (7)	1989	Saudi Arabia	72	5.6	3.2
Silverman Jr et al. (8)	1991	USA	214	2.3	7.5
Sigurgeirsson & Lindelöf (9)	1991	Sweden	2071	0.4	9.9
Voûte et al. (10)	1992	Holland	113	2.7	7.8
Barnard et al. (11)	1993	United Kingdom	241	3.3	–
Moncarz et al. (12)	1993	Israel	280	2.1	–
Gorsky et al. (13)	1996	Israel	157	1.3	1.5
Markopoulos et al. (14)	1997	Greece	326	1.3	4.8
Silverman & Bahl (15)	1997	USA	95	3.2	6.1
Lo Muzio et al. (16)	1998	Italy	263	4.9	5.3
Rajentheran et al. (17)	1999	United Kingdom	832	0.8	11
Mignogna et al. (18)	2001	Italy	502	3.6	–
Chainani-Wu et al. (19)	2001	USA	229	1.7	–
Eisen (20)	2002	USA	723	0.8	4.5
Lanfranchi-Tizeira et al. (21)	2003	Argentina	719	4.5	–
Van der Meij et al. (22)	2003	Holland	173	1.7	2.7
Rödström et al. (23)	2004	Sweden	1028	0.5	6.8
Xué et al. (24)	2005	China	674	0.6	–
Laeijendecker et al. (25)	2005	Holland	200	1.5	4.3
Bornstein et al.(26)	2006	Switzerland	145	2.8	–
Ingafou et al.(27)	2006	United Kingdom	690	1.9	–
Hsue et al.(28)	2007	Taiwan	143	2.1	1.2
Zhang & Zhou (29)	2007	China	724	2.1	1.8

## Discussion

Since the beginning of the 20<sup>th</sup> century, several studies have drawn attention to the malignant transformation potential of oral lichen planus. Even recently, prospective and retrospective epidemiological studies in several countries suggested that patients with oral lichen planus present a higher risk for developing squamous cell carcinoma than the general population (6-29). However, these studies are criticized due to the lack of clear clinical and histopathological criteria for the diagnosis of the disease. In 1978, Krutchkoff et al. (30) alerted about the lack of data to support the malignant transformation of cases of oral lichen planus described in the literature. Such statement was corroborated by Van der Meij et al. (3), in 1999, which suggested that two thirds of the malignant transformation cases of oral lichen planus were not sufficiently documented to be considered. For these authors, the majority of the cases described in the literature regarding malignant transformation of oral lichen planus may have resulted from a misinterpreted initial diagnosis of the disease.

In fact, the diagnosis of oral lichen planus demands expertise and experience of clinicians and pathologists. For example, Van der Meij & Van der Waal (31) reported no consensus on histopathological diagnosis for 42% of the cases with full agreement on the clinical diagnosis of the disease.

Furthermore, in 50% of the cases with such a consensus there was a lack of clinical agreement. This fact probably occurs because oral lichen planus is likely associated with the differential diagnosis of several other diseases, such as lichenoid reactions, erythematosus lupus, leukoplakia, erythroleukoplakia, and proliferative verrucous leukoplakia (1).

Despite the controversial results in the literature, large variability of incidence across populations, and criticism regarding the inclusion criteria used in most studies, it seems impossible to deny the malignant transformation potential of oral lichen planus. Since 2005 the WHO classifies oral lichen planus as a potentially malignant disorder. The present study reviewed 24 articles of oral lichen planus cases (6-30) and revealed an annual malignant transformation rate of 0.27%, which is 27 times higher than the incidence of oral cancer in Brazil as estimated by the National Cancer Institute (INCA) for the male gender in 2008. It is important to mention that such estimation does not consider risk habits such as alcohol abuse and/or tabagism, and some authors (3,30) did not exclude patients with such habits in the cases of malignant transformation. Nonetheless, the literature does not relate alcohol abuse and/or tabagism to an increase in the malignant transformation rate of oral lichen planus (6,7,13). Conversely, the clinical presentation of the disease seems to be relevant for potential malignancy. The atypical forms

(atrophic, erosive, "in plaque") had higher risk for malignant transformation than the reticular form (8,11,14,16,20-22,24), which is fortunately the most common clinical presentation. Tongue lesions also had higher risk of malignancy in comparison with other locations (11,16,21).

Finally, it should be emphasized the importance of long-term follow-up of patients with oral lichen planus, especially those who present atypical forms of the disease, which is a consensus of all studies (6-29). In addition, another aspect that should be considered is the lack of epidemiological studies on the malignant potential of oral lichen planus in

Brazil, which makes the national casuistic impossible. Other limitation of the present study is the search of articles only in PubMed MEDLINE as some relevant papers may have been indexed in other databases.

## Conclusions

Despite the great controversy, epidemiological studies in the last 20 years revealed a malignant transformation rate of oral lichen planus of 0.27% per year. This reinforces the importance of clinical follow-up of patients with this disease.

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