Malignant transformation in oral lichen planus and lichenoid lesions: a 14-year longitudinal retrospective cohort study of 829 patients in New Zealand

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Objective. The aim of this study was to identify the rate of malignant transformation in a longitudinal cohort of patients with oral lichen planus and oral lichenoid lesion (OLP/OLL) and to assess the associations between clinicopathologic aspects and malignant transformation.

Study Design. Data were taken from the records of 829 patients histologically diagnosed with OLP/OLL in the years 2005 to 2018.

Results. Of the study patients, 548 (66.1%) were females and 281 (33.9%) were males. The average age at diagnosis was 57.3 years. The hyperplastic type was the most frequent (58.5%). Most patients had multiple sites of involvement, with the buccal mucosa being the most frequent site of biopsy. Oral epithelial dysplasia developed in 5 (0.6%) patients with a previous histologic diagnosis of OLP/OLL and developed oral squamous cell carcinoma (OSCC) in 23 patients (2.8%) during the follow-up period. The atrophic/ulcerative forms are 25.8 times more likely to progress to OSCC compared with the hyperplastic types (hazard ratio [HR] 25.8; $P < .05$). The HR increases by 5% with every year of age (HR 1.05; 95% confidence interval; $P < .05$).

Conclusions. In our study, oral epithelial dysplasia developed in less than 1% of patients with OLP/OLL, and OSCC in 2.8%during the follow-up period. The atrophic/ulcerative forms are 25.8 times more likely to progress to OSCC compared with the hyperplastic types. The HR increases by 5% with every year of age. (Oral Surg Oral Med Oral Pathol Oral Radiol 2020;130:411−418)

The association between oral lichen planus (OLP) and oral cancer has been debated for decades. The World Health Organization (WHO) defined OLP as a potentially malignant disorder, associated with a small increased risk of oral cancer.[1] Recent systematic reviews have suggested that the erosive type, female gender, and tongue site are risk factors for malignant transformation.[2,3] The modified 2003 WHO diagnostic criteria suggested that oral epithelial dysplasia should not be present for a diagnosis of OLP, in an attempt to reduce the controversy relating to the so-called oral lichenoid dysplasia (OLD), a term proposed by Krutchkoff and Eisenberg in 1985 to describe lesions with the histologic features of both OLP and oral epithelial dysplasia.[4-6] Lichenoid dysplasia has a significantly higher risk of malignant transformation compared with OLP/oral lichenoid lesion (OLL).[4,7] The rate of malignant transformation varies from 0% to 5% in both retrospective and prospective cohort studies.[8-10] However, when lichenoid dysplasia is excluded, the malignant transformation rate can be as low as 0.9%.[7,11] The term *OLL* and the diagnosis have been discussed for many years.[12,13] The exact etiology of OLL remains unknown. OLL may present as a unilateral lesion, rather than bilateral lesions, which can usually be seen in OLP.[13] OLL may be associated with the use of several dental materials and medications, such as antihypertensives, nonsteroidal anti-inflammatory drugs, anticonvulsants, and antimalarials.[14] The histopathologic features of OLL are similar to those of OLP. However, some studies have suggested that OLL may have a higher number of apoptotic keratinocytes, more diffused mixture of plasma and eosinophil cells, and deeper inflammatory infiltration compared with OLP.[13,15]

There are no reports on the incidence rate of malignant transformation in OLP/OLL in a New Zealand population. The aim of this study was to identify the rate of malignant transformation in a retrospective study of a cohort of patients histologically diagnosed with OLP/OLL to assess the associations between malignant transformation and clinicopathologic characteristics.

MATERIAL AND METHODS

The study was approved by the Human Research Ethics Committee, University of Otago, Dunedin, New Zealand (HD 18/075). This retrospective study included all patients with histopathologic a diagnosis of OLP or

Statement of Clinical Relevance

Atrophic/ulcerative oral lichen planus is 25.8 times more likely to progress to oral cancer compared with the hyperplastic forms. The expected hazard ratio increases by 5% with every year of age.

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OLL, provided by registered oral pathologists at the Oral Pathology Centre, University of Otago (Dunedin, New Zealand), in the years 2005 to 2018. Data collected from the biopsy request forms included gender, age at the time of the initial biopsy, clinical characteristics of the lesion (appearance and sites of oral involvement), and histologic diagnosis. This information was anonymized and recorded on an Excel spreadsheet. Patients who did not fulfill the clinical and histologic criteria for OLP and OLL were excluded from the analysis.

The diagnosis was made as OLP and related lesions, according to the modified 2003 WHO criteria.[4,16,17] According to these criteria, the histologic features to note are the presence of a well-defined, band-like zone of inflammatory cells in the superficial connective tissue; signs of liquefaction degeneration in the basal cell layer; and absence of oral epithelial dysplasia. For the present study, any case with histologically identified features of OLP but also no dysplasia (the so-called OLD) was excluded. In addition, the oral pathologists referred to patient notes and clinical photographs and, if necessary, discussed the case with the clinician to confirm various clinical features before a histologic diagnosis was made. Nevertheless, the diagnostic laboratory reported the diagnosis as one entity, OLP or OLL, with the expectation that the clinician would be responsible for excluding a lichenoid reaction. Clinically, reticular, papular, and plaque-like lesions were considered to be the hyperplastic type, and the atrophic, erosive, ulcerative, or bullous lesions were considered to be the atrophic/ulcerative type.[7,9,18,19] For a clinical diagnosis of OLP, the following criteria had to be met:

1. Presence of bilateral, more or less symmetric lesions
2. Presence of a lace-like network of slightly raised white lines (reticular pattern)
3. Erosive, atrophic, bulbous, and plaque-type lesions, which were only accepted as a subtype in the presence of reticular lesions elsewhere in the oral mucosa

For the purpose of this study, OLP, OLL, or oral lichenoid reaction were considered to be one entity and included the following scenarios:

1. Clinically typical of OLP but histopathologically only compatible with OLP
2. Histopathologically typical of OLP but clinically only compatible with OLP
3. Clinically compatible with OLP and histopathologically compatible with OLP[4]
4. All lesions with initial biopsy showing OLP/OLL and concurrent epithelial dysplasia (i.e., OLD excluded).

