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# Relation between Chronic Periodontitis and Prevalence of Head-Neck Carcinoma in Association with Quality of Life*

SUMMARY

***Background and Aim**: Substantial evidence supports an association between chronic infections/inflammation, and cancer. The aim of this study was to assess the effect of chronic periodontitis on head and neck squamous-cell carcinoma (HNSCC). **Materials and Methods**: The study population consisted of 46 patients, divided into two groups. Cases were patients diagnosed with primary HNSCC (n=26). Controls were all patients seen during the same period of time but negative for malignancy (n=20). The severity of periodontitis was assessed through clinical determination of the bleeding index, periodontal index, tooth mobility degree and alveolar bone loss (ABL) on standardized panoramic radiographs. All patients were asked to fill in a questionnaire regarding aspects of quality of life before the diagnostic was established. **Results**: Each millimetre of ABL was associated with >4-fold increased risk for HNSCC. The strength of the association was greatest in the oral cavity, followed by the oropharynx and larynx. The association persisted in subjects who never used tobacco and alcohol. Patients with periodontitis, whose bleeding and periodontal indices and tooth mobility values were higher, were more likely to have poorly differentiated oral cavity SCC than those without periodontitis (32.8% versus 11.5%; P = 0.038). The patients in the study group had higher values regarding the questionnaire points compared to those in the control group. **Conclusions**: This study suggests that chronic periodontitis is a risk factor for the development of HNSCC. These results have implications for practical and improved strategies for prevention, diagnosis, and treatment of HNSCC.*

**Keywords:** Chronic Periodontitis; Carcinoma, Head and Neck; Alveolar Bone Loss; Bleeding Index; Periodontal Index; Tooth Mobility; Quality of Life

**Diana-Cristala Nitescu[1], Sorina Solomon[1], Irina Ursarescu[1],IoanaMartu, Cristian Martu[2], Silvia Martu[1]**

[1]Periodontology Department, Faculty of Dental Medicine, „Gr.T.Popa"UMPh, Iaşi, Romania
[2]ENT Department, Clinical Rehabilitation Hospital, Faculty of Medicine „Gr.T.Popa"UMPh, Iaşi, Romania

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## Introduction

Chronic periodontitis is a bacterial inflammatory disease in which the maintenance and sustenance tissues of the tooth in its respective alveolar socket are destroyed. Through migration of the attachment epithelia apically and, at the same time, loss of alveolar bone, the teeth become mobile and, ultimately, are avulsed. The periodontal disease represents one of the major causes for tooth loss in adults. The etiologic factor of this disease is represented by bacterial plaque and, moreover, of the presence of gram-negative anaerobe or optionally anaerobe bacteria of its constitution. Periodontitis is the result of local inflammatory bacterial processes, constant liberation of bacteria and inflammatory biomarkers into saliva, crevicular fluid and blood stream of the patient. Thus, the quantity of pro-inflammatory cytokines and periodontal pathogens that end up in the blood stream through micro-ulcerations within the sulcus, reach sites at a distance from where they can affect the general status of the patient.

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Cancer is a worldwide problem, with over 12 million newly diagnosed cases in 2008, of which 985 200 were reported to be located in Eastern and Central Europe. Malignancies occupied first place in developed countries and second place in developing countries from the mortality rate point of view[1].Globally, the prevalence of periodontal disease in the adult population can reach up to 90% after a study published in 2005 by Pihlstromet al[2].

There are several studies that prove the inter-relationship between periodontal disease and some systemic diseases in the sense that the treatment of one leads to the amelioration of the other[3-6], and some studies that sustain the relation between cancer and chronic inflammation[7-9].

The morbidity and mortality of head and neck squamous-cell carcinoma (HNSCC) have high values even to this day, regardless of how complex the cancer treatment is. Thus, the aim of this study was to further understand the aetiology, risk factors and interactions between the risk factors in order to develop new views on the cancerous treatment, to complement the therapy used presently and to understand the impact these afflictions have on the quality of life of patients.

