Clinical–pathologic Agreement for Oral Lesions in an Oral Medicine Setting

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Abstract

Background: Histopathological examination remains the gold standard for the diagnosis of oral mucosal lesions. To date little is known on the clinical–pathologic agreement for oral lesions diagnosed by oral medicine experts. Objective: This retrospective study attempts to quantify the clinical–pathologic agreement for oral lesions diagnosed by oral medicine experts.

Methods: Data were collected retrospectively from the medical records of all new oral medicine consultations. The clinical diagnosis provided by an oral medicine expert was compared to the histopathological diagnosis. Clinical–pathologic agreement was estimated as the percentage agreement and was measured using weighted Kappa.

Results: The most common oral lesions were oral lichen planus (34.7%), traumatic fibroma (23.4%), squamous cell carcinoma (SCC) or severe dysplasia (6.7%), mucous membrane pemphigoid (MMP) (5.7%), leukoplakia (5.6%) and squamous papilloma (4.3%). The overall clinical–pathologic agreement for all lesions had a weighted kappa of 0.81 [95%CI 0.78% to 0.85%]. The concordance for the most common oral lesions in the study population was 90.2%, with a weighted kappa of 0.88 [95%CI 0.85% to 0.92%]. The clinical–pathologic agreement for SCC/severe dysplasia was 78.7%, for traumatic fibroma 91.4%, for leukoplakia 97.4%, for oral lichen planus 93.8%, for squamous papilloma 96.7% and for MMP 65%.

Conclusions: The overall concordance between clinical and histopathological diagnosis for oral lesions was excellent. Dentists have the unique opportunity to refer patients to oral medicine experts for diagnosis and management of oral diseases. Given their expertise patients may require fewer visits for diagnostic purposes.

Keywords: Concordance; Oral lesions; Oral medicine expert

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1. Introduction

Oral medicine is defined as "the discipline of dentistry concerned with the oral health care of medically compromised patients and with the diagnosis and non-surgical management of medically-related disorders or conditions affecting the oral and maxillofacial region."(Bilde, von Buchwald, Dabelsteen, Therkildsen, & Dabelsteen, 2009) Oral medicine clinicians have broad knowledge of head and neck pathology and focus their practice on diseases of the adjacent oral-maxillo-facial complex, particularly the oral mucosa. Although oral medicine training programs are present in many countries, the overall number of available clinicians is still limited and the practice of oral medicine is largely unknown among medical and dental practitioners (Rogers et al., 2011).

Oral medicine experts use visual inspection and palpation to diagnose oral conditions in addition to perform biopsies on a daily basis for definitive diagnosis. Histopathological examination remains the gold standard for the diagnosis of oral mucosal lesions (Patton, Epstein, & Kerr, 2008). The American Academy of Oral and Maxillofacial Pathology recommends that all abnormal tissue be submitted promptly for microscopic evaluation and analysis (Melrose, Handlers, Kerpel, Summerlin, & Tomich, 2007). Knowledge gained through histopathologic examination is not only necessary for diagnosis, but it is also useful in estimating clinical behavior along with disease prognosis, and assessing the need for follow-up or additional therapy. Scalpel biopsy (both excisional and incisional) and punch biopsy are the most common techniques and usually produce the most satisfactory samples (Eisen, 1992; Oliver, Sloan, & Pemberton, 2004).

Although oral biopsy is a relatively simple procedure, it may cause pain and anxiety in patients. In 2012, Navabi et al. evaluated the pain experience of 60 patients using a 10-point visual analogue scale after an oral mucosal biopsy on the day of the biopsy and after three days following the biopsy. Forty percent of patients reported moderate pain on the day of biopsy and 58% of patients experienced no pain on the third day after the biopsy (Navabi, Salehi, Zarei, & Borna, 2012).

In 2011, Patel et al. evaluated the agreement between the clinical and histopathologic diagnoses in all clinicians, general dental practitioners, and dentists with registered postgraduate qualifications (specialists)(Patel, De Silva, Tong, & Love, 2011). The authors found that the overall concordance for both groups was 50.6%, with specialists being more accurate in diagnosing malignant or potentially malignant disorders. To date, little is known on the level of concordance achieved by the oral medicine expert' clinical diagnosis and the histopathological diagnosis. As such, we conducted a retrospective study to quantify the clinical–pathologic agreement for oral lesions diagnosed by a team of oral medicine experts.

