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Introduction

- OSCC accounts for about 90% of all oral malignancies.
- Well-known risk factors are tobacco, alcohol, betel quid ingestion, malnutrition as well as viral infections.
- Bacterial and viral infections may also induce a chronic inflammation with the potential for malignant transformation. Carcinogenesis(癌變) represents the end point of a cascade in which bacterial toxin, inflammatory factors and mediators cause direct or indirect DNA damage.
- Chronic periodontitis is caused by G (-), anaerobic bacteria.
 - Microbial toxins, proteases and endotoxins
 - Inflammation stimulates further excretion of mediators like prostaglandin E2, interleukin-1, -6, -8, -17, TNF and collagenases .
- Clinical manifestations are **increased gingival pocket depth with loss of gingival attachment and destruction of alveolar bone**, abscess formation and increased teeth mobility with subsequent teeth loss.
- 因發炎反應產生的毒素被發現對細胞造成惡性轉變，加上慢性牙周病很常見，抗發炎的治療又具有抑制惡性疾病的效果，於是臨床上有了 OSCC 和慢性牙周病的關聯似乎是相關的假定。
- 這兩者的關聯經由放射學影像的比較(bone loss)，及從口腔衛生、菸與酒精的攝取來分類。

Materials and methods

Patients

- A group of patients with OSCC and a control group, each treated in our department between 01/2002 and 12/2010, were examined retrospectively in the time between 01/2011 and 01/2012.
- The inclusion criteria(受試者納入條件) were as follows: (1)**Untreated, primary OSCC** limited to the area of periodontitis with preoperative panoramic x-ray (2)At least 6 remaining teeth (3)No other malignant tumors beside the oral cavity (4)No inflammatory diseases of the jaws as well as autoimmune disorders or infectious diseases (5)No prior intake of medication affecting the periodontium (6)No pregnancy (7)No trauma or fractures affecting the periodontium prior evaluation and informed consent.
- Patients in the control group had to be without malignant diseases in and beyond the oral cavity. All other criteria were the same as in the OSCC-group.

Radiological evaluation

- Radiological signs were evaluated in a **blinded manner** by one trained observer.
- Bone loss of **non-retained teeth** was determined by panoramic x-ray with software SIDEXIS XG.
- Two vertical lines parallel to the axis of tooth at **the CEJ to the crestal bone**

were drawn at the M & D aspect of each tooth. Horizontal lines orthogonal to the prior characterized vertical lines were drawn at the M & D CEJ. Distance between the cross point of each vertical and its horizontal line to the **crestal bone** specified the respective bone loss. The **lower edge of the filling** served as reference point if the CEJ was not visible.

4. Alveolar bone loss of **less than 2 mm** is considered as **healthy periodontium** .
5. A second examiner reviewed the calculations in order to assure the reproducibility.

Questionnaire

1. Data with regards to:
 - (1) **Age, gender, body weight and height, marital status and level of education.**
 - (2) **Habitual oral hygiene(刷牙漱口口水牙線), date of the last dental examination, gingival bleeding, halitosis, periodontal treatment, dental prosthesis.**
 - (3) **Tobacco and alcohol** use and were investigated
 - (4) Stress before examination(visual analogue scale)

Statistics

1. Absolute and relative frequencies were calculated.
2. Categorical data were visualized via bar charts, consistent data via boxplots. The influence of **categorical variables** was shown with chi-square tests 卡方檢定 and cross tables.

Results

Patients(A total of 301 patients were included.)