## Material and Methods

Our study comprised 46 patients investigated at the Clinical Hospital of Recovery from Iasi, Romania, ENT section, in the period between January 2013 and June 2014. The subjects were split into 2 groups. The first group, the cases, consisted of 26 patients diagnosed with primary HNSCC and the second group, the controls, consisted of 20 malignancy-free patients. All patients included in this study were investigated in the same period of time by a single examiner to exclude error in this sense.

The cases (n=26) consisted of newly diagnosed primary HNSCC patients who fulfilled all the inclusion criteria. The carcinoma diagnosis was generated in accordance to the clinical examination findings, following the TNM staging (primary tumour size, cancer affected lymph nodes and the existence or absence of metastasis). The squamous-cell carcinoma localizations were represented by: oral cavity (floor of the mouth, gingiva, hard palate, buccal mucosa, retromolar area and other regions of the oral cavity), oropharynx (base of the tongue, soft palate, tonsil region and oropharynx) and larynx.

The controls (n=20) comprised patients examined at the same time with the cases, but who were not diagnosed with head and neck or systemic cancer. Patients in the control group were diagnosed with benign tumours (cysts, hyperplasia, lipoma, mucocellae), traumatic lesions, chemical burns, allergic reactions. However, we excluded patients that presented a local pathology that was associated with periodontal pathology.

We chose to exclude patients that had other systemic diseases that could interfere with the evolution of the periodontal disease, total edentulous patients, those younger than 25 and, also, patients that had a history of malignancies for which they were treated, purely surgically or in association with radio/chemotherapy. The patients with an immunocompromised status were also excluded for the reason that the results regarding the periodontal disease might have been influenced, as well as patients with autoimmune conditions (pemphigus, lupus, herpetiform dermatitis). In order to ensure homogenous data and results, we have also excluded patients with some localizations of oral cancer (lip cancer, salivary glands, mandible and maxillary, rhino-pharynx).

Each patient was asked to fill in a questionnaire that qualified a series of aspects related to quality of life. In the questionnaire we included general data of the patient and the date at which the filling in was done, questions regarding the level of pain endured by the patient, swallowing, whether there were any modifications of the senses, problems regarding speech, mental status and level of social contact of the patient. To each sub-point we attributed values between 0 and 5, 0 representing no complaints and 5 high complaints and a low quality of life.

The analysis of the status of the periodontal disease was done with the help of standard panoramic radiographs that were done in the moment of patient admission, and before diagnostic and the commencing of treatment. We have analysed quantitatively the alveolar bone loss (ABL))by measuring on the ortopantomographs in mesial and distal sites of the present teeth. This method of evaluation of the status of periodontal disease is an established one and frequently used in literature[10,11]. At the same time, we determined the number of absent teeth on the x-rays of each patient.

During clinical examination of the subjects of both groups, we evaluated the bleeding index and the periodontal index. The measurements were done on Ramfjord teeth (#16, #21, #24, #36, #41 and #44) in 6 points (3 buccal and 3 oral). The data was gathered on periodontal observation papers in the moment of evaluation of the patients. The instruments used included: WHO periodontal probe, standard dentistry consultation kit (mirror, forceps and dental probe). Before the measurements, we have isolated the oral field with 6 cotton rolls in order to avoid contamination of sites and to optimize visibility. All measurements were done by a single examiner.

Other variables taken into account in both groups were obtained from the hospital medical history documentation and included age (in years), gender (female, male), marital status (married, single, divorced, separated), smoking status (number of cigarettes per day) and alcohol consumption (number of glasses per day, never or occasionally).