After this baseline sample was collected, the medical and dental records, available at the Faculty of Dentistry, University of Otago, of every patient diagnosed with OLP or OLL between 2005 and 2018 were checked prospectively to determine whether or not they were subsequently diagnosed with oral squamous cell carcinoma (OSCC) or oral epithelial dysplasia. Furthermore, as an additional check, all cases of OSCC or oral epithelial dysplasia diagnosed in the Oral Pathology Centre at the University of Otago between 2005 and 2018 were checked to see whether or not there was a previous diagnosis of OLP or OLL.

Statistical analysis of the data was performed by using Stata/IC version 15.0 (StataCorp, College Station, TX). Continuous variables were expressed as mean ± standard deviation (SD) if normally distributed or as median and quartiles if they had a skewed distribution. Categorical variables were described as counts and percentages. The Cox proportional hazard regression model was used to estimate hazard ratio (HR), and a multivariable model was used to adjust the potential confounders, including patient age and gender and lesion location and clinical appearance. A P value of less than 0.05 was considered to indicate statistical significance.

RESULTS

Data from a total of 829 patients with OLP/OLL were analyzed retrospectively; 548 (66.1%) were females, and 281 (33.9%) were males, giving a female-to-male ratio 2.0:1 (Figure 1). The youngest patient was 9 years old, and the oldest was 90 years old. The average age at diagnosis of OLP/OLL was 57.3 years. The mean age at diagnosis was 55.1 years for males and 58.5 years for females. The hyperplastic type of OLP/OLL was observed in 485 patients (58.5%), of which 184 were males and 301 were females. The mean age at diagnosis of the hyperplastic type was 54.2 years and 57.1 years for males and females, respectively (Table I). The atrophic/ulcerative forms of OLP were diagnosed in 344 patients (41.5%), including 97 males and 247 females. The mean age at diagnosis of the atrophic/ulcerative form was 56.7 years and 60 years for males and females, respectively. Most patients had multiple oral lesions. The buccal mucosa was the most common site of biopsy (56.3%), followed by the gingivae (18.8%) and the tongue (18.7%). Biopsy of lesions on the floor of the mouth and on the soft palate was uncommon (Figure 2).

Of the 829 patients, 5 patients (0.6%) previously diagnosed histologically with OLP/OLL developed an oral mucosal dysplastic lesion, and 23 patients (2.8%) developed OSCC during the follow-up period (Table II). None of the 23 patients reported smoking and heavy alcohol consumption. The mean duration of

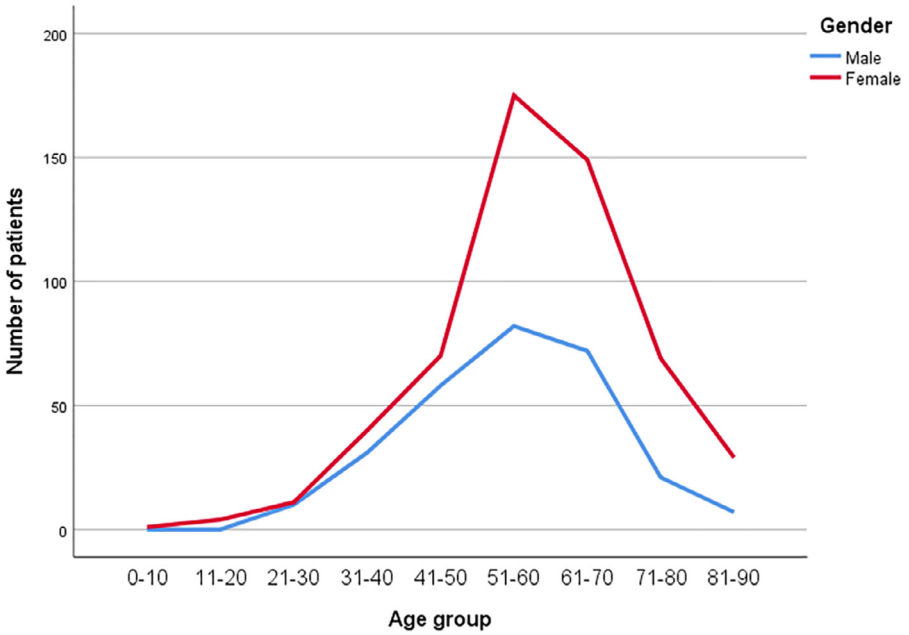

Fig. 1. Age and gender of 829 patients with oral lichenoid lesion (OLL)/oral lichen planus (OLP).

