



## **University of Pennsylvania School of Dental Medicine**

### ***QUALITY OF LIFE IN PATIENTS WITH ORAL POTENTIALLY MALIGNANT DISORDERS: ORAL LICHEN PLANUS AND ORAL EPITHELIAL DYSPLASIA***

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## **Abstract**

### **Background**

Oral potential malignant disorders (OPMDs) are lesions and conditions that increase the risk for malignant transformation. OPMDs have an impact on patients' health status and Quality of life (QoL). The aim of our study is to evaluate and compare QoL in patients with oral lichen planus and oral epithelial dysplasia as a setting of clinical leukoplakia.

### **Methods**

This is a cross-sectional study with a sample size of 100 patients divided into, 53 subjects with Oral Lichen Planus (53.0%), 39 patients with oral epithelial dysplasia as a setting of solitary leukoplakia (39.0%), and 8 subjects with oral lichen planus with oral epithelial dysplasia (8.0%). Patients who fit the criteria were asked to fill out three different questionnaires. 26-item Chronic Oral Mucosal Disease Questionnaire (COMDQ-26), Hospital Anxiety and Depression Scale (HADS), and the Oral potentially malignant disorders QoL questionnaire (OPMDsQoL).

### **Results**

Both the COMD-26 and OPMDQoL questionnaire scores were significantly different across the three disease groups. Relative to patients aged >65, the 40-64 age group added 6.8 points to the COMD-26 survey score ( $P < 0.05$ ). Relative to oral epithelial dysplasia, oral lichen planus added 15.7 points to the COMD-26 survey score ( $P < 0.001$ ). Relative to oral epithelial dysplasia, oral lichen plus added 8.9 points to the OPMDQoL survey score ( $P = 0.003$ ).

### **Conclusion**

Within the limitation of our study OLP shows significant poorer QoL in compared to OED as a setting of clinical OL. Younger individuals affected with OLP, and OED showed significant impact in QoL in compared to older individuals.

### **Keywords**

Oral potential malignant disorders, Oral lichen planus, Oral epithelial dysplasia, oral health QoL, COMD-26 questionnaire, HADS, OPMDs QoL questionnaire.

## **Introduction**

Worldwide, an estimated 19.3 million new cancer cases were diagnosed in 2020, resulting in 10 million cancer death. There are approximately 378,000 cases of oral cavity cancer worldwide in 2020, which caused an estimated 178,000 deaths. (AICR 2020). There are multiple risk factors for malignant transformation. These include tobacco and alcohol, while betel, radiation exposure, and infections are relevant in some cases.<sup>1</sup>

Oral potential malignant disorders (OPMDs) are lesions and conditions that increase the risk for malignant transformation.<sup>2</sup> The term OPMDs is defined as “a group of disorders of varying etiologies, usually tobacco; characterized by mutagen associated, spontaneous or hereditary alterations or mutations in the genetic material of oral epithelial cells with or without clinical and histomorphological alterations that may lead to oral squamous cell carcinoma transformation.”<sup>3</sup> Premalignant lesions OPMDs are leukoplakia, erythroplakia, proliferative verrucous leukopakia, candida leukoplakia, and actinic keratosis. Premalignant conditions include oral lichen planus (OLP), discoid lupus erythromatosus and epidermolysis bullosa.<sup>2</sup> Monitoring and managing such lesions by a specialist is important to minimize risk for malignant transformation.

Oral epithelial dysplasia is a specific alternation of the epithelial layer caused by an accumulation of genetic changes associated with progression towards malignancy. According to WHO 2017 criteria, dysplasia involves cellular and architectural changes, such as loss of epithelial cell cohesion.<sup>4</sup>

WHO classified oral epithelial dysplasia in 2017 in three categories: mild, moderate and severe.<sup>5</sup> Mild dysplasia is defined as mild cellular changes with limited architecture disturbance up to the lower third of the epithelium. The histopathological features of moderate oral epithelial dysplasia entail architecture disturbance that extend to middle third of epithelium. Lastly, severe oral epithelial dysplasia characterized by cellular architecture disturbance that extend to the upper third of epithelium with severe cellular changes.<sup>4</sup> The risk of malignant transformation for mild oral epithelial dysplasia is approximately <5%.<sup>6</sup> Moderate oral epithelial dysplasia carries a risk of around 3-30%.<sup>6</sup> Severe oral epithelial dysplasia has a 50% chance of malignant transformation.<sup>6</sup>