2. Materials and Methods

The data for this study were collected retrospectively from all new oral medicine patients seen at the Unit of Oral Diagnosis at San Paolo Hospital, University of Milano from January 1, 2002, through July 31, 2012. Follow up visits were excluded for the purpose of this analysis. The scientific board of the dental hospital approved this study (exempt category; prot. 45/13).

2.1 Study population

The study population consisted of individuals who had been seen in the Unit of Oral Diagnosis for oral lesions for which a biopsy and histopathological examination was required for definitive diagnosis. Patients who reported an oral mucosal problem or who were seen by their primary care physician or other health care providers for an oral problem were referred to this specialty clinic. Patients with primarily dental problems were referred separately to another dental specialist for consultation and were excluded from this study.

At each visit patients received a full medical and dental history and had a thorough examination of the oral cavity. All clinical examinations were carried out by dental students and the final diagnosis was confirmed by oral medicine experts (two doctors) trained to recognize oral diseases according to the WHO criteria (Kramer, Pindborg, Bezroukov, & Infirri, 1980).

Oral medicine expert received formal training in the subspecialty of oral medicine. The oral exam was performed on each subject using two mouth mirrors for retraction of soft tissues. A sterile piece of gauze was used to retract the tongue. The examination procedure followed a systematic assessment of the gingiva and alveolar ridges, tongue, floor of the mouth, hard and soft palate, buccal mucosa and sulcus, commissures, lips, and labial mucosa (Scully, 1993). No adjunct screening tools were used. Patients were discharged after their condition was treated and were instructed to return for follow up as needed or at scheduled intervals depending on the type of oral disease.

2.2 Data collection

Medical records were reviewed. Clinical data was collected from the medical charts using a standardized data collection form and entered into a Microsoft Excel spreadsheet (Microsoft Corporation, Redmond, USA). Data collected included patient demographics (age, sex, date of birth, and date of first visit), whether or not a biopsy was obtained at the consultation visit, clinical diagnosis, anatomic site of the lesion (lip, tongue, floor of the mouth, buccal mucosa, gingiva, hard palate, soft palate, maxilla and mandible), and histopathological diagnosis.

2.3 Statistical Analysis

During the 10-year period, 2007 new patients with oral mucosal lesions were evaluated. Of these, 697 patients were identified as having a histologically confirmed diagnosis and were therefore included for purpose of this study. We evaluated the distribution of participant characteristics, including demographics. Descriptive frequencies were calculated to: 1) describe the distribution of clinical and histopathological diagnoses (including the anatomic site), 2) identify the most common oral lesions, and 3) determine the concordance between clinical diagnosis and histological diagnosis for the most common oral diseases.

The distribution of the most common oral lesions was evaluated by age and sex. None of the leukoplakias that were biopsied had a histopatholigical diagnosis of hyperkeratosis. As such, severe dysplasia was incorporated under the "SCC". Clinical–pathologic agreement was estimated as the percentage agreement and was measured using weighted Kappa test and 95% confidence intervals