malignant transformation after the first biopsy was 4.3 ± 2.2 years. The mean duration of oral mucosal dysplasia transformation was 5.8 ± 2.5 years. A Cox proportional hazards model was used to estimate the HR and 95% confidence interval (CI) for malignant transformation among patients with OLP/OLL (Table III). The Cox proportional hazards model showed a 5.2-fold increase in hazard (malignant transformation) in females compared with males, and it was statistically significant (HR 5.2; 95% CI 1.2−22.3). However, after being adjusted for different sites of biopsy, clinical appearance of the lesion, and patient age, no statistical significance was found. The atrophic/ulcerative forms were 32.2 times more likely to progress to OSCC compared with the hyperplastic types (HR 32.2; 95% CI 4.3−239.3; $P < .05$). After adjustment for patient gender and age and lesion location, the association of malignant transformation with the atrophic/ulcerative forms was still statistically significant (HR 25.8; 95% CI 3.4−191.8; $P < .01$). The HR increased by 5% with every year of age (HR 1.05; 95% CI 1.01−1.09; $P < .01$), and it was statistically significant. Although the floor of the mouth and the tongue had HRs of 2.8 and 1.3, respectively, they were not statistically significant in both the adjusted and unadjusted models.

DISCUSSION

This study analyzed patients with OLP/OLL and the association with malignant transformation. Our study had several limitations. First, we did not separate OLP

Table I. Clinical characteristics of OLP/OLL lesions

	Current/ ex-smoker N (%)	*Alcohol consumption N (%)*	*Hepatitis C infection N (%)*	*Age at the OLP/OLL diagnosis (Mean ± SD)*	*Types of OLP/OLL N (%)*
Male	60 (7.2%)	86 (10%)	2 (0.2%)	55.1 ± 13.0	281 (33.9%)
Hyperplastic type	33 (4%)	57 (7%)	0 (0%)	54.2 ± 13.1	184 (22.2%)
Atrophic/Ulcerative form	27 (3.2%)	29 (3%)	2 (0.2%)	56.7 ± 12.7	97 (11.7%)
Female	56 (6.8%)	110 (13.3%)	0 (0%)	58.5 ± 13.3	548 (66.1%)
Hyperplastic type	34 (4.1%)	64 (8%)	0 (0%)	57.1 ± 13.0	301 (36.3%)
Atrophic/Ulcerative form	22 (2.7%)	46 (6%)	0 (0%)	60.0 ± 13.4	247 (30%)
Total	116 (14%)	196 (24%)	2 (0.2%)	57.3 ± 13.3	829 (100%)
Hyperplastic type	54 (6.5%)	121 (15%)	0 (0%)	56.0 ± 13.2	485 (58.5%)
Atrophic/Ulcerative form	62 (7.5%)	75 (9%)	2 (0.2%)	59.1 ± 13.3	344 (41.5%)

OLL, oral lichenoid lesion; *OLP,* oral lichen planus; *SD,* standard deviation.

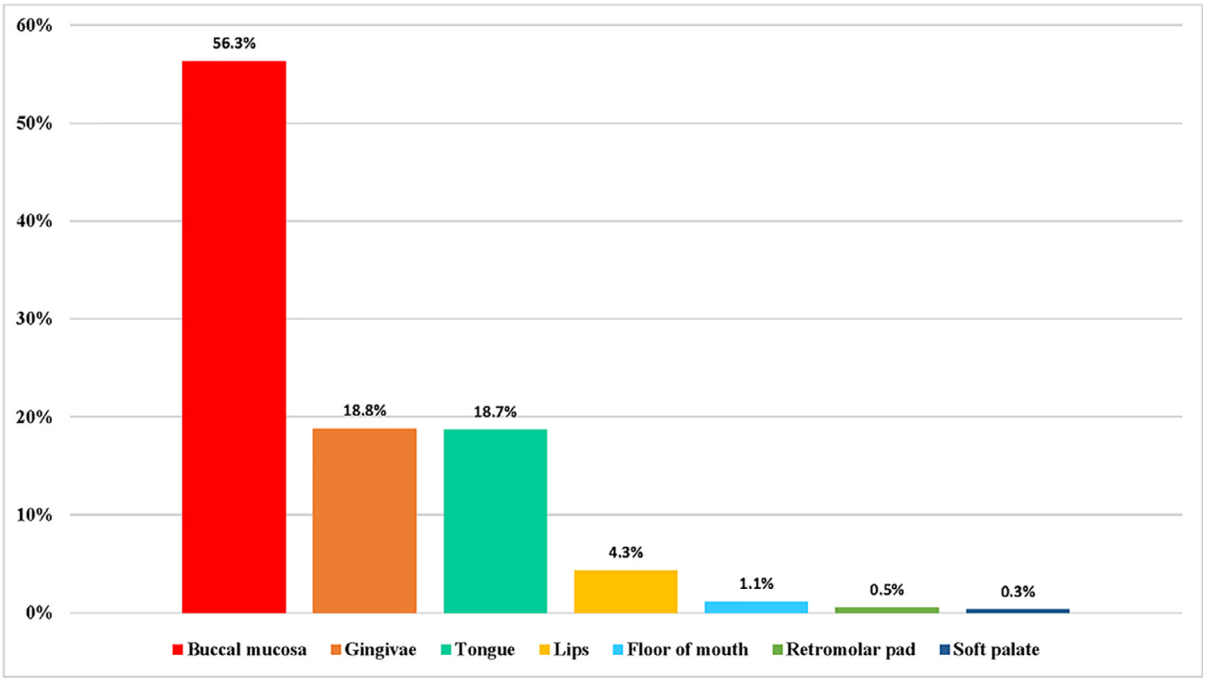

Fig. 2. Different sites of biopsy.

