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ORIGINAL ARTICLE

Gustatory function and taste perception in patients with oral lichen planus and tongue involvement

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Abstract
Objectives The aim of the study was to evaluate if patients with oral lichen planus (OLP) and tongue involvement have impaired taste function and if there is an association to the perception of pain.
Material and methods The test group included patients with OLP and involvement of the tongue without treatment ($n = 20$). Control subjects had no mucosal or systemic disease affecting taste function and were matched for age and gender ($n = 20$). Patients' intraoral pain and subjective perception of taste were recorded on a visual analog scale. Taste function was assessed by means of the "taste strips."
Results Measured taste function was slightly but significantly decreased in OLP patients compared to control subjects ($p = 0.01$). Self-rated taste perception did not differ in both groups ($p = 0.8$). Post hoc analysis showed that particularly the taste quality "sour" was most affected by the OLP status ($p = 0.01$). There were no correlations between pain and subjective/objective taste perception.
Conclusion Untreated OLP subjects have lower gustatory function, which they are not aware of.
Clinical relevance Impaired gustatory function in patients with OLP may affect patient's quality of life. Further studies on larger samples sizes are requested.

Keywords Oral lichen planus · Taste · Tongue · Pain · Treatment

Introduction

Oral lichen planus (OLP) is a common chronic inflammatory mucocutaneous disease. The etiology remains unknown, but there is some evidence that it is an immunological process triggered by an antigen that alters basal keratinocytes. The degeneration of basal keratinocytes is attributed to CD8+ T-lymphocytes and the involvement of proinflammatory cytokines [1–3]. It primarily affects the adult population with an estimated prevalence of 1–2 % [4–6] and is more common in women with a female to male ratio of about 2:1 [4, 5, 7].

OLP has typical clinical features and affects multiple intraoral sites with a characteristic bilateral distribution. The presence of slender white lines (Wickham's striae) is pathognomonic. This reticular pattern is often interspersed with papules, rings, or a white plaque-like appearance. The reticular lesions are frequently accompanied by symptomatic erythematous/erosive patches or ulcerations [8–11]. The most common sites affected are the buccal mucosa followed by the tongue (dorsum and border), gingiva, palate, labial mucosa, and vermillion of the lips [11–15]. Involvement of the dorsum of the tongue is typically located at the anterior two thirds and presents as mucosal thickening with white striae and plaques or atrophy of the papillary structure. Symptoms reported are a burning sensation and pain that may compromise oral hygiene, eating, and swallowing [15–20].

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Gustatory function is provided by taste receptor cells, which are embedded in taste buds distributed throughout the tongue surface. The highest densities of taste buds and thus function are found in the front, rear, and sides of the tongue, whereas the dorsum has a little lower sensibility to gustatory stimuli [21]. Taste disorders are relatively rare compared to olfactory disorders that occur much more frequently in specialized chemosensory outpatient clinics [22]. The most frequent reasons for taste disorders are medication side effects and neurological defects including surgical damage of taste nerves and idiopathic taste alteration [23]. Quantitative taste function can be measured by means of previously described psychophysical tests [24]. Qualitative taste disorders can only be assessed by patients' own reports [23].

As OLP can affect the tongue, it would be conceivable that taste function may be disturbed. However, the literature shows only one report about gustatory complaints in OLP patients and it seems to be rare (less than 1 %) [19]. Furthermore, perceived taste function does not always reflect measured taste function [25]. Thus, the aim of this study was to assess taste perception and function in patients with OLP and tongue involvement compared to a group of healthy persons and if there is a correlation to the perception or pain.

Materials and methods

Study sample and inclusion and exclusion criteria

The prospective study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the local ethics committee of the state of Bern, Switzerland (approval number 166/13). All patients referred or in annual follow-up at the Department of Oral Surgery and Stomatology, University of Bern, diagnosed with OLP were initially eligible. Subjects were only eligible for inclusion in the study, when both clinical and histopathological criteria enabling the final diagnosis of OLP were met (Table 1) [13, 17, 26–28]. All microscopic evaluations were performed by pathologists not involved in the study adhering to strict histopathological criteria to be concomitant with the diagnosis of OLP. Only patients without an ongoing treatment for OLP were included. Patients with smell disorders; acute or chronic rhinosinusitis; head, neck, and throat diseases; and previous ENT surgeries were excluded. Furthermore, patients with medical conditions (i.e., pregnancy, diabetes mellitus) or taking medication known to induce taste disturbances or with a previous radiochemotherapy were excluded. Control subjects were recruited from the patient pool of the Department of Oral Surgery and Stomatology provided that the tongue had a normal clinical appearance. The abovementioned exclusion criteria for the test group were also applied for the control subjects. All included subjects provided written informed consent.