## Results and Discussion

The statistical analysis of the 2 lots showed that the subjects in the study group (which had HNSCC) were older, smoked more, consumed more alcohol, presented a higher number of missing teeth and ABL had higher values than in the cases of the control group. The bleeding and periodontal index were also higher within the study group. Correlating the lifestyle of patients with HNSCC and clinical examination, we could highlight the fact that smoking more and the consumption of more alcohol in these patients, along with the presence of cancer in the territory, could aggravate the oral status in the sense of a higher number of missing teeth and higher values of bleeding index and periodontal index. It is demonstrated that smokers had a higher prevalence of periodontitis than non-smokers and the number of periodontal pockets deeper than 4 mm was higher than in non-smokers, a fact that has already been reported in literature[12]. We must, however, take into consideration psychological particularities related to these cases. The questionnaire regarding quality of life indicated the fact that patients in the study group had an altered mental status compared to patients in the control group (Fig. 1). This can be correlated to the results of the clinical and para-clinical examination, forming a vicious cycle in which the patients of the study group seemed to be in.

Even though the senses did not present significant modifications, the patients accused pain and difficulty in swallowing, especially in the more posterior localization of oral SCC and oropharyngeal SCC (Tab. 1). De Graeffet al[13] noticed that oncological patients had a high depressive level before and after anti-tumour treatment, but that there was an improvement in the emotional function a while after treatment, probably as a result of adaption and coping processes. Also, the patients in the study group had a lower level of social contact compared to the control group patients, probably as a result of their mental status in accordance with the moment of oncological diagnosis.

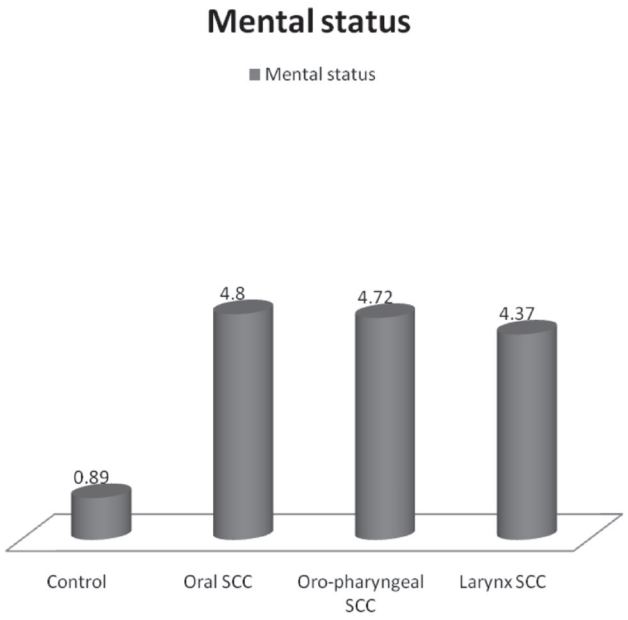


*Figure 1. Mental status of investigated patients*

*Table 1. Quality of life questionnaire - average values*

| | Controls | Oral cavity SCC | Oropharyngeal SCC | Laryngeal SCC |
|---|---|---|---|---|
| Pain | 0.78 | 4.23 | 4.19 | 3.49 |
| Swallowing | 0 | 3.73 | 4.71 | 4.38 |
| Senses | 0.65 | 1.27 | 1.35 | 0.46 |
| Speech | 0 | 3.84 | 3.96 | 4.14 |
| Mental status | 0.89 | 4.8 | 4.72 | 4.37 |
| Social contact status | 1.63 | 3.58 | 3.76 | 3.87 |

The risk factors for oral cancer include smoking, alcohol consumption and poor nutrition, family history, low socioeconomic status, and certain viral infections, such as infections with the human papilloma virus[14,15], as well as poor oral hygiene[16]. The association between periodontitis and poor oral hygiene can be related to other risk factors like smoking, alcohol, diabetes and poor nutrition, thus generating an inter-relationship between these factors. Poor oral hygiene is a well-known factor in the etiopathogenesis of periodontal diseases, allowing colonization of bacteria and disturbing the balance in the sulcus. These microorganisms implicated in the genesis of periodontitis lead to destruction of the profound and superficial periodontium, generating friability in the local tissues and blood vessels. These bacteria along with the bacterial products and pro-inflammatory cytokines end up in the blood stream. Thus oral microorganisms can be implicated in the aetiology of oral cancer[17].