and OLL in our study. A recent systemic review had stated that the malignant transformation rates of OLP and OLL were 1.14% and 1.88%, respectively.[3,7] Second, we excluded lesions histologically showing dysplasia (*i.e.,* lichenoid dysplasia) because it is not clear whether lichenoid dysplasia is a distinct histopathologic entity, whether oral epithelial dysplasia shows OLP-like inflammatory features, or whether

Table II. Clinical details of patients with malignant transformation

Patient No.	*Age at oral cancer onset (year)*	*Age at OLP/OLL onset (year)*	*Duration of malignant transformation (year)*	*Clinical appearance of OLP/OLL*	*Gender*	*Tumor Location*	*Current/ Ex-smoker*	*Alcohol consumption*
1	82	77	5	Atrophic/Ulcerative form	F	Gingivae	No	No
2	81	78	3	Atrophic/Ulcerative form	F	Tongue	No	Once to twice/week
3	81	76	5	Atrophic/Ulcerative form	F	Buccal mucosa	No	No
4	80	73	7	Atrophic/Ulcerative form	F	Gingivae	No	No
5	79	73	6	Atrophic/Ulcerative form	F	Gingivae	No	Once to twice/week
6	79	73	6	Atrophic/Ulcerative form	F	Tongue	No	No
7.	75	74	1	Atrophic/Ulcerative form	F	Buccal mucosa	No	Once to twice/week
8	72	69	6	Atrophic/Ulcerative form	F	Buccal mucosa	No	No
9	70	67	3	Atrophic/Ulcerative form	F	Tongue	No	No
10	69	67	2	Atrophic/Ulcerative form	F	Gingivae	No	No
11	68	57	11	Atrophic/Ulcerative form	F	Tongue	No	Once to twice/week
12	64	59	5	Atrophic/Ulcerative form	F	Floor of mouth	No	No
13	64	63	1	Atrophic/Ulcerative form	M	Buccal mucosa	No	No
14	62	59	3	Atrophic/Ulcerative form	F	Tongue	No	No
15	62	57	5	Atrophic/Ulcerative form	F	Buccal mucosa	No	No
16	62	58	4	Atrophic/Ulcerative form	F	Tongue	No	No
17	60	59	1	Atrophic/Ulcerative form	F	Tongue	No	No
18	60	57	3	Atrophic/Ulcerative form	F	Tongue	No	No
19	58	53	5	Atrophic/Ulcerative form	M	Gingivae	No	Once to twice/week
20	58	55	3	Hyperplastic type	F	Gingivae	No	Once to twice/week
21	57	53	4	Atrophic/Ulcerative form	F	Floor of mouth	No	No
22	56	52	4	Atrophic/Ulcerative form	F	Gingivae	No	No
23	55	49	6	Atrophic/Ulcerative form	F	Tongue	No	No

OLL, oral lichenoid lesion; *OLP,* oral lichen planus.

Table III. Cox proportional hazards model

	Hazard ratio	*Standard error*	*Z value*	*P value*	*95% confidence interval*
Age (adjusted)	1.05	0.02	3.04	.00*	1.01−1.09
Gender (adjusted)	3.78	2.81	1.79	.07	0.88−16.22
Biopsy site (adjusted)	1.39	0.25	1.87	.06	0.98−1.97
Clinical appearance (adjusted)	25.77	26.39	3.17	.00*	3.4−191.86

*$P < .05$ considered significant.

OLP lesions gain dysplastic features. Third, some of our patients' medical records had insufficient details. Finally, our results were dependent on the site of biopsy, and we did not tabulate patients with concurrent multiple sites of involvement. However, this is the first study to show that there was a 5% increase in the expected hazard relating to a 1-year increase in age (i.e., the expected hazard was 0.05 times higher in a patient who was 1 year older than another), holding patient gender and the lesion location and clinical appearance constant. The atrophic/ulcerative forms were 25.8 times more likely to progress to OSCC compared with the hyperplastic forms. These results imply that the atrophic/ulcerative forms OLP/OLL should be managed more aggressively because a cumulative effect could significantly increase the rate of malignant transformation year over year. In general, the results of the present New Zealand study were compatible with those of previous studies (Table IV). Although it is clearly reported in the international literature that OLP/OLL does occur in all age groups, our study confirmed that in New Zealand, middle-aged females were most commonly affected.[18,20,21] The age at diagnosis of OLP/OLL was usually between 50 and 70 years, with an incidence peak in both males and females in the age group 51 to 60 years. In agreement with other similar studies, the majority of our patients with OLP/OLL were females (F:M ratio = 2:1), with an average age of 57 years at the time of diagnosis. Only 1 child and 3 teenagers were present in this study, perhaps reflecting the rarity of OLP/OLL in individuals younger than 20 years of age.[22-24]

As expected clinically, a mixture of white and red lesions with a bilateral symmetric pattern were seen in these patients. The hyperplastic type, with a reticular pattern, white papules, and plaque-like (white) lesions, represented more than half the patients (58.5%). This proportion of patients was less compared with that reported in a previous series; in Chinese,[25] Swedish,[26] Italian,[19] and American[27] studies, the atrophic/ulcerative forms were more predominant.