Clinical examination and subjective assessment

Medical, ENT, and dental history was recorded for all included subjects. A thorough intraoral examination, including examination of the dorsum of the tongue, was performed by VS or MB. An ENT examination was done by SN or HF. The clinical findings of the dorsum of the tongue were allocated to two possible phenotypes of OLP: (1) keratotic or (2) atrophic/mixed keratotic-atrophic. To record patients' intraoral pain due to OLP, a visual analog scale (VAS; ranging from 0 to 100) was filled in before any further questioning or tests. Then, subjects were instructed to fill in a second VAS scale (ranging from 0 to 100; 0 = My taste function is very poor, 100 = I have extraordinarily good taste function) to rate their own gustatory function. They also filled in a taste perception questionnaire. The first question was "Did you notice any impairment of taste since you have had a mucosal disease?". The further question was if "Food is tasting different" with four optional answers "never," "seldom," "often," and "always." This question was repeated with the same optional answers for the four different qualities of taste: "sweet," "sour," "salty," and "bitter."

Taste testing

Taste testing was performed in each subject by SN or HF using a validated test with taste strips (Taste Strips, Burghart, Wedel, Germany) [24]. It consists of filter paper strips of 8 cm with an impregnated tip area of 2 cm^2. Each

Table 1 Clinical and histopathologic criteria for the diagnosis of OLP as initially proposed by the WHO Collaborating Centre for Oral Precancerous Lesions [26] and applied in previous investigations [13, 17] and the present study

Clinical criteria	Histopathologic criteria
– Bilateral distribution of the mucosal lesions – Presence of a gray-white reticular pattern on the oral mucosa (Wickham's striae) alone or together with plaque-like, erosive, atrophic, and bullous lesion types – Exclusion of lesions suggesting a direct association/contact with a dental restoration (lichenoid reaction)	– Band-like lymphocytic infiltrate at the epithelial-stromal junction, confined to the superficial part of the connective tissue – Signs of a basal cell liquefaction – Additional but not mandatory features: spindly/"saw-tooth"-like rete ridges, civatte bodies, parakeratosis, acanthosis, increased number of intraepithelial lymphocytes

Table 2 Demographic data of the 40 subjects included regarding age, gender, and smoking habits

	Overall	Group 1 Patients with OLP	Group 2 Control subjects
Patients (*n*)	40	20	20
Age (years)			
Mean	59.53	59.75	59.3
Median (p25, p75)	58 (52.75, 64.25)	58 (53.75, 64.25)	58 (51.75, 64.25)
Minimum	43	45	43
Maximum	82	82	82
Gender (*n*)			
Female, *n* (%)	23 (57.5)	12 (60)	11 (55)
Male, *n* (%)	17 (42.5)	8 (40)	9 (45)
Smoking			
Yes, *n* (%)	4 (10)	3 (15)	1 (5)
No, *n* (%)	36 (90)	17 (85)	19 (95)

p25 25th percentile, *p75* 75th percentile

side of the anterior tongue was tested with 16 taste strips. Each quality was tested in four different concentrations: "sweet"—0.4, 0.2, 0.1, 0.05 g/ml sucrose; "sour"—0.3, 0.165, 0.09, 0.05 g/ml citric acid; "salty"—0.25, 0.1, 0.04, 0.016 g/ml sodium chloride; and "bitter"—0.006, 0.0024, 0.0009, 0.0004 g/ml quinine hydrochloride. For each side and taste, a value of 0–4 was attributed with one point given for each correctly identified taste. All scores were transferred to a table and total scores calculated for the right and left sides of the tongue.

Statistical analysis

In the control group, a total of 26 subjects were recruited initially. For further analysis, an age- and gender-matched controlled selection to the test group was performed resulting in 20 patients for inclusion. For initial data distribution, a descriptive analysis was performed using box plots. To evaluate differences of the subjective and objective taste perception (overall, "sweet," "sour," "salty," and "bitter") for the two groups, Wilcoxon rank-sum tests were performed. For detection of a potential correlation between pain and subjective/objective taste perception, Spearman's rank correlation coefficients were calculated.