OLP is a chronic mucocutaneous disease that affects 0.5 to 2.2% of the population.<sup>7</sup> Although the exact etiology of OLP is unclear, it has been suggested that lichen planus is a T-cell mediated hypersensitivity disorder.<sup>7</sup> Lichen planus occurs in both skin and mucosa in about 40% of cases, skin only in 35% of cases, and mucosa only in about 25% of cases.<sup>6</sup> OLP typically manifests between the third and seventh decade of life. Females are more likely to develop OLP than males.<sup>6-7</sup> OLP is associated with increased risk for malignant transformation. Based on current literature the overall malignant transformation risk for OLP is 0.9%-1.9% and 0.28% per year.<sup>8</sup> The current diagnostic criteria according to WHO for OLP is based on clinical and histopathological correlation.<sup>9</sup> OLP clinically occurs in three main clinical pattern: reticular, erosive/atrophic, and a plaque-like pattern.<sup>7-10</sup>

The reticular form is a raised lacework or reticular appearance and referred to as Wickham's Striae. Patients with this form typically complain of raised painless lesions. Reticular OLP usually presents in the buccal mucosa followed by the buccal vestibule, tongue, gingiva, and

labial mucosa. The erosive/atrophic form of OLP is a mixed erythematous and white lesion with irregular yellow ulceration and pseudo-membrane. If the erythema extends along the gingival mucosa, it will produce a pattern described as “desquamative gingivitis.” Patients usually experience burning sensation that might interfere with their lifestyle and eating habits. Finally, plaque-like OLP is a raised white flat area that usually present in the dorsum of the tongue.<sup>7-10</sup>

The WHO defined quality of life (QoL) as a ‘the perception of each individual of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns’. The impact of health status on QoL has become an important component of patient care. OPMDs are commonly encountered in the clinical practice of oral medicine - and their management can be very challenging in the field. Our knowledge on the QoL in patients with OPMDs is very limited. The aim of our study is to evaluate and compare QoL in patients with oral lichen planus and oral epithelial dysplasia as a setting of clinical leukoplakia.

## **Material and methods**

### Study procedure

Subjects were recruited from the oral maxillofacial surgery/oral medicine practices at University of Pennsylvania from January to June 2021. The study protocol was approved by the institutional review board at the University of Pennsylvania. OLP group inclusion criteria: newly diagnosed and established patients with clinical and histopathological confirmation of OLP including lichenoid reaction. Individuals with histopathological confirmation of either atypia, mild, moderate, or severe epithelial dysplasia were included in oral epithelial dysplasia group. The following cases were excluded from the study: prior history of head and neck cancer, history of psychiatric disease prior to diagnosis of OLP or OED, patients with skin or genital lesions, graft versus host disease related lichenoid reaction, systemic lupus erythematosus related lichenoid reaction, proliferative verrucous leukoplakia. Patients who fit the criteria were asked to fill out the forms. Patient were given the option to either fill out the form in clinic, mail the questionnaire to their attending, scan their survey via *myPennMedicine* application and send it to their attending, or set up a phone call.

## **Results**

This is a cross-sectional study with a sample size of 114 patients. Four patients refused to participate in the study, 11 patients didn't send back their survey. The final sample consisted of 100 subjects. There were 53 subjects with Oral Lichen Planus (53.0%), 39 patients with oral epithelial dysplasia as a setting of solitary leukoplakia (39.0%), and 8 subjects with oral lichen planus with oral epithelial dysplasia (8.0%). With regards to sex, 37 (37.0%) subjects were male and 63 (63.0%) were female. Patients were divided according to age group: 4 (4.0%) were <40 years old, 38 (38.0%) were 40-64 years old, and 58 (58.0%) were >64 years old (**Table 1**). There were 60 ever drinkers (60.0%), five ex-drinkers (5.0%), two current drinkers (2.0%), and 33 never drinkers (33.0%). There were two ever-smokers (2.0%), 35 ex-smokers (35.0%), eight current smokers (8.0%), and 55 subjects who never smoked in their life (55.0%) (**Table 1**). Mean duration of OED (months)  $25.8 \pm 25.6$  and mean duration of OLP (months)  $53.3 \pm 50.3$  (**Table 1**).

OLP group was classified three different clinical forms: erosive 11(18.0%), erythematous 38(62.3%), and keratotic form 12(19.7%). OLP was also classified according to clinical severity – there were 44 subjects with mild OLP (72.1%), 17 subjects with moderate OLP (27.9), and none with severe OLP (0.0%) (**Table 2**).

OED was classified according to histopathological confirmation of epithelial hyperplasia and hyperkeratosis with atypia (17.4%), mild epithelial dysplasia (52.2%), moderate epithelial dysplasia (17.4%), and severe epithelial dysplasia (13.0%). Regarding previous history management of OED, 26 subjects received clinical monitoring (56.5%), 13 subjects received complete Co2 laser ablation of lesion (28.3%), and seven subjects had previous complete exclusion of lesion (15.2%). OED was also categorized according to the anatomical biopsy location. Five were in the buccal mucosa (10.9%), five were in the floor of mouth (10.9%), two were in the palate (4.3%), three were in the lower gingiva (6.5%), 26 were in the tongue (56.5%), and five in the upper gingiva (10.9%) (**Table 3**).