(CIs). Weighting is used to determine the sources of disagreement between histopathological examination and clinical exam on a nominal scale with more than two categories (Brennan & Silman, 1992). The strength of agreement was assessed with the benchmarks of Landis and Koch (Landis & Koch, 1977). All statistical analyses were completed using SAS, version 9.2 (SAS Institute Inc., Cary, NC, USA).
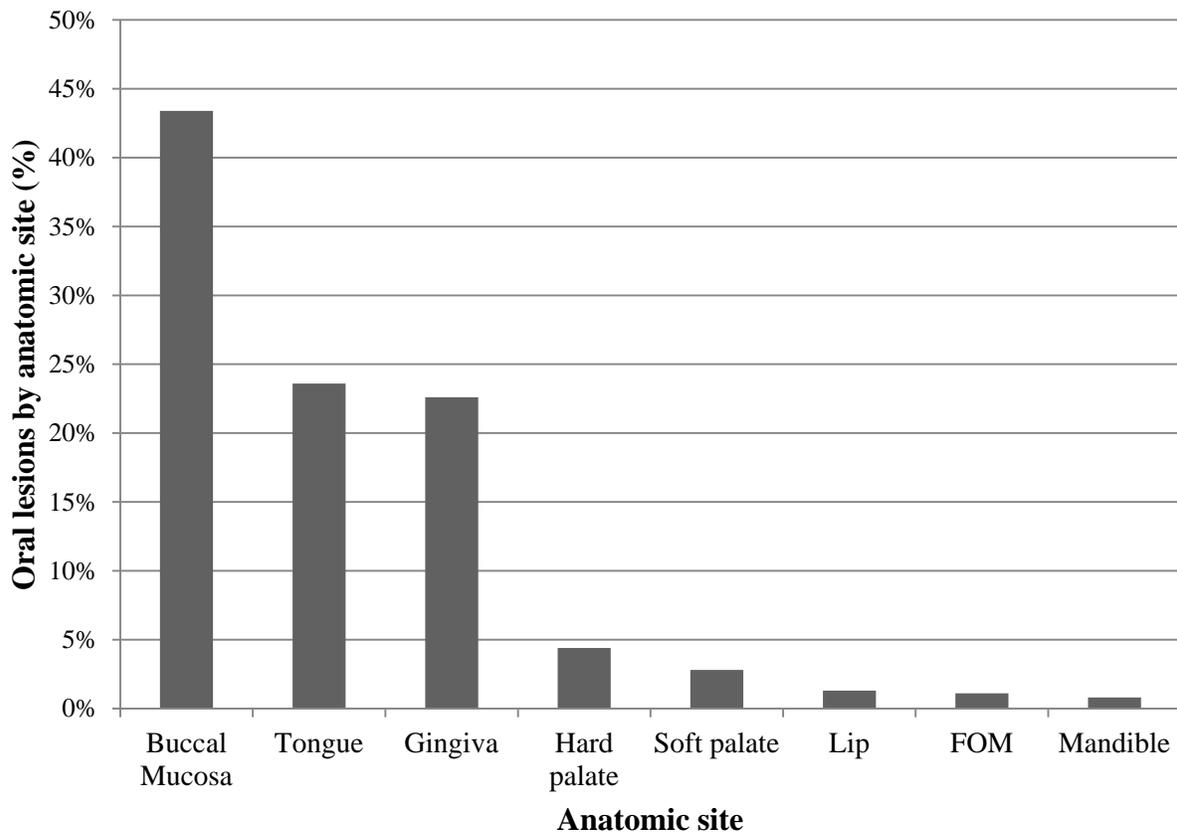
3. Results

Fig. 1. Anatomic distribution of oral lesions
Legend: FOM, floor of the mouth.

A total of 697 patients (301 men and 396 women) were included. Overall, patients ranged in age from 14 to 99 years; the median age was 60 years (interquartile range 45-70 years). Around 43% patients had lesions of the buccal mucosa, 24% had tongue involvement, 23% had gingival lesions, 4% had lesions of the hard palate, 3% had soft palate, and the remaining 1% had lesions of the lip, floor of the mouth and mandible (Figure 1).

A summary of the clinical and histological diagnosis is presented in Table 1. The most common oral lesions (confirmed by histopathological examination) were oral lichen planus (34.7%), traumatic fibroma (23.4%), squamous cell carcinoma (SCC) or severe dysplasia (6.7%), mucous membrane

pemphigoid (MMP) (5.7%), leukoplakia (5.6%) and squamous papilloma (4.3%). Oral lichen planus was more prevalent among female patients (59.9%) and people aged 45-69 (60.2%) (Table 2). Traumatic fibroma was equally present in males and females (47.8% vs. 52.2%) and was more common in people older than 45 years (84.5%). SCC or severe dysplasia had a higher prevalence in females (61.7%) and patients older than 45 years (83%).

Of all MMP patients, 70% were females and 88.9% were age 45 or older. Leukoplakia was more common in female patients (56.4%) and patients older than 45 years (89.7%). Squamous papilloma was more prevalent in males (63.3%) and in patients aged 45 or older (83.3%). The clinical–pathologic agreement for all lesions had a weighted kappa of 0.81 [95%CI 0.78% to 0.85%].