All analyses were performed with the statistical software R (version 3.0.1 for Windows, Institute for Statistics and Mathematics of the WU Wien, Vienna, Austria; http://www.R-project.org). Due to the explorative nature of the study, no correction has been applied for multiple testing. Significance levels were set at $p \leq 0.05$.

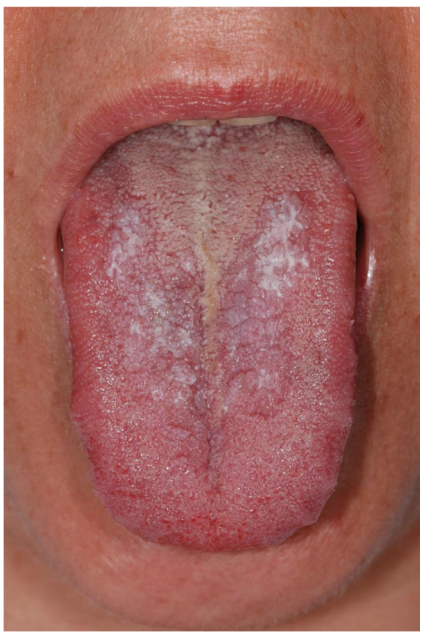

Fig. 1 Typical clinical aspect of a 55-year-old female patient with OLP and tongue involvement on the dorsum that manifests as hyperkeratotic white striae and patches

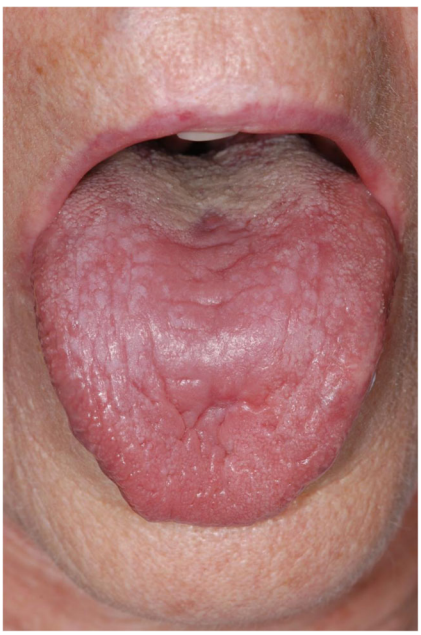

Fig. 2 Typical clinical aspect of an 84-year-old female patient with OLP and tongue involvement on the dorsum that manifests as a mixed keratotic-atrophic type

Table 3 Pain and phenotype of oral lichen planus on the dorsum of the tongue

	All patients ($n=20$)	Phenotype 1 Keratotic ($n=12$)	Phenotype 2 Atrophic or atrophic/keratotic ($n=8$)
Pain (VAS 1–100 mm)			
Mean	10.8	13	7.5
Median (p25, p75)	6.0 (0.0, 17.25)	13.5 (1.5, 18.0)	0.0 (0.0, 10.0)
Minimum	0	0	0
Maximum	50	50	36

p25 25th percentile, *p75* 75th percentile

Results

Of the 20 OLP patients included, 12 were female and 8 were male, resulting in a male to female ratio of 3:2. In the control group, the male to female ratio of 11:9 was similar. The mean age was 59 years in both groups. The demographic distribution and smoking habits of the 40 subjects is presented in Table 2. Nearly one third of the patients had atrophic or both atrophic and keratotic lesions on the dorsum of the tongue (Figs. 1 and 2; Table 3). The mean pain value (VAS 1–100) of OLP patients was 10.8.

Measured taste function was significantly different and lower in the OLP patients compared to controls ($p=0.01$, Fig. 3). Post hoc analysis showed that taste decrease was most pronounced for the taste quality sour ($p=0.01$; Table 4, Fig. 4), whereas the other taste qualities were less concerned ("sweet": $p=0.11$; "bitter": $p=0.28$; "salty": $p=0.25$). For the OLP patients, there was no significant difference ($p=0.35$) regarding the overall objective taste perception and the type of OLP lesion (keratotic versus atrophic/mixed).