**Table 1.** Demographics and alcohol & smoking history for Oral Lichen Planus (OLP) and Oral Epithelial Dysplasia (OED) patients

	Number of patients, n (%)
<b>Total</b>	100
<b>Disease</b>	
<b>Oral epithelial dysplasia</b>	39 (39.0%)
<b>Oral lichen planus</b>	53 (53.0%)
<b>Oral lichen planus with oral epithelial dysplasia</b>	8 (8.0%)
<b>Sex</b>	
<b>Male</b>	37 (37.0%)
<b>Female</b>	63 (63.0%)
<b>Age Group</b>	
<b>&lt; 40</b>	4 (4.0%)
<b>40 - 64</b>	38 (38.0%)
<b>&gt; 65</b>	58 (58.0%)
<b>Alcohol use history</b>	
<b>Current Drinker</b>	2 (2.0%)
<b>Ever drinker</b>	60 (60.0%)
<b>Ex-drinker</b>	5 (5.0%)
<b>Never drinker</b>	33 (33.0%)
<b>Smoking history</b>	
<b>Current smoker</b>	8 (8.0%)
<b>Ever smoker</b>	2 (2.0%)
<b>Ex- smoker</b>	35 (35.0%)
<b>Never smoker</b>	55 (55.0%)
<b>Duration OED, mean (months)</b>	25.8 ± 25.6
<b>Duration OLP, mean (months)</b>	53.3 ± 50.3

**Table 2.** Characteristics of Oral Lichen Planus (OLP)

	Number of patients, n (%)
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<b>Total</b>	61 (100.0%)
<b>Oral lichen planus - form</b>	
<b>Erosive</b>	11 (18.0%)
<b>Erythematous</b>	38 (62.3%)
<b>Keratotic</b>	12 (19.7%)
<b>Oral lichen planus – clinical severity</b>	
<b>Mild</b>	44 (72.1%)
<b>Moderate</b>	17 (27.9%)

**Table 3.** Characteristics of Oral Epithelial Dysplasia (OED)

	<b>Number of patients, n (%)</b>
<b>Total</b>	46 (100.0%)
<b>Oral epithelial dysplasia – histopathological grading</b>	
<b>Epithelial hyperplasia and hyperkeratosis with atypia</b>	8 (17.4%)
<b>Mild epithelial dysplasia</b>	24 (52.2%)
<b>Moderate epithelial dysplasia</b>	8 (17.4%)
<b>Severe epithelial dysplasia</b>	6 (13.0%)
<b>Previous history management</b>	
<b>Clinical monitoring</b>	26 (56.5%)
<b>Previous complete CO<sub>2</sub> laser ablation of lesion</b>	13 (28.3%)
<b>Previous complete excision of lesion</b>	7 (15.2%)
<b>Oral cavity anatomical</b>	
<b>Buccal mucosa</b>	5 (10.9%)
<b>Floor of mouth</b>	5 (10.9%)
<b>Hard palate</b>	2 (4.3%)
<b>Lower gingiva</b>	3 (6.5%)
<b>Tongue</b>	26 (56.5%)
<b>Upper gingiva</b>	5 (10.9%)

Both the COMD-26 and OPMDQoL questionnaire scores were significantly different across the three disease groups – Oral lichen planus had the highest score in both the COMD-26 and OPMDQoL questionnaires. No significant differences were seen for the HADS questionnaire. Sex, age, and alcohol use history were not significant predictors of disease group. However, ex-smokers ( $p < 0.05$ ) and never smokers ( $p < 0.05$ ) were unequally distributed between the disease groups (Table 4).

**Table 4.** Demographics and alcohol & smoking history stratified by disease

	<b>Oral epithelial dysplasia</b>	<b>Oral lichen planus</b>	<b>Oral lichen planus with oral epithelial dysplasia</b>	<b>p-value</b>
<b>Total</b>	39	53	8	-
<b>COMD-26 questionnaire, mean</b>	22.7	38.6	34.0	0.000*
<b>OPMDQoL questionnaire, mean</b>	18.8	28.0	24.8	0.010*
<b>HADS questionnaire, mean</b>	8.4	8.0	6.1	0.518