One of the most important issues concerning OLP/OLL is its potential for malignant transformation. Although the WHO has categorized OLP as a potentially malignant disorder, the risk of malignant transformation has been a subject of debate.[6] The overall malignant transformation rate is estimated to be 0% to 5%, with the highest rate noted with the atrophic/ulcerative forms (see Table III). Although there are no known histopathologic predictive factors of malignant transformation of OLP, the clinical presence of the atrophic/ulcerative forms is known to indicate a greater predisposition to cancer development.[2,28] It has been suggested that the atrophic/ulcerative forms predispose the oral mucosa to damage from carcinogenic agents, such as alcohol and tobacco, and/or to infections, such as with *Candida albicans*.[28] However, not all patients in whom cancer developed were tobacco smokers or drank alcohol daily, suggesting that malignant transformation may be part of the natural evolution of OLP or is related to other unknown factors. We found that malignant transformation was uncommon but still a significant risk. Of the patients in our study, OSCC developed in 23 (2.8%), as reported by other studies as well.[9,10,18-21,25,27,29-48]

In our study, we confirmed the findings of other studies which demonstrated that the atrophic/ulcerative forms had a higher malignant transformation rate compared with the hyperplastic forms.[25-28,47,49] It has been suggested that chronic inflammation might play an important role in the progression of OLP/OLL lesions to OSCC.[50] Current research has suggested that cytokines released as part of chronic inflammatory processes might participate in malignant transformation.[51-53] Cytokines, such as interleukin-6 (IL-6), IL-17, and IL-23 have been shown to contribute to tumor progression, and tumor necrosis factor (TNF)-α/-β and IL-6 promote cancer cells to grow and survive.[54] Multiple cells that expressed IL-17 were found in both OLP and OSCC, indicating that IL-17 might play a role in the pathogenesis of OSCC.[55,56] In addition, elevated levels of salivary TNF-α, IL-6, and IL-10 were found in the saliva of patients with OLP/OLL with high-grade dysplasia and OSCC.[51,57-60] Long-standing chronic inflammation is associated with increased risk of malignant transformation in some conditions, such as inflammatory bowel diseases.[61] Chronic inflammation induces constant healing and repair, thereby improving cellular survival, and is associated with the release of numerous cytokines and other molecules into the local environment.[62] Potentially, genetic predisposition of basal keratinocytes, in

Table IV. Studies on OLP/OLL malignant transformation published over last 20 years

Study	*Year*	*Country*	*OLP/OLL cases*	*Mean Age*	*F:M*	*Most common clinical form*	*Most common sites*	*Malignant Transformation*
Shearston et al.[7]	2019	Australia	206 OLP 31 OLL 41 OLD	60		N/A	Buccal, tongue, gingiva	1 (0.49%) OLP 0 (0%) OLL 3 (6.81%) OLD
Gonzalez-Mole et al.[10]	2017	Spain	102 OLP 81 OLL	58	2.9:1	Reticular	Buccal, mucosa, tongue, gingiva	4 (3.9%)
Lauritano et al.[18]	2016	Italy	87 OLP	59.2	1.8:1	Hyperplastic type	Buccal mucosa, tongue, gingiva	1 (1.2%)
Casparis et al.[9]	2015	Switzerland	381 OLP 102 OLL	58	1.6:1	Hyperplastic type	Buccal mucosa, tongue, floor of mouth	5 (5%) OLP 5 (1.3%) OLL
Radochova et al.[29]	2014	Czech Rep	171 OLP	55.2	2.1:1	Reticular form	Buccal mucosa, tongue, gingiva	0 (0%)
Budimir et al.[30]	2014	Croatia	563 OLP	58	2.7:1	Reticular form	Buccal mucosa, tongue, gingiva	4 (0.7%)
Wang et al.[34]	2014	Taiwan	381 OLP	51.2	1.5:1	N/A	Buccal mucosa, tongue, gingiva	2 (0.52%)
Gumru et al.[31]	2013	Turkey	370 OLP	49.8	2.3:1	Hyperplastic type	Buccal mucosa, tongue, gingiva	1 (0.27%)
Bardellini et al.[20]	2013	Italy	204 OLP	54.5	3.9:1	Reticular form	Buccal mucosa, tongue, gingiva	2 (0.98%)
Tovaru et al.[33]	2013	Romania	633 OLP	52	3.5:1	White type	Buccal mucosa, tongue, gingiva	6 (0.95%)
Shen et al.[21]	2012	China	518 OLP	46.3	2.1:1	Reticular	Buccal mucosa, tongue, gingiva	5 (0.96%)
Kaplan et al.[40]	2012	Israel	171 OLP	59.1	2.4:1	Hyperkeratotic	Buccal mucosa, tongue, gingiva	6 (3.5%)
Bombeccari et al.[41]	2011	Italy	327 OLP	57.7	2.3:1	N/A	N/A	8 (2.4%)
Bermejo-Fenoll et al.[32]	2010	Spain	550 OLP	56.4	3.2:1	Reticular	Buccal mucosa, tongue, gingiva	5 (0.9%)
Torrente-Castells et al.[38]	2010	Spain	65 OLP	59	1.5:1	Hyperkeratotic	Buccal mucosa, tongue, gingiva	2 (1.5%)
Pakfetrat et al.[35]	2009	Iran	420 OLP	41.6	1.8:1	Reticular	Buccal mucosa, tongue, gingiva	3 (0.7%)
Fang et al.[25]	2009	China	2119 OLP	52	N/A	Erosive	N/A	23 (1.1%)
Carbone et al.[42]	2009	Netherlands	808 OLP	61	1.5:1	Reticular and plaque	Buccal mucosa, tongue, gingiva	15 (1.85%)
Van der Meij et al.[45]	2007	Netherlands	67 OLP 125 OLL	55.9	2:1	N/A	N/A	0 (0%) OLP 4 (3.2%) OLL
Ingafou et al.[36]	2006	England	690 OLP	52	1.75:1	Reticular	Buccal mucosa, tongue, gingiva	13 (1.9%)
Bornstein et al.[43]	2006	Switzerland	145 OLP	56.3	2.1:1	Reticular and papular	Buccal mucosa, tongue, gingiva	4 (2.7%)
Xue et al.[37]	2005	China	674 OLP	50.4	1.93:1	Reticular	Buccal mucosa, lip, gingiva	4 (0.6%)
Laeijendecker et al.[44]	2005	Netherlands	200 OLP	53	1.6:1	hyperkeratotic	Buccal mucosa, tongue, gingiva	3 (1.5%)
Rodstrom et al.[26]	2004	Sweden	1028 OLP	55	1.9:1	Erythematous or ulcerative	Buccal mucosa, floor of mouth, gingiva	5 (0.5%)
Gandolfo et al.[46]	2004	Italy	402 OLP	N/A	N/A	N/A	N/A	9 (2.2%)
Lanfranchi et al.[47]	2003	Argentina	719 OLP	54.5	2.0:1	Keratotic (Plaque-like)	Tongue	32 (4.5%)
Eisen[39]	2002	USA	723 OLP	52	3:1	Reticular	Buccal mucosa, tongue, gingiva	6 (0.8%)
Chainani-Wu et al.[27]	2001	USA	229 OLP	55	2.0:1	Erosive	N/A	4 (1.7%)
Mignogna et al.[48]	2001	Italy	502 OLP	55.4	1.6:1	N/A	N/A	18 (3.7%)
Rossi & Colasanto[19]	2000	Italy	100 OLP	58.6	1.3:1	Atrophic-erosive	Buccal mucosa, tongue, Gingiva	N/A