In contrast to measured taste function, the mean self-reported, subjective taste perception did not differ between the two groups ($p=0.834$; Table 4). None of the subjects of the OLP group and of the control group mentioned that food was "always" or "often" tasting differently. Only four subjects of the OLP and two subjects from the control group mentioned that food "seldom" tastes different. Most of the participants (16 in the OLP group and 18 in the control group) reported to have "never" noticed any change in taste perception while eating.

There was no significant correlation between pain and psychophysical taste function (correlation coefficient −0.034, $p=0.89$). Furthermore, there was no significant correlation between pain in OLP patients and subjective taste perception (correlation coefficient −0.362, $p=0.12$).

Discussion

The present cohort study is the first to show that patients with OLP and tongue involvement have impaired gustatory function in comparison to age- and gender-matched control subjects without mucosal or systemic disease affecting taste. Measured taste function assessed with the "taste strips" in both groups exhibited that there is a significant difference ($p=0.01$)

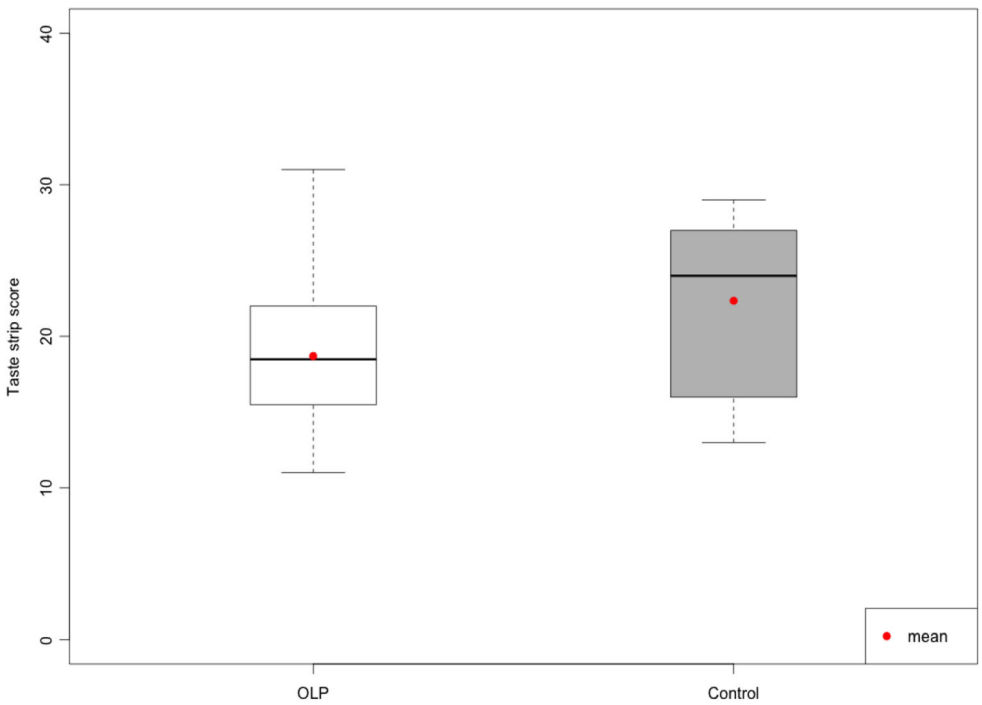

Fig. 3 Box and whisker plots exhibiting the data distribution for the measured overall taste function for OLP patients ($n=20$) compared to controls ($n=20$)

regarding the overall objective taste function between OLP and control patients and also more specifically for the taste quality "sour." To standardize the included patients with OLP and to avoid possible bias due to a variability in the clinical and histologic assessment of OLP, the WHO diagnostic criteria to obtain a more reproducible diagnosis were strictly applied in this study [26].

The disease of OLP is often asymptomatic when presenting with reticular, papular, or plaque-like features. Atrophic and erosive forms of OLP can cause various symptoms ranging from severe pain, burning sensation to recurrent bleeding [7, 9, 14, 18, 29]. Less frequently reported complaints include mucosal roughness and gingival soreness [30]. These symptoms—alone or in a combined effect—may result in an impairment of oral functions such as speaking, eating, swallowing, or oral hygiene [10, 17]. This may also have a negative impact on the quality of life of patients, which has been demonstrated in several studies [29, 31–33].

