

STUDY REGARDING THE ASSOCIATION BETWEEN CHRONIC PERIODONTITIS AND THE PREVALENCE OF HEAD-NECK CARCINOMA

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ABSTRACT

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). **Material 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. **Results and discussions:** Each millimeter of ABL was associated with >4-fold increased risk of 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). **Conclusions** This study suggests that chronic periodontitis is a risk factor for HNSCC. These results have implications for practical and improved strategies for prevention, diagnosis, and treatment of HNSCC.

Keywords: chronic periodontitis, head and neck carcinoma, alveolar bone loss, bleeding index, periodontal index, tooth mobility

INTRODUCTION

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. Thus, malignancies occupied first place in

developed countries and second place in developing countries from the mortality rate point of view [1]]. 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 is to further understand the etiology, risk factors and interactions between the risk factors in order to develop new views on the cancerous treatment and to complement the therapy used presently. There are several studies that support the relationship between cancer and chronic inflammatory processes [2, 3, 4].

On the global scale, the prevalence of periodontal diseases reaches up to 90% of the adult population [5] according to a study published in 2005. Chronic periodontitis is a chronic inflammatory disease that leads to epithelial attachment loss and its migration towards the apical extremity of the root, the formation of periodontal pockets and the loss of alveolar bone around the tooth which, in turn, is a major cause for tooth loss in the adult population. The etiological factor of periodontal diseases are represented by the Gram-negative, anaerobe bacteria located in the dental biofilm. Periodontitis is the result of bacterial loads and inflammatory biomarkers constantly being released into the saliva and into the blood stream. In this way, periodontal pathogens and pro inflammatory cytokines reach distant sites of the body, thus affecting the general health status of the patient. There are various studies that support the inter-relationship between periodontal disease and some systemic disorders in the sense that the treatment of one will lead to the amelioration of the other [6, 7, 8, 9].

MATERIAL AND METHODS

Our study included a number of 46 patients investigated at the Clinical Hospital of Recovery from Iași, Romania, ENT section, in the period of time between January 2013 - June 2014. The subjects were split into two groups. The first group, the cases, consisted of 26 patients diagnosed with primary head and neck squamous-cell carcinoma 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 calibrated examiner.

The cases (n=26) consisted of newly diagnosed patients with primary head and neck carcinoma who fulfilled all the inclusion criteria that were examined during the time of the study. 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 we included in this study 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 control group (n=20) included patients examined at the same time with the cases, but were not diagnosed with head and neck or systemic cancer, these patients also fulfilling the inclusion criteria. Patients in the control group were diagnosed with benign tumours (cysts, hyperplasia, lipoma, mucocel), traumatic lesions, chemical burns, allergic reactions etc.

However, we excluded patients that had a pathology which could be associated with periodontal disease (periodontal traumas, congenital anomalies, genetic disorders etc) in order to reach significant results in our study.

The exclusion criteria used to build the two groups referred to patients that did not have other systemic disorders that might have interfered with the evolution of the periodontal disease, total edentulous patients, patients younger than 25 and patients who had a history of malignancies and oncologic treatment. We also excluded immunocompromised patients (HIV

infections/ AIDS, amiloidosis, chemotherapy) and patients that presented oral lesions associated with autoimmune diseases (like pemphigus vulgaris, cicatriceal or bullous pemphigoid, dermatitis herpetiformis, lupus erythematosus). Considering the necessity for homogeneity within gathered data and derived results, the exclusion of patients with particular localizations of oral cancer was necessary: lip carcinoma, salivary gland carcinoma, maxillary and mandible bone carcinoma, nasopharynx.