Table 1 Clinical and histological diagnosis of the oral lesions

Oral mucosal lesions (*N*=697)	Clinical Diagnosis *n (%)*	Histopathological Diagnosis *n (%)*
BARK	8 (1.1)	8 (1.1)
Erythema multiforme	1 (0.1)	0 (0.0)
Geographic tongue	4 (0.6)	2 (0.3)
HSV infection	4 (0.6)	1 (0.1)
Hyperkeratosis	12 (1.7)	16 (2.3)
Inflammatory fibrous hyperplasia	13 (1.9)	13 (1.9)
Leukoplakia*	59 (8.5)	39 (5.6)
Lipoma	0 (0.0)	4 (0.6)
Melanotic macule	15 (2.2)	11 (1.6)
MMP	28 (4.0)	40 (5.7)
Mucocele	6 (0.9)	8 (1.1)
Normal epithelium	0 (0.0)	24 (3.4)
Odontogenic infection	10 (1.4)	7 (1.0)
ONJ	5 (0.7)	4 (0.6)
Oral lichen planus	266 (38.2)	242 (34.7)
Pemphigus vulgaris	6 (0.9)	4 (0.6)
Pyogenic granuloma	1 (0.1)	3 (0.4)
SCC/severe dysplasia	37 (5.3)	47 (6.7)
Squamous papilloma	33 (4.7)	30 (4.3)
Sjogren Syndrome	13 (1.9)	17 (2.4)
Traumatic ulcer	18 (2.6)	10 (1.4)
Traumatic fibroma	154 (22.1)	163 (23.4)
Varix	4 (0.6)	4 (0.6)

Legend: BARK, benign alveolar ridge keratosis; **HSV,** Herpes Simplex Virus; **MMP,** mucous membrane pemphigoid; **ONJ,** osteonecrosis of the jaw; **SCC,** squamous cell carcinoma.
*It includes a histopathological diagnosis of mild and/or moderate dysplasia.

The overall concordance between clinical and histopathological diagnosis for the most common oral lesions in the study population was 90.2%, with a weighted kappa of 0.88 [95%CI 0.85% to 0.92%]. The clinical–pathologic agreement for SCC/severe dysplasia was 78.7%, for traumatic

fibroma 91.4%, for leukoplakia 97.4%, for oral lichen planus 93.8%, for squamous papilloma 96.7% and for MMP 65.0% (Table 3). Forty-five percent of biopsy-proven MMP cases were given a clinical diagnosis of oral lichen planus. 21.3% of SCCs/severe dysplasias had an initial clinical diagnosis of oral lichen planus or traumatic ulcer. One case of leukoplakia was diagnosed as oral lichen planus (data not shown).

Table 2 Most common oral diseases (histological diagnosis) by sex and by age

Most common oral lesions	**Sex** *n* (%)		**Age** *n* (%)		
	Female (*N*=396)	Male (*N* =301)	<45 (*N*=387)	45-69 (*N*=387)	≥ 70 (*N*=157)
Oral lichen planus	145 (59.9)	97 (40.1)	37 (15.5)	144 (60.2)	58 (24.3)
Fibroma	85 (52.2)	78 (47.8)	58 (36.0)	77 (47.8)	26 (16.2)
SCC/Severe dysplasia	29 (61.7)	18 (38.3)	8 (17.0)	24 (51.1)	15 (31.9)
MMP	28 (70.0)	12 (30.0)	4 (11.1)	19 (52.8)	13 (36.1)
Leukoplakia*	22 (56.4)	17 (43.6)	4 (10.3)	28 (71.8)	7 (17.9)
Squamous Papilloma	11 (36.7)	19 (63.3)	5 (16.7)	19 (63.3)	6 (20.0)

Legend: SCC, squamous cell carcinoma; **MMP,** mucous membrane pemphigoid.

*It includes a histopathological diagnosis of mild and/or moderate dysplasia.

Table 3 Concordance between clinical diagnosis and histological diagnosis for most common oral diseases.

Concordance		*n* (%)
Leukoplakia*		
	No	1 (2.6)
	Yes	38 (97.4)
MMP		
	No	14 (35.0)
	Yes	26 (65.0)
Oral lichen planus		
	No	15 (6.2)
	Yes	227 (93.8)
SCC/Severe dysplasia		
	No	10 (21.3)
	Yes	37 (78.7)
Squamous papilloma		
	No	1 (3.3)
	Yes	29 (96.7)
Traumatic fibroma		
	No	14 (8.6)
	Yes	149 (91.4)

Legend: MMP, mucous membrane pemphigoid; **SCC,** squamous cell carcinoma;

*It includes a histopathological diagnosis of mild and/or moderate dysplasia.