<b>Sex</b>					0.307
	<b>Male</b>	17	16	4	
	<b>Female</b>	22	37	4	
<b>Age Group</b>					
	<b>&lt; 40</b>	1	2	1	0.423
	<b>40 - 64</b>	16	20	2	0.695
	<b>&gt; 65</b>	22	31	58	0.945
<b>Alcohol use history</b>					
	<b>Current Drinker</b>	1	1	0	0.891
	<b>Ever drinker</b>	23	34	3	0.353
	<b>Ex-drinker</b>	3	1	1	0.269
	<b>Never drinker</b>	12	17	4	0.562
<b>Smoking history</b>					
	<b>Current smoker</b>	6	1	1	0.055
	<b>Ever smoker</b>	0	2	0	0.405
	<b>Ex- smoker</b>	11	18	6	0.040*
	<b>Never smoker</b>	22	32	1	0.039*

**Table 5** illustrates the COMD-26 questionnaire scores across predictor variables. The scores proved to be significantly different across sex, age group, alcohol use history, disease group, oral lichen planus form, oral lichen planus severity, and previous history management of oral epithelial dysplasia ( $P < 0.15$ ). Univariate linear regression to determine which categories were associated with increased score for each variable (**Table 6**). After controlling for covariates, multivariate linear regression was conducted (**Table 7**). Relative to patients aged  $>65$ , the 40-64 age group added 6.8 points to the COMD-26 survey score ( $P < 0.05$ ). Relative to oral epithelial dysplasia, oral lichen planus added 15.7 points to the COMD-26 survey score ( $P < 0.001$ ).

**Table 5.** Comparison of COMD-26 instrument for each predictor variable

\*, Statistically significant for regression ( $P < .15$ )

	COMD-26 score, Mean	p-value
<b>Sex</b>		0.037*
	<b>Male</b>	29.6
	<b>Female</b>	33.5
<b>Age Group</b>		0.113*
	<b>&lt; 40</b>	38.3
	<b>40 – 64</b>	35.6
	<b>&gt; 65</b>	29.3
<b>Alcohol use history</b>		0.136*

<b>Current Drinker</b>	35.5	
<b>Ever drinker</b>	30.0	
<b>Ex-drinker</b>	24.0	
<b>Never drinker</b>	36.9	
<b>Smoking history</b>		0.912
<b>Current smoker</b>	31.3	
<b>Ever smoker</b>	32.5	
<b>Ex- smoker</b>	30.6	
<b>Never smoker</b>	33.1	
<b>Disease</b>		0.000*
<b>Oral epithelial dysplasia</b>	22.7	
<b>Oral lichen planus</b>	38.6	
<b>Oral lichen planus with oral epithelial dysplasia</b>	34.0	
<b>Oral lichen planus – clinical pattern</b>		0.136*
<b>Erosive</b>	45.1	
<b>Erythematous</b>	37.9	
<b>Keratotic</b>	31.9	
<b>Oral lichen planus – clinical severity</b>		0.021*
<b>Mild</b>	35.2	
<b>Moderate</b>	45.5	
<b>Oral epithelial dysplasia – histopathological grading</b>		0.573
<b>Epithelial hyperplasia and hyperkeratosis with atypia</b>	21.0	
<b>Mild epithelial dysplasia</b>	25.2	
<b>Moderate epithelial dysplasia</b>	21.9	
<b>Severe epithelial dysplasia</b>	28.3	
<b>Oral epithelial dysplasia - previous history management</b>		0.128*



<b>Clinical monitoring</b>	21.5	
<b>Previous complete CO<sub>2</sub> laser ablation of lesion</b>	28.9	
<b>Previous complete excision of lesion</b>	26.1	
<b>Oral epithelial dysplasia - oral cavity anatomical</b>		0.670
<b>Buccal mucosa</b>	27.2	
<b>Floor of mouth</b>	28.4	
<b>Hard palate</b>	30.0	
<b>Lower gingiva</b>	28.0	
<b>Tongue</b>	23.0	
<b>Upper gingiva</b>	19.2	
<b>Duration of OLP</b>		0.583
<b>0-6 months</b>	32.1	
<b>6-24 months</b>	39.4	
<b>24-60 months</b>	38.8	
<b>60 and more</b>	39.6	
<b>Duration of OED</b>		0.710
<b>0-6 months</b>	23.2	
<b>6-24 months</b>	23.9	
<b>24-60 months</b>	27.5	
<b>60 and more</b>	21.3	

**Table 6.** Univariate linear regression model for COMD-26 instrument score

\*, Ref – reference group is the standard with which all other variables are compared to