The clinical examination of the subjects from both the control and the study groups consisted of determining the bleeding index, the periodontal index and the degree of mobility. The measurements for these indices was done on Ramfjord teeth (16, 21, 24, 36, 41 and 44) and the probing consisted of 6 probing sites for each of those teeth: 3 sites on the vestibular face (mesial, central, distal) and 3 sites on the oral face (mesial, central, distal). The clinical dental mobility was determined using dental pliers (Dumitriu technique) and measured in mobility degrees. The data was consigned in periodontology observation charts elaborated during the patient evaluation. The instruments used during clinical determinations were: WHO periodontal probe, standard dentistry consultation kit (dental mirror, dental pliers, dental probe). The determination field was isolated prior to the determinations by using a total of 6 cotton rolls per patient placed buccally for the prevention of saliva contamination and insuring optimal visibility. All evaluations were done by a single examiner to exclude error in measurement as much as possible.

The analysis of periodontal disease in all patients consisted of a quantitative analysis of alveolar bone loss (ABL) on orthopantomographs taken from all patients when they were first admitted, before oncologic diagnosis and before any treatment

had been prescribed. The ABL level was measured in millimetres on the orthopantomographs in both mesial and distal sites of all teeth present on the arches by a calibrated examiner. This periodontal disease status evaluation is an established method frequently used in literature [10, 11] and in association with various systemic diseases [12]. At the same time, we determined the number of missing teeth on the same standardized orthopantomographs.

Other variables that were taken into consideration for the two groups and obtained from the observation medical charts were: age (in years), gender (men, women), marital status (married, not married, divorced, widow, separated), medical insurance (insured, not insured), smoking status (number of cigarettes per day), alcohol consumption (number of glasses per day, never, sometimes).

The statistical analysis was conducted using the SPSS computerized program in which all data and variables from the observation papers were added, including the number of missing teeth and alveolar bone loss measured in millimeters on the orthopantomographs. We also determined mean values, proportions and frequencies among relevant variables which were used to describe the study population. Only p values lower than 0.05 were considered statistically significant. Thus, using multiple logistic analyses, enabled us to estimate the independent association between ABL values, number of missing teeth and HNSCC, including all the other variables of age, gender, marital status, smoking status and alcohol consumption.

RESULTS AND DISCUSSIONS

The total number of subjects included in this study that fulfilled all inclusion criteria was 46, of which 20 patients were in the control group and 26 were cases. After

statistical analysis, we found that the cases were older, smoked a higher number of cigarettes per day, consumed more alcohol, had a higher number of missing teeth and the ABL levels were greater. Clinically, the cases presented a bleeding index with values between 0 and 1 determined on Ramfjord teeth, but the periodontal index had higher values, between 4-6, compared to the control group who presented values between 2-5. 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 larynx 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 two carcinoma localizations. Patients with laryngeal SCC were older, consumed

more alcohol, smoked more and had a higher number of missing teeth than the other two. In addition, all patients with larynx SCC were current smokers.

After statistic analysis, we found that chronic periodontitis is 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, oropharynx SCC and larynx SCC had higher periodontal index values compares to the controls, the index having the highest values in patients with oral cavity SCC.

After data stratification, the association was stronger for oral cavity SCC (OR 4.52) compared to oropharynx SCC (OR 3.64) and larynx SCC (OR 2.72) (Table 1).

Table 1: Association between periodontal variables (ABL and absent teeth) and HNSCC by localization

	Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Total HNSCC		
ABL (per millimeter)	3.85	4.36
Absent teeth (per tooth)	1.04	1.02
Oral cavity SCC		
ABL (per mm)	3.26	4.52
Absent teeth (per tooth)	1.04	1.03
Oropharynx SCC		
ABL (per mm)	3.06	3.64
Absent teeth (per tooth)	1.01	0.99
Larynx SCC		
ABL (per mm)	3.75	2.72
Absent teeth (per tooth)	1.09	1.05

The absence of teeth was significantly associated with HNSCC in the univariated analysis, however after adjustment for periodontal disease history and the other

variables, the association lost its statistical significance. Other studies support the fact that teeth loss is a surrogate marker of periodontitis, however the aetiology of

missing teeth is not just limited to periodontitis [3]. Divaris et al. [13] confirmed the fact that dental mobility is a more certain parameter for the quantification of periodontitis in relation with HNSCC in comparison to absent teeth. The patients in the study group had dental mobility (degree 1 to 3) especially in teeth 16 and 41. Thus, dental mobility generally had higher