OSCC: 178 (F: n□=□56, M: n□=□122; mean age: **60** years). gender ratio: 2.1

Control: 123 (F: n□=□65, M: n□=□58; mean age: **57** years). gender ratio: balanced

Table 1

Location of OSCCs

Location

Mouth floor next to alveolar bone	n = 44 (25%)
Tongue next to alveolar bone	n = 41 (23%)
Alveolar bone mandible	n = 36 (20%)
Alveolar bone maxilla	n = 9 (5%)
Palate next to maxillary alveolar bone	n = 7 (4%)
Cheek next to alveolar bone	n = 6 (3%)
Multiple locations including proximity of alveolar bone	n = 35 (20%)

Location of OSCCs

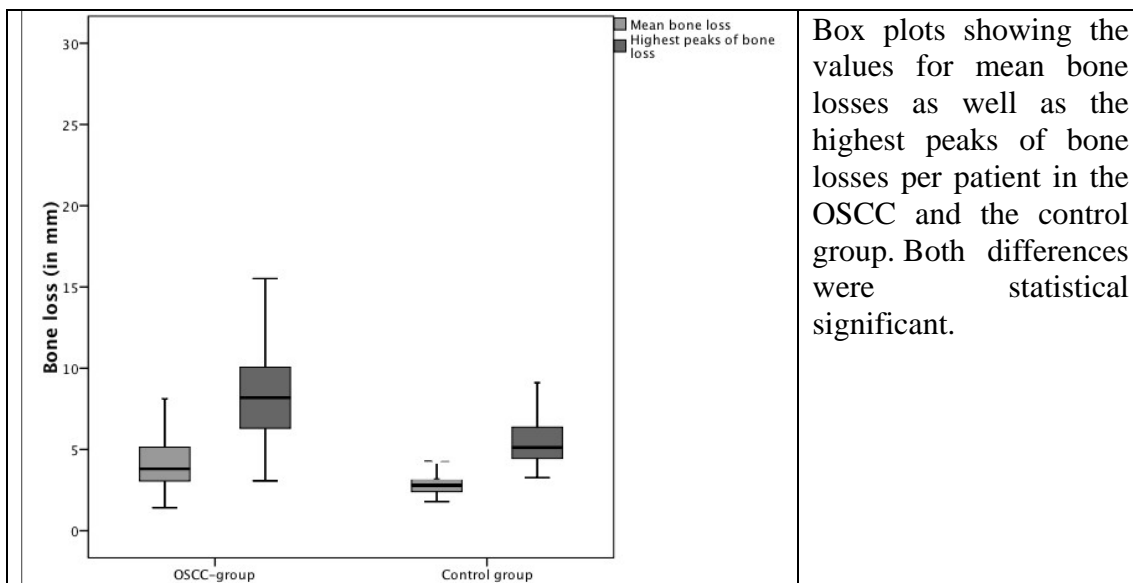
Univariate analysis

Radiological evaluation

Mean bone loss	
OSCC: 4.3 mm	Control: 2.9 mm

Highest peaks of bone loss	
OSCC: 8.6 mm	Control: 5.5 mm

Figure. 1



1. In 46 OSCC patients (26%), **the most distinct bone loss** was observed in **direct proximity to the malignant tumor**.
2. Whereas the highest total bone losses were seen from the **postcanine region (67%) up to the second molar** in all quadrants, the **highest frequency** of bone loss were in the precanine (17%) followed by the canine (10%) and the postmolar region (6%). This tendency was observed in both groups.

Questionnaire

1. 178 位 OSCC 病人裡, 40% 否認腫瘤復發, 15% 死亡, 6% 拒絕填寫問卷。整體來說, 39% 的 OSCC 病人和 100% 的對照組有良好反應。
2. 兩組的 BMI 值與婚姻狀態是相似的; OSCC 的病人相對下教育程度較低。
3. 對照組的刷牙頻率及使用牙線較高; OSCC 則是較常使用漱口水, 接受牙周病治療的次數較低, 其他牙科治療也較低。對照組喝較多的酒; OSCC 則是較常抽菸。

Table 3

Variables of the multiple logistic regression models together with each Odds Ratio (OR), 95% confidence interval and p-values

Variable	OR (95% CI)	p-value
Gender	0.7 (0.3-1.5)	0.33
Age	1 (1-1.1)	0.4
Teeth with caries	1.3 (0.8-2.2)	0.38
Teeth with fillings	0.9 (0.9-1)	0.09
Missing teeth	1 (0.9-1)	0.16
Mean bone loss	2.4 (1.5-3.8)	<0.001
Periodontal treatment	0.2 (0.1-0.5)	<0.001
Alcohol	1 (0.9-1)	0.28
Tobacco/pack years	1 (1-1.1)	<0.001

Multivariate analysis

1. **Gender, age, decayed, missing & filled teeth, bone loss as well as prior periodontal therapy, tobacco and alcohol abuse**, the radiological parameter “**mean bone loss**” was identified to be an **independent risk factor** for the presence of OSCC.
2. **Smoking had a significant but clinical not relevant effect** on the OSCC incidence.