\*, CI- confidence interval

	<b>COMD score</b>
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	<b>Coefficient</b>	<b>95% CI</b>	<b>p-value</b>
<b>Sex</b>			
<b>Male</b>	Ref	-	-
<b>Female</b>	3.8	-2.6, 10.3	0.241
<b>Age Group</b>			
<b>&lt; 40_1</b>	9.0	-7.0, 24.9	0.267
<b>40 – 64_3</b>	6.3	-0.1, 12.8	0.054
<b>&gt; 65_2</b>	Ref	-	-
<b>Alcohol use history</b>			
<b>Current Drinker</b>	11.5	-14.3, 37.3	0.379
<b>Ever drinker</b>	6.0	-8.4, 20.3	0.413
<b>Ex-drinker</b>	Ref	-	-
<b>Never drinker</b>	12.8	-2.0, 27.6	0.088
<b>Disease</b>			
<b>Oral epithelial dysplasia_1</b>	Ref	-	-
<b>Oral lichen planus_2</b>	16.0	10.1, 21.8	0.000*
<b>Oral lichen planus with oral epithelial dysplasia_3</b>	11.3	0.6, 22.1	0.038*
<b>Oral lichen planus - form</b>			
<b>Erosive</b>	13.2	0.2, 26.1	0.047*
<b>Erythematous</b>	6.0	-4.3, 16.3	0.248
<b>Keratotic</b>	Ref	-	-
<b>Oral lichen planus - severity</b>			
<b>Mild_2</b>	Ref	-	-
<b>Moderate_3</b>	10.3	1.6, 19.0	0.021*

<b>Oral epithelial dysplasia - previous history management</b>			
<b>Pediatric evaluation without management_2</b>	Ref	-	-
<b>Previous complete CO<sub>2</sub> laser ablation of lesion_3</b>	7.3	-0.0, 14.7	0.050
<b>Previous complete excision of lesion_4</b>	4.6	-4.6, 13.9	0.315

**Table7.** Multivariate linear regression model for COMD-26 instrument score

\*, Ref – reference group is the standard with which all other variables are compared to

\*, CI- confidence interval

	<b>COMD score</b>		
	<b>Coefficient</b>	<b>95% CI</b>	<b>p-value</b>
<b>Sex</b>			
<b>Male</b>	Ref	-	-
<b>Female</b>	1.8	-4.0, 7.5	0.538
<b>Age Group</b>			
<b>&lt; 40</b>	11.5	-2.7, 25.8	0.112
<b>40 - 64</b>	6.8	1.2, 12.5	0.017*
<b>&gt; 65</b>	Ref	-	-
<b>Alcohol use history</b>			
<b>Current Drinker</b>	11.1	-11.8, 34.0	0.338
<b>Ever drinker</b>	1.4	-11.4, 14.3	0.825
<b>Ex-drinker</b>	Ref	-	-
<b>Never drinker</b>	8.6	-4.7, 22.0	0.202
<b>Disease</b>			
<b>Oral epithelial dysplasia</b>	Ref	-	-

<b>Oral lichen planus</b>	15.7	10.0, 21.4	0.000*
<b>Oral lichen planus with oral epithelial dysplasia</b>	10.3	-0.2, 20.9	0.054

**Table 8** illustrates the OPMDQoL questionnaire scores across predictor variables. The scores were significantly different for sex, alcohol use history, disease group, oral lichen planus severity, and previous history management of oral epithelial dysplasia ( $P < 0.15$ ). As was done for COMD-26 questionnaire scores, univariate linear regression to determine which categories were associated with increased score for each variable (**Table 9**). After controlling for covariates, multivariate linear regression was conducted (**Table 10**). Relative to oral epithelial dysplasia, oral lichen plus added 8.9 points to the OPMDQoL survey score ( $P = 0.003$ ).

**Table 8.** Comparison of OPMDQoL instrument for each predictor variable

\*, Statistically significant for regression ( $P < .15$ )

	<b>OPMDQoL score, Mean</b>	<b>p-value</b>
<b>Sex</b>		0.073*
<b>Male</b>	20.7	
<b>Female</b>	26.2	
<b>Age Group</b>		0.380
<b>&lt; 40</b>	24.0	
<b>40 – 64</b>	26.7	
<b>&gt; 65</b>	22.5	
<b>Alcohol use history</b>		0.031*
<b>Current Drinker</b>	28.0	
<b>Ever drinker</b>	21.1	
<b>Ex-drinker</b>	20.0	
<b>Never drinker</b>	30.1	
<b>Smoking history</b>		0.790
<b>Current smoker</b>	24.8	
<b>Ever smoker</b>	18.5	
<b>Ex- smoker</b>	22.5	