(*continued*)

Table IV. Continued

Study	*Year*	*Country*	*OLP/OLL cases*	*Mean Age*	*F:M*	*Most common clinical form*	*Most common sites*	*Malignant Transformation*
Present study	2019	New Zealand	829 OLP/OLL	57	3:1	Hyperplastic	Buccal mucosa, tongue, gingiva	23 (2.8%)

OLD, oral lichenoid dysplasia; *OLL,* oral lichenoid lesion; *OLP,* oral lichen planus.

conjunction with ongoing chronic inflammation, might lead to the initiation of carcinogenesis.

CONCLUSIONS

The present study has provided information about the epidemiologic and clinical characteristics of patients with OLP/OLL in New Zealand and about the rate of malignant transformation in this cohort. The atrophic/ulcerative clinical forms were more likely to progress to OSCC compared with the hyperplastic types. The malignant transformation rate in the present study was 2.8%, with a 5% increase in the HR with every year of age. The mechanisms that are related to malignant transformation in OLP are still unclear but are likely linked to persistent chronic inflammation. It is important that patients with OLP/OLL, especially those with the atrophic/ulcerative type, be monitored through their entire life by clinicians so that any concerning clinical changes can be observed and investigated as early as possible.

REFERENCES

1. Pindborg JJ, Wahi PN. *Histological Typing of Cancer and Precancer of the Oral Mucosa*. 2nd ed. New York: Springer; 1997.
2. Giuliani M, Troiano G, Cordaro M, et al. Rate of malignant transformation of oral lichen planus: a systematic review. *Oral Dis*. 2019;25:693-709.
3. Gonzalez-Moles MA, Ruiz-Avila I, Gonzalez-Ruiz L, Ayen A, Gil-Montoya JA, Ramos-Garcia P. Malignant transformation risk of oral lichen planus: a systematic review and comprehensive meta-analysis. *Oral Oncol*. 2019;96:121-130.
4. van der Meij EH, van der Waal I. Lack of clinicopathologic correlation in the diagnosis of oral lichen planus based on the presently available diagnostic criteria and suggestions for modifications. *J Oral Pathol Med*. 2003;32:507-512.
5. Krutchkoff DJ, Eisenberg E. Lichenoid dysplasia: a distinct histopathologic entity. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1985;60:308-315.
6. Kramer IR, Lucas RB, Pindborg JJ, Sobin LH. Definition of leukoplakia and related lesions: an aid to studies on oral precancer. *Oral Surg Oral Med Oral Pathol*. 1978;46:518-539.
7. Shearston K, Fateh B, Tai S, Hove D, Farah CS. Oral lichenoid dysplasia and not oral lichen planus undergoes malignant transformation at high rates. *J Oral Pathol Med*. 2019;48:538-545.
8. Warnakulasuriya S, Kovacevic T, Madden P, et al. Factors predicting malignant transformation in oral potentially malignant disorders among patients accrued over a 10-year period in South East England. *J Oral Pathol Med*. 2011;40:677-683.
9. Casparis S, Borm JM, Tektas S, et al. Oral lichen planus (OLP), oral lichenoid lesions (OLL), oral dysplasia, and oral cancer: retrospective analysis of clinicopathological data from 2002-2011. *Oral Maxillofac Surg*. 2015;19:149-156.
10. Gonzalez-Moles MA, Gil-Montoya JA, Ruiz-Avila I, Bravo M. Is oral cancer incidence among patients with oral lichen planus/oral lichenoid lesions underestimated? *J Oral Pathol Med*. 2017;46:148-153.
11. Aghbari SMH, Abushouk AI, Attia A, et al. Malignant transformation of oral lichen planus and oral lichenoid lesions: a meta-analysis of 20095 patient data. *Oral Oncol*. 2017;68:92-102.
12. Shivhare P, Gupta A, Yadav M, Konidena A, Shankarnarayan L. Evaluation of different diagnostic criteria of diseases manifesting the oral cavity—a review. Part-1. *J Oral Biol Craniofac Res*. 2016;6:135-141.
13. Cheng Y-SL, Gould A, Kurago Z, Fantasia J, Muller S. Diagnosis of oral lichen planus: a position paper of the American Academy of Oral and Maxillofacial Pathology. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2016;122:332-354.
14. Schlosser BJ. Lichen planus and lichenoid reactions of the oral mucosa. *Dermatol Ther*. 2010;23:251-267.
15. Al-Hashimi I, Schifter M, Lockhart PB, et al. Oral lichen planus and oral lichenoid lesions: diagnostic and therapeutic considerations. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;103. S25.e21-e22.
16. van der Waal I. Potentially malignant disorders of the oral and oropharyngeal mucosa: terminology, classification and present concepts of management. *Oral Oncol*. 2009;45:317-323.
17. Ismail SB, Kumar SK, Zain RB. Oral lichen planus and lichenoid reactions: etiopathogenesis, diagnosis, management and malignant transformation. *J Oral Sci*. 2007;49:89-106.
18. Lauritano D, Arrica M, Lucchese A, et al. Oral lichen planus clinical characteristics in Italian patients: a retrospective analysis. *Head Face Med*. 2016;12:18.
19. Rossi L, Colasanto S. Clinical considerations and statistical analysis on 100 patients with oral lichen planus. *Minerva Stomatol*. 2000;49:393-398.
20. Bardellini E, Amadori F, Flocchini P, Bonadeo S, Majorana A. Clinicopathological features and malignant transformation of oral lichen planus: a 12-years retrospective study. *Acta Odontol Scand*. 2013;71:834-840.
21. Shen ZY, Liu W, Zhu LK, Feng JQ, Tang GY, Zhou ZT. A retrospective clinicopathological study on oral lichen planus and malignant transformation: analysis of 518 cases. *Med Oral Patol Oral Cir Bucal*. 2012;17:e943-e947.
22. Horowitz MR, Vidal MdL, Resende MO, Teixeira MAG, Cavalcanti SMdM, Alencar ERBd. Linear lichen planus in children—case report. *An Bras Dermatol*. 2013;88:139-142.
23. Chatterjee K, Bhattacharya S, Mukherjee CG, Mazumdar A. A retrospective study of oral lichen planus in paediatric population. *J Oral Maxillofac Pathol*. 2012;16:363-367.
24. Mohan Das U, Beena Jp. Oral lichen planus in children. *Int J Clin Pediatr Dent*. 2009;2:49-51.
25. Fang M, Zhang W, Chen Y, He Z. Malignant transformation of oral lichen planus: a retrospective study of 23 cases. *Quintessence Int*. 2009;40:235-242.
26. Rodstrom PO, Jontell M, Mattsson U, Holmberg E. Cancer and oral lichen planus in a Swedish population. *Oral Oncol*. 2004;40:131-138.