The relation between ABL and smoking was significant. The association was weaker between ABL and HNSCC in current smokers (OR 2.85) compared with former smokers (OR 7.59) and never smokers (OR 5.96). Oral cancer is one of the top ten most common types of cancers in the world, representing approximately 7% of the total number of malignant tumours[18,19]. It is known that smoking, alcohol consumption and betel quid chewing have a synergic effect: in Taiwan, those who combine all these 3 habits exhibit a 123-fold incidence of oral cavity cancer than those who do not have any of the habits[20]. Alcohol consumption did not represent a significant factor in our study, the association between ABL and HNSCC in the 2 groups being similar: alcohol users (OR 4.45) and non-alcohol users (OR 4.31).

Out of 26 patients from the cases: 10 were diagnosed with oral cavity SCC (38.4%), 11 with oropharyngeal SCC (42.3%) and 5 with laryngeal SCC (19.2%). The patients with oral cavity SCC had a higher percentage of well differentiated tumours in comparison to the patients with oropharyngeal and laryngeal SCC. On the other hand, the patients diagnosed with oropharyngeal SCC had a higher frequency of weak differentiated tumours and were younger compared to the other 2 carcinoma localizations. Moreover, all patients with laryngeal SCC were current smokers. After a statistical analysis, we found that chronic periodontitis was generally associated with HNSCC, but also with each type of SCC in turn, and after adjustment for the other variables taken into consideration in this study (gender, marital status, smoking, alcohol consumption, age and absent teeth) we found that each millimetre of ABL were associated with 4 fold increased risk of developing HNSCC (OR 4.36). Clinically, all patients who were diagnosed with oral cavity SCC, oropharyngeal SCC and laryngeal SCC had higher periodontal index values compared to the controls, the index having the highest values in patients with oral cavity SCC. Association was stronger for oral cavity SCC (OR 4.52) compared to oropharyngeal SCC (OR 3.64) and laryngeal SCC (OR 2.72). The absence of teeth was significantly associated with SCCHN; however, after adjustment for periodontal disease history and other variables, the association lost its statistical significance.

Other studies support the fact that tooth loss is a surrogate marker of periodontitis; however, the aetiology of missing teeth is not just limited to periodontitis[8,21]. Divariset al[22] confirmed the fact that dental mobility is a more certain parameter for quantification of periodontitis in relation with HNSCC in comparison to absent teeth. The patients in the study group had dental mobility, especially in teeth 16 and 41. Thus, dental mobility generally had higher values in the lateral maxillary area and in the anterior mandibular area. This predilection for certain areas can also be explained by local anatomical particularities regarding the disposition and quantity of alveolar bone. Most patients presented missing teeth in the lateral mandibular region, a fact also confirmed on panoramic radiographs.

Overall, periodontal history was not associated in a significant manner with tumour staging and differentiation degree. However, patients with a periodontal disease history, who presented higher values of the bleeding index, periodontal index and in correlation with high values of dental mobility, had a higher percentage of weakly differentiated oral cavity tumours in comparison with patients who did not have a periodontitis history (32.8% versus 11.5%, $p$=0.038).

## Conclusions

Our study suggests that chronic periodontitis is a risk factor for HNSCC. Patients affected by cancer in the oral, oral-pharyngeal and laryngeal regions had a lower quality of life through alteration of mental status, pain, swallowing and lower social contact than those without cancer. These results have implications for practical and safe strategies in prevention, diagnosis and treatment of HNSCC.

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Correspondence and request for offprints to:

Diana-CristalaNitescu
„Gr.T.Popa" UMPh
Faculty of Dental Medicine
Periodontology Department
Iași, Romania
E-mail: cristala.nitescu@gmail.com