<b>Never smoker</b>	25.3	
<b>Disease</b>		0.010*
<b>Oral epithelial dysplasia</b>	18.8	
<b>Oral lichen planus</b>	28.0	
<b>Oral lichen planus with oral epithelial dysplasia</b>	24.8	
<b>Oral lichen planus – clinical pattern</b>		0.313
<b>Erosive</b>	33.6	
<b>Erythematous</b>	27.1	
<b>Keratotic</b>	23.7	
<b>Oral lichen planus – clinical severity</b>		0.020*
<b>Mild</b>	24.7	
<b>Moderate</b>	35.1	
<b>Oral epithelial dysplasia – histopathological grading</b>		0.243
<b>Epithelial hyperplasia and hyperkeratosis with atypia</b>	13.0	
<b>Mild epithelial dysplasia</b>	22.0	
<b>Moderate epithelial dysplasia</b>	21.1	
<b>Severe epithelial dysplasia</b>	18.0	
<b>Oral epithelial dysplasia - previous history management</b>		0.036*
<b>Clinical monitoring</b>	16.6	
<b>Previous complete CO<sub>2</sub> laser ablation of lesion</b>	26.2	
<b>Previous complete excision of lesion</b>	19.7	
<b>Oral epithelial dysplasia - oral cavity anatomical</b>		0.332
<b>Buccal mucosa</b>	25.4	
<b>Floor of mouth</b>	21.0	
<b>Hard palate</b>	29.0	
<b>Lower gingiva</b>	26.0	

	<b>Tongue</b>	18.2	
	<b>Upper gingiva</b>	13.4	
<b>Duration of OLP</b>			0.697
	<b>0-6 months</b>	23.9	
	<b>6-24 months</b>	30.7	
	<b>24-60 months</b>	25.5	
	<b>60 and more</b>	28.7	
<b>Duration of OED</b>			0.693
	<b>0-6 months</b>	18.5	
	<b>6-24 months</b>	19.9	
	<b>24-60 months</b>	22.9	
	<b>60 and more</b>	16.0	

**Table9.** Univariate linear regression model for OPMDQoL instrument score

\*, Ref – reference group is the standard with which all other variables are compared to

\*, CI- confidence interval

	QoL score		
	Coefficient	95% CI	p-value
<b>Sex</b>			
<b>Male</b>	Ref	-	-
<b>Female</b>	5.4	-0.5, 11.4	0.073
<b>Age Group</b>			
<b>&lt; 40_1</b>	1.5	-13.5, 16.5	0.840
<b>40 – 64_3</b>	4.3	-1.8, 10.3	0.165
<b>&gt; 65_2</b>	Ref	-	-

<b>Alcohol use history</b>			
<b>Current Drinker</b>	8.0	-15.6, 31.6	0.502
<b>Ever drinker</b>	1.1	-12.0, 14.2	0.870
<b>Ex-drinker</b>	Ref	-	-
<b>Never drinker</b>	10.1	-3.4, 23.6	0.140
<b>Disease</b>			
<b>Oral epithelial dysplasia</b>	Ref	-	-
<b>Oral lichen planus</b>	9.2	3.3, 15.1	0.003*
<b>Oral lichen planus with oral epithelial dysplasia</b>	6.0	-4.9, 16.8	0.279
<b>Oral lichen planus - severity</b>			
<b>Mild</b>	Ref	-	-
<b>Moderate</b>	10.4	1.7, 19.0	0.020*
<b>Oral epithelial dysplasia - previous history management</b>			
<b>Pediatric evaluation without management</b>	Ref	-	-
<b>Previous complete CO<sub>2</sub> laser ablation of lesion</b>	9.6	2.4, 16.8	0.010*
<b>Previous complete excision of lesion</b>	3.1	-5.9, 12.2	0.487

**Table10.** Multivariate linear regression model for OPMDQoL instrument score

\*, Ref – reference group is the standard with which all other variables are compared to

\*, CI- confidence interval

	QoL score		
	Coefficient	95% CI	p-value
<b>Sex</b>			
<b>Male</b>	Ref	-	-

<b>Female</b>	4.2	-1.6, 10.0	0.156
<b>Age Group</b>			
<b>&lt; 40</b>	5.4	-9.1, 19.8	0.462
<b>40 - 64</b>	4.6	-1.1, 10.3	0.110
<b>&gt; 65</b>	Ref	-	-
<b>Alcohol use history</b>			
<b>Current Drinker</b>	4.9	-18.2, 28.1	0.672
<b>Ever drinker</b>	-3.3	-16.3, 9.7	0.615
<b>Ex-drinker</b>	Ref	-	-
<b>Never drinker</b>	5.8	-7.7, 19.3	0.396
<b>Disease</b>			
<b>Oral epithelial dysplasia</b>	Ref	-	-
<b>Oral lichen planus</b>	8.9	3.1, 14.6	0.003*
<b>Oral lichen planus with oral epithelial dysplasia</b>	4.7	-5.9, 15.4	0.379

**Table 11** illustrates the HADS scores across predictor variables. The scores were not significantly different for any variable ( $P < 0.15$ ). Nevertheless, sex and age group were further analyzed via univariate linear regression since they are biologically relevant variables. Further, disease group was also analyzed via regression analysis since it is the primary predictor variable of our study (**Table 12**). After controlling for covariates, multivariate linear regression was conducted. No significant results were observed (**Table 13**).