27. Chainani-Wu N, Silverman S. Jr., Lozada-Nur F, Mayer P, Watson JJ. Oral lichen planus: patient profile, disease progression and treatment responses. *J Am Dent Assoc*. 2001;132:901-909.
28. van der Meij EH, Schepman KP, van der Waal I. The possible premalignant character of oral lichen planus and oral lichenoid lesions: a prospective study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2003;96:164-171.
29. Radochova V, Drizhal I, Slezak R. A retrospective study of 171 patients with oral lichen planus in the East Bohemia, Czech Republic—single center experience. *J Clin Exp Dent*. 2014;6:e556-e561.
30. Budimir V, Richter I, Andabak-Rogulj A, Vucicevic-Boras V, Budimir J, Brailo V. Oral lichen planus—retrospective study of 563 Croatian patients. *Med Oral Patol Oral Cir Bucal*. 2014;19:e255-e260.
31. Gumru B. A retrospective study of 370 patients with oral lichen planus in Turkey. *Med Oral Patol Oral Cir Bucal*. 2013;18:e427-e432.
32. Bermejo-Fenoll A, Sanchez-Siles M, Lopez-Jornet P, Camacho-Alonso F, Salazar-Sanchez N. A retrospective clinicopathological study of 550 patients with oral lichen planus in south-eastern Spain. *J Oral Pathol Med*. 2010;39:491-496.
33. Tovaru S, Parlatescu I, Gheorghe C, Tovaru M, Costache M, Sardella A. Oral lichen planus: a retrospective study of 633 patients from Bucharest, Romania. *Med Oral Patol Oral Cir Bucal*. 2012;18:e201-e206.
34. Wang Y-Y, Tail Y-H, Wang W-C, et al. Malignant transformation in 5071 southern Taiwanese patients with potentially malignant oral mucosal disorders. *BMC Oral Health*. 2014;14. 99-99.
35. Pakfetrat A, Javadzadeh-Bolouri A, Basir-Shabestari S, Falaki F. Oral lichen planus: a retrospective study of 420 Iranian patients. *Med Oral Patol Oral Cir Bucal*. 2009;14:e315-e318.
36. Ingafou M, Leao JC, Porter SR, Scully C. Oral lichen planus: a retrospective study of 690 British patients. *Oral Dis*. 2006;12:463-468.
37. Xue JL, Fan MW, Wang SZ, Chen XM, Li Y, Wang L. A clinical study of 674 patients with oral lichen planus in China. *J Oral Pathol Med*. 2005;34:467-472.
38. Torrente-Castells E, Figueiredo R, Berini-Aytes L, Gay-Escoda C. Clinical features of oral lichen planus. A retrospective study of 65 cases. *Med Oral Patol Oral Cir Bucal*. 2010;15:e685-e690.
39. Eisen D. The clinical features, malignant potential, and systemic associations of oral lichen planus: a study of 723 patients. *J Am Acad Dermatol*. 2002;46:207-214.
40. Kaplan I, Ventura-Sharabi Y, Gal G, Calderon S, Anavi Y. The dynamics of oral lichen planus: a retrospective clinicopathological study. *Head Neck Pathol*. 2012;6:178-183.
41. Bombeccari GP, Guzzi G, Tettamanti M, et al. Oral lichen planus and malignant transformation: a longitudinal cohort study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2011;112:328-334.
42. Carbone M, Arduino PG, Carrozzo M, et al. Course of oral lichen planus: a retrospective study of 808 northern Italian patients. *Oral Dis*. 2009;15:235-243.
43. Bornstein MM, Kalas L, Lemp S, Altermatt HJ, Rees TD, Buser D. Oral lichen planus and malignant transformation: a retrospective follow-up study of clinical and histopathologic data. *Quintessence Int*. 2006;37:261-271.