An impairment or alteration of taste function in patients with OLP prior to treatment is not regarded as a characteristic complaint. Therefore, taste alterations—subjective or objective—are not considered as relevant clinical features for establishing the diagnosis of OLP. The present data further shows that this taste impairment remains totally unnoticed by the patients since the subjective ratings were similar as for the control group. Previous studies investigating the reliability of taste self-rating [34] and patients with middle ear or tonsillar surgery [25, 35]—both surgeries prone to disrupt taste nerves—acknowledged that self-reported taste disorders do not necessarily reflect measured objective taste function. Our results add another example of a pathology with a gap between perceived and measured gustatory function. To the best of our knowledge, patients with OLP initially complaining of taste impairment have only been reported once in a study from Croatia retrospectively analyzing a group of 563 subjects with known OLP [19]. In this study, 0.5 % of the patients

Table 4 Subjective and objective taste perception in the two groups (patients with OLP and healthy control subjects)

	Overall	Group 1 Patients with OLP	Group 2 Control subjects	*p* value
Subjects, *n*	40	20	20	
Subjective taste perception (VAS 1–100 mm)				
Mean	70.70	69.80	71.60	0.834
Median (p25, p75)	71.5 (50.75, 84)	67.5 (49.75, 90.5)	72 (64.75, 80)	
Minimum	31	31	35	
Maximum	100	100	100	
Objective taste perception				
Overall score (0–32)				
Mean	20.52	18.70	22.35	**0.01**
Median (p25, p75)	20.5 (16, 24.25)	18.5 (15.75, 22.0)	24.0 (16.0, 27.0)	
Minimum	11	11	13	
Maximum	31	31	29	
Sweet score (0–8)				
Mean	6.35	6.1	6.6	0.106
Median (p25, p75)	6.5 (5.0, 7.25)	6.0 (5.0, 7.25)	7.0 (5.75, 8.0)	
Minimum	4	4	4	
Maximum	8	8	8	
Sour score (0–8)				
Mean	4.05	3.25	4.85	**0.01**
Median (p25, p75)	4.0 (3.0, 5.25)	3.0 (3.0, 4.0)	5.5 (3.0, 6.25)	
Minimum	1	2	1	
Maximum	8	4	8	
Bitter score (0–8)				
Mean	5.15	4.8	5.5	0.278
Median (p25, p75)	6.0 (3.0, 7.0)	6.0 (2.75, 7.0)	6.0 (4.75, 7.0)	
Minimum	0	0	0	
Maximum	8	8	8	
Salty score (0–8)				
Mean	5.125	4.85	5.4	0.253
Median (p25, p75)	5.0 (4.0, 6.0)	5.0 (3.75, 6.0)	6.0 (4.0, 6.25)	
Minimum	2	2	2	
Maximum	8	8	8	