**Table 11.** Comparison of HADS for each predictor variable

\*, Statistically significant for regression ( $P < .15$ )

	<b>HADS score, Mean</b>	<b>p-value</b>
<b>Sex</b>		0.657



	<b>Male</b>	7.7	
	<b>Female</b>	8.2	
<b>Age Group</b>			0.257
	<b>&lt; 40</b>	11.0	
	<b>40 - 64</b>	7.4	
	<b>&gt; 65</b>	8.6	
<b>Alcohol use history</b>			0.716
	<b>Current Drinker</b>	4.5	
	<b>Ever drinker</b>	7.9	
	<b>Ex-drinker</b>	7.4	
	<b>Never drinker</b>	8.5	
<b>Smoking history</b>			0.170
	<b>Current smoker</b>	10.0	
	<b>Ever smoker</b>	1.0	
	<b>Ex- smoker</b>	7.9	
	<b>Never smoker</b>	8.0	
<b>Disease</b>			0.518
	<b>Oral epithelial dysplasia</b>	8.4	
	<b>Oral lichen planus</b>	8.0	
	<b>Oral lichen planus with oral epithelial dysplasia</b>	6.1	
<b>Oral lichen planus – clinical pattern</b>			0.697
	<b>Erosive</b>	6.5	
	<b>Erythematous</b>	7.9	
	<b>Keratotic</b>	8.3	
<b>Oral lichen planus – clinical severity</b>			0.351
	<b>Mild</b>	7.3	

<b>Moderate</b>	8.8	
<b>Oral epithelial dysplasia – histopathological grading</b>		0.787
<b>Epithelial hyperplasia and hyperkeratosis with atypia</b>	7.8	
<b>Mild epithelial dysplasia</b>	8.5	
<b>Moderate epithelial dysplasia</b>	7.1	
<b>Severe epithelial dysplasia</b>	6.5	
<b>Oral epithelial dysplasia - previous history management</b>		0.794
<b>Clinical monitoring</b>	8.1	
<b>Previous complete CO<sub>2</sub> laser ablation of lesion</b>	8.1	
<b>Previous complete excision of lesion</b>	6.7	
<b>Oral epithelial dysplasia - oral cavity anatomical</b>		0.698
<b>Buccal mucosa</b>	8.0	
<b>Floor of mouth</b>	5.8	
<b>Hard palate</b>	9.5	
<b>Lower gingiva</b>	11.7	
<b>Tongue</b>	7.6	
<b>Upper gingiva</b>	8.2	
<b>Duration of OLP</b>		0.737
<b>0-6 months</b>	6.5	
<b>6-24 months</b>	8.7	
<b>24-60 months</b>	7.5	
<b>60 and more</b>	8.3	
<b>Duration of OED</b>		0.833
<b>0-6 months</b>	8.1	
<b>6-24 months</b>	8.6	
<b>24-60 months</b>	7.2	

<b>60 and more</b>	6.3	
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**Table 12.** Univariate linear regression model for HADS score

\*, Ref – reference group is the standard with which all other variables are compared to

\*, CI- confidence interval

	HADS score		
	Coefficient	95% CI	p-value
<b>Sex</b>			
<b>Male</b>	Ref	-	-
<b>Female</b>	0.5	-1.6, 2.6	0.657
<b>Age Group</b>			
<b>&lt; 40</b>	3.6	-1.6, 8.8	0.173
<b>40 - 64</b>	Ref	-	-
<b>&gt; 65</b>	1.2	-0.9, 3.3	0.257
<b>Disease</b>			
<b>Oral epithelial dysplasia</b>	2.3	-1.7, 6.3	0.253
<b>Oral lichen planus</b>	1.9	-2.0, 5.7	0.341
<b>Oral lichen planus with oral epithelial dysplasia</b>	Ref	-	-

**Table 13.** Multivariate linear regression model for HADS score

\*, Ref – reference group is the standard with which all other variables are compared to

\*, CI- confidence interval

	HADS score		
	Coefficient	95% CI	p-value

<b>Sex</b>			
<b>Male</b>	Ref	-	-
<b>Female</b>	0.7	-1.4, 2.9	0.508
<b>Age Group</b>			
<b>&lt; 40</b>	4.3	-1.1, 9.6	0.115
<b>40 - 64</b>	Ref	-	-
<b>&gt; 65</b>	1.1	-1.0, 3.3	0.289
<b>Disease</b>			
<b>Oral epithelial dysplasia</b>	2.5	-1.5, 6.5	0.218
<b>Oral lichen planus</b>	1.9	-2.0, 5.8	0.325
<b>Oral lichen planus with oral epithelial dysplasia</b>	Ref	-	-