44. Laeijendecker R, van Joost T, Kuizinga MC, Tank B, Neumann HA. Premalignant nature of oral lichen planus. *Acta Derm Venereol*. 2005;85:516-520.
45. van der Meij EH, Mast H, van der Waal I. The possible premalignant character of oral lichen planus and oral lichenoid lesions: a prospective five-year follow-up study of 192 patients. *Oral Oncol*. 2007;43:742-748.
46. Gandolfo S, Richiardi L, Carrozzo M, et al. Risk of oral squamous cell carcinoma in 402 patients with oral lichen planus: a follow-up study in an Italian population. *Oral Oncol*. 2004;40:77-83.
47. Lanfranchi-Tizeira HE, Aguas SC, Sano SM. Malignant transformation of atypical oral lichen planus: a review of 32 cases. *Med Oral*. 2003;8:2-9.
48. Mignogna MD, Lo Muzio L, Lo Russo L, Fedele S, Ruoppo E, Bucci E. Clinical guidelines in early detection of oral squamous cell carcinoma arising in oral lichen planus: a 5-year experience. *Oral Oncol*. 2001;37:262-267.
49. Rajentheran R, McLean NR, Kelly CG, Reed MF, Nolan A. Malignant transformation of oral lichen planus. *Eur J Surg Oncol*. 1999;25:520-523.
50. Sun Y, Liu N, Guan X, Wu H, Sun Z, Zeng H. Immunosuppression induced by chronic inflammation and the progression to oral squamous cell carcinoma. *Mediators Inflamm*. 2016;2016:1-12.
51. Landskron G, De la Fuente M, Thuwajit P, Thuwajit C, Hermoso MA. Chronic inflammation and cytokines in the tumor microenvironment. *J Immunol Res*. 2014;2014:149185.
52. Aivaliotis IL, Pateras IS, Papaioannou M, et al. How do cytokines trigger genomic instability? *J Biomed Biotechnol*. 2012;2012:536761.
53. Neagu M, Caruntu C, Constantin C, et al. Chemically induced skin carcinogenesis: updates in experimental models [Review]. *Oncol Rep*. 2016;35:2516-2528.
54. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. *Cell*. 2010;140:883-899.
55. Avadhani AV, Parachuru VP, Milne T, Seymour GJ, Rich AM. Multiple cells express interleukin 17 in oral squamous cell carcinoma. *J Oral Pathol Med*. 2017;46:39-45.
56. Javvadi LR, Parachuru VP, Milne TJ, Seymour GJ, Rich AM. Regulatory T-cells and IL17 A(+) cells infiltrate oral lichen planus lesions. *Pathology*. 2016;48:564-573.
57. Rhodus NL, Cheng B, Myers S, Miller L, Ho V, Ondrey F. The feasibility of monitoring NF-kappaB associated cytokines: TNF-alpha, IL-1 alpha, IL-6, and IL-8 in whole saliva for the malignant transformation of oral lichen planus. *Mol Carcinog*. 2005;44:77-82.
58. Juretic M, Cerovic R, Belusic-Gobic M, et al. Salivary levels of TNF-alpha and IL-6 in patients with oral premalignant and malignant lesions. *Folia Biol*. 2013;59:99-102.
59. Lisa Cheng YS, Jordan L, Gorugantula LM, Schneiderman E, Chen HS, Rees T. Salivary interleukin-6 and -8 in patients with oral cancer and patients with chronic oral inflammatory diseases. *J Periodontol*. 2014;85:956-965.
60. Tampa M, Caruntu C, Mitran M, et al. Markers of oral lichen planus malignant transformation. *Dis Markers*. 2018;2018:1-13.
61. Dyson JK, Rutter MD. Colorectal cancer in inflammatory bowel disease: what is the real magnitude of the risk? *World J Gastroenterol*. 2012;18:3839-3848.
62. Kurago ZB. Etiology and pathogenesis of oral lichen planus: an overview. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2016;122:72-80.

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