4. Discussion

We conducted a retrospective study to determine the clinical–pathologic agreement for oral lesions in new patients who were seen in consultation by a team of oral medicine experts; few studies have addressed questions on the oral medicine experts' accuracy and competencies to clinically diagnose oral diseases.

The most common lesion found in our clinic was oral lichen planus (34.7%), followed by traumatic fibroma (23.4%), SCC or severe dysplasia (6.7%), MMP (5.7%), leukoplakia (5.6%) and squamous papilloma (4.3%). Similarly, an Italian study on referrals to an Italian oral medicine practice found that oral lichen planus was present in 29.5% of the patients who received a consultation, 13.8% had a traumatic fibroma, 1.6% SCC, 13.1% MMP, 11.8% leukoplakia and 1.3% had squamous papilloma (Sardella et al., 2007).

The buccal mucosa (43%) with the tongue (24%) remained the most common affected sites in our patients. This is in agreement with previous studies on the prevalence of oral diseases in patients seen in consultation in oral medicine clinics (Farah, Simanovic, & Savage, 2008; Riordain, O'Sullivan, & McCreary, 2011). Kappa values between 0.81 and 1.00 represent an "excellent strength of agreement" (Landis & Koch, 1977).

Our findings show that the overall concordance between clinical and histopathological diagnosis for all oral lesions had a weighted kappa of 0.81 [95%CI 0.78% to 0.85%]. When the most common oral diseases were considered, the weighed kappa for agreement was even higher (0.88 [95%CI 0.85% to 0.92%]) with a clinical–pathologic concordance of 90.2%. The concordance was high for squamous papilloma (97%), leukoplakia (97%), oral lichen planus (94%), traumatic fibroma (91%), but was lower for malignancies (SCC/severe dysplasia [79%]) or vesiculobullous diseases (MMP [65%]).

A study by Williams et al. showed that general practitioners had a clinical–pathologic concordance of 56.4% (Williams, Hey, & Browne, 1997). In a similar study from Spain, the diagnostic specificity of the general dental practitioners for oral cancer detection was 86.5 and the sensitivity was 61.4 (Seoane, Warnakulasuriya, Varela-Centelles, Esparza, & Dios, 2006). Diagnostic sensitivity for oral cancer and precancer versus benign lesions was 57.8 and specificity of 53.0. The mean concordance between general dentists' diagnoses and clinical cases was poor (kappa=0.25 ± 0.14). Patel et al. reported that the clinical diagnosis of oral lesions provided by general dental practitioners had a concordance of 49.4% with histological diagnosis, while specialists in oral and maxillo-facial surgery had a concordance of 51.0% (Patel et al., 2011). In our analysis, the overall concordance was higher than the findings from other studies (Patel et al., 2011; Seoane et al., 2006; Williams et al., 1997). This high concordance could be explained by the fact that oral medicine experts are well trained to diagnose, treat and manage conditions affecting the oral and maxillofacial region (Sollecito et al., 2013).

A visit to the oral medicine expert for the diagnosis of oral mucosal diseases may require fewer visits for when compared to other providers thus reducing the costs, anxiety, and pain associated

with this procedure. However, for MMP or SCC the oral medicine experts misdiagnosed the lesions for oral lichen planus or traumatic ulcers.

As such, histopathological examination remains the gold standard for diagnosis of certain oral mucosal disorders. One important limitation to note for this study is that the histopathological examination was considered as gold standard; it might have been useful to have the slides read by at least two pathologists in a blind fashion to reduce possible biases. Also, for the cases of dysplasias it is known that the agreements among pathologists remain low. In addition only a group of oral medicine experts from a single center was included to test the clinical–pathologic agreement for oral lesions; as such, our results may not be generalizable to all the oral medicine experts.

It would have been interesting to see whether several oral medicine experts provide the same clinical diagnosis when they evaluate the same patients. Finally, not all oral lesions were included in our sample population. Larger studies may provide additional data on the clinical–pathologic agreement for oral mucosal diseases.

5. Conclusion

Oral medicine experts have a unique opportunity to diagnosis, manage and treat a wide variety of orofacial conditions. Medical doctors and dentists may refer patients to an oral medicine expert and reduce the delay in the diagnosis of mucosal, salivary gland or bone pathology (Gomez et al., 2010). Additional research on the clinical–pathologic agreement for oral lesions among oral medicine and other specialists is needed to support such initial results.

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Conflict of interest

None.

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