Values in bold indicate statistically significant findings

p25 25th percentile, p75 75th percentile

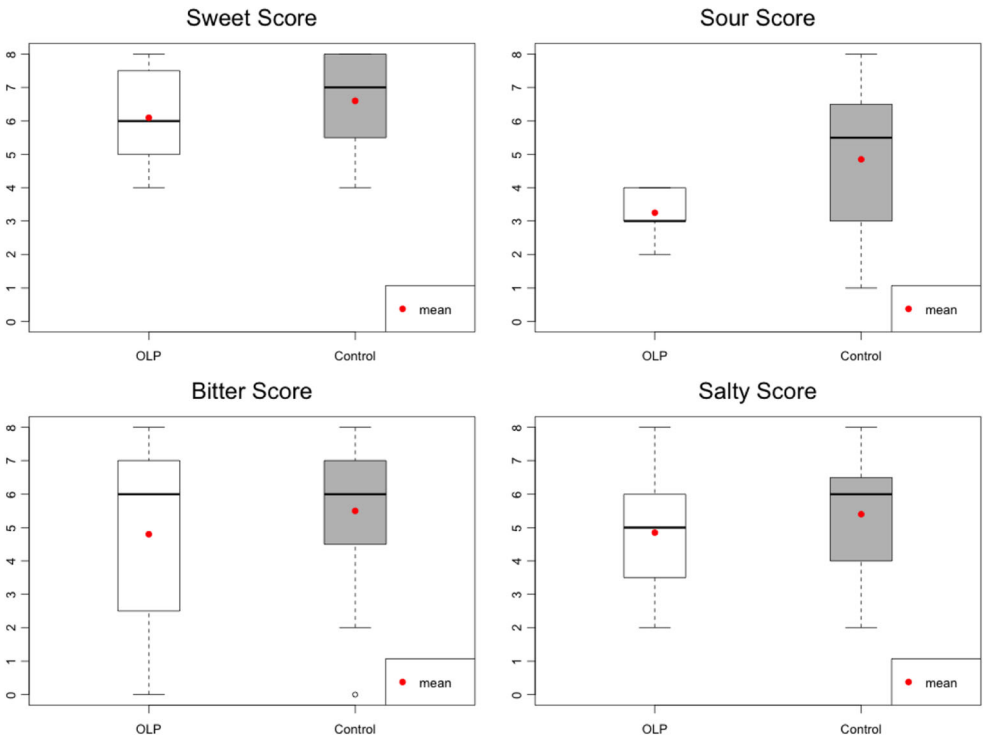

Fig. 4 Box and whisker plots exhibiting the data distribution for the specific taste qualities "sweet," "bitter," "sour," and "salty." Only for the perception of "sour" was there a significant difference between OLP and control patients ($p = 0.01$)

complained of an altered taste. Based on our observations, it would not be surprising that, if the authors had tested gustatory function, they might have found a higher percentage of taste impairments. In both groups evaluated in the present study, most of the subjects, irrespective of the presence or absence of OLP, had "never" noticed any change in taste perception while eating (16 in the OLP and 18 in the control group). Thus, without specifically addressing taste disorders using an objective assessment method, this symptom would not have been diagnosed. This further emphasizes that the only way of drawing an accurate picture of taste function is to measure it using standardized methods. Whether taste impairment is an important issue for OLP patients or even affects quality of life needs to be addressed in future studies.

In the present study, healthy subjects exhibited higher scores than OLP patients for measured taste function. It has to be emphasized that this finding was seen in subjects prior to active treatment, as taste alterations have been frequently reported during treatment of symptomatic OLP due to side effects of different pharmaceutical agents tested [36–39]. Nevertheless, regarding the limited number of patients included in the present investigation (20 patients each in the test and control groups), the findings have to be interpreted with caution. Furthermore, the statistical significance can be regarded as borderline ($p = 0.01$) and needs to be validated with a larger sample size. Finally, it is not clear whether taste alterations were present as a result of the tongue involvement due to OLP and the concomitant damage of the gustatory receptor cells in the taste buds alone, or if there also are taste alterations in patients with other mucosal sites affected by the disease. Therefore, future studies are needed including patients with known OLP with and without involvement of the tongue to assess the clinical significance of taste alterations as a diagnostic factor or means to evaluate the effectiveness of the therapy in the course of the disease.

The main causes of taste disorders reported in the literature are head trauma, infections of the upper respiratory tract, exposure to toxic substances, iatrogenic causes (e.g., dental treatment/surgery or exposure to radiation), side effects of pharmaceutical agents, and the "burning mouth syndrome" [40]. Other more infrequent causes of taste disorders include tumors, bulimia, hypothyroidism, Cushing's disease, diabetes mellitus and liver disease, poor oral hygiene, and the use of mouth rinses. Still, many cases of taste dysfunction have to be categorized as idiopathic [23]. Oral mucosal diseases are rarely mentioned as causes for taste alterations [41] and mainly refer to dry mouth or problems related to removable dentures.

Conclusions

Based on the findings of the present investigation, the following statements can be made:

- Untreated OLP subjects with involvement of the tongue showed significantly less overall gustatory function as assessed using objective testing.

- Regarding the different taste qualities, only the gustatory function of "sour" was significantly different between the two groups evaluated.
- Although the patients have lower taste function, they are not aware of it.
- Whether or not an impaired gustatory function is a typical finding for patients with OLP in general or only for patients with involvement of the tongue needs to be addressed in future studies with larger sample sizes.

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Compliance with ethical standards The study was approved by the local ethics committee of the state of Bern, Switzerland (approval number 166/13). All procedures in this prospective study were conducted in accordance with the Declaration of Helsinki (1964) and its later amendments.

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent Informed consent was obtained from all individual participants included in the study.

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