## **Discussion**

This study compared oral health quality of life between two OPMDs: OLP and OED. The general mean score for determining mood disorders for all groups is below average. The general mean value in COMD-26 instrument for OED is 22.7, 38.6 for OLP, and 34.0 for OLP with OED. The COMD-26 instrument scores were significantly different among the three disease groups ( $P < 0.01$ ). The OPMD QoL questionnaire scores were also significantly different ( $P < 0.05$ ) among the three disease groups, also being highest for OLP. From this result we can conclude that patients with either OLP or OED is not affecting patients' general well-being QoL. Both diseases are locally affecting oral health.

We hypothesized that Patients diagnosed with OED were more likely to show signs of mood disorder than patients diagnosed with OLP since OED the potential to malignancy transform much more than OLP. However, our analysis showed the contrary. Patients diagnosed with OED has lower score compared to OLP for two different questionnaires, COMD-26 questionnaire and OPMD QoL questionnaire. The results of our multivariate linear regression model were consistent with the results of Karbach et al., Tadakamadla et al.

Our study showed that age group has a significant impact in QoL in OPMDs. Patients aged 40-64 had poorer QoL than patients aged above 64. Whereas Karbach et al., Tadakamadla et al. showed that age group has no influence in QoL in patients with OPMDs (OLP, OL and Oral squamous cell carcinoma).

Patients with erosive pattern of OLP showed poorer QoL in compared to keratotic OLP. This result was consistent with Villanueva et al., Karbach et al., Zucoloto et al., Parlatescu et al., showed no significant different in OHQoL between both clinical patterns. In the other hand, Pippi et al., found high depression and lower self-control among keratotic OLP subjects in compared to erosive/erythematous type.

Our results showed that clinical periodic evaluation of lesion had a negative impact on patients QoL in compared to perform a complete Co2 laser ablation of lesion. It makes sense that surgical intervention can influence patients QoL. But, due to lack of literature comparing both approach's in regarding to patients QoL, this finding might need further investigation.

Gender, social history (smoking behavior and alcohol intake), severity of disease and previous management of disease has no influence on QoL in patient with OPMDs.

One of the limitations in our study lies in its cross-sectional design, which does not allow for identifying any causal relationship between OLP, OED and QoL. Another is due to the fact that the trial was conducted during the COVID-19 pandemic, which may have affected the result. We recommend enhancing knowledge and understanding of comprehensive management of patients with OLP and OED among dentists to improve the patient's experience and reduce oral discomfort.

## **Conclusion**

Within the limitation of our study OLP shows significant poorer QoL in compared to OED as a setting of clinical OL. Younger individuals affected with OLP, and OED exhibited higher COMD-26 scores compared to older individuals. Further, the QoL decreased as OLP disease severity increased. Future directions to investigate the quality of life among patients with proliferative verrucous leukoplakia (PVL) and whether their QoL is better or worse than patients oral lichen planus.

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## **Appendix**

### Variables

The following instruments were used to assess the patient's general QoL and specific oral health related QoL:

- The Hospital Anxiety and Depression Scale [HADS] is a brief 14-item survey that assesses anxiety and depression using general well-being questions. This instrument is widely used in medical practices. This instrument is divided into parts: the first part is seven items that assess anxiety (HAD-A). The second part is seven items that assess depression (HAD-D). The total score ranges from 0-21. A score that ranges from 0-7 points is considered normal. A score that ranges from 8-10 points indicates moderate risk of mood disorder. A score that ranges from 11-21 points indicates the presence of mood disorder.<sup>14</sup>
- Chronic Oral Mucosal Disease Questionnaire-26 [COMDQ-26] is an instrument that assess patient with chronic oral mucosal disease. This instrument is categorized into 4 different aspects: pain and functional limitation-9 items, medication and treatment-6 items, social and emotional 7-items, patient support-4 items. The total score ranges from 0-104. The higher the score, the poorer the oral health QoL.<sup>15</sup>
- Oral Potential Malignant Disorder QoL Questionnaire [OPMDQoL] is an instrument that assess Oral health QoL specifically for OPMDs. This instrument consists of 20 items categorized into difficulties with diagnosis, physical impairment and functional limitation, psychological and social well-being, effect of treatment on daily life. The total score ranges from 0-80 points. The greater the score, the poorer the oral health QoL.<sup>2</sup>