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Discussion

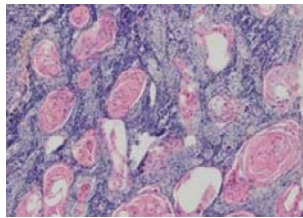
1. 早期診斷與初步預防對病人是關鍵的，延遲診斷可能導致罹病及致死率上升。臨床上，短期的回診對 OSCC 高風險的患者是有益的。
2. 除了普遍接受的菸與酒外，細菌感染與黏膜發炎也被視為致癌因子。
3. The **major limitation** of this study that **only** radiographic features were assessed. Further limitations are the **low response rate of the questionnaire** and the **significant higher number of males** in the test group.
4. In the present investigation “mean” and “highest” **bone loss** could be confirmed in univariate and multivariate analysis as **independent risk factor for OSCC**. As the alveolar bone resorption is a very slow progress in general, it can be hypothesized that there was a **chronic periodontitis prior to cancer diagnosis**. This underlines the high clinical relevance to **treat oral chronic inflammations** and is in accordance to the study of Tezal et al.
5. Possible bone loss due to **spreading of the cancerous lesions**(而非發炎造成) has to be taken into account as well.
6. A general association between inflammatory processes and malignant tumors is known. Parkin recently quoted that nearly 18% of all **malignant diseases** worldwide are possibly caused by **inflammation**.
7. 慢性牙周病為 G(-)及牙菌斑造成的慢性發炎，增效(Synergistically)的病毒環境可能導致 **deep periodontal pockets**。
8. An association between chronic periodontitis and OSCC is explainable by **direct toxic effects** of microorganisms and their products as well as through activated inflammatory cells. (發炎反應中的環氧核酶-2 可能造成 periodontal attachment 減少)
9. In addition to the positive correlation between chronic periodontitis and OSCC, we obtained a hint that **periodontal therapies including mechanical scaling and antimicrobial therapies**(抗生素治療) may have a protective impact on OSCC incidence.
10. 藉由 scaling and root planning 機械式清除牙齦上與下的牙菌斑可削弱發炎反應並穩定疾病。
11. In the multivariate regression model, neither dental hygiene, tobacco, alcohol, nor concomitant diseases could be found to be associated with OSCC. Though, **smoking** was confirmed to be a factor **associated with OSCC** in **univariate analysis** with poor clinical relevance within the multivariate regression model.

Conclusions

1. Association between chronic periodontitis and OSCC is completed by a possible

beneficial effect of periodontal therapy that may possibly inhibit the occurrence of OSCC.

- Due to high frequency of periodontal diseases, this could be of **high clinical relevance**. Present data was gathered within **retrospective setting** and a **low response rate** to the questionnaire, further prospective clinical studies are needed.

題號	題目
1	慢性牙周炎 (chronic periodontitis) 和一些 risk factors 有所關聯，下列何者尚未證實有重要的關聯性？ (A) 系統性疾病例如糖尿病 (diabetes mellitus) (B) 遺傳學 (genetics) (C) 營養缺乏 (nutritional deficiencies) (D) 環境壓力 (stress)
答案(C)	出處：100 年第二次高等考試, 牙醫學(三)
題號	題目
2	根據顯微鏡的發現 (如下圖)，病患的口腔病灶的病理診斷為鱗狀細胞癌 (squamous cell carcinoma)，此癌症屬：  (A) 分化良好 (well-differentiated) (B) 中度分化 (moderately-differentiated) (C) 分化不良 (poorly-differentiated) (D) 無法判斷
答案(A)	出處：102 年第一次高等考試, 牙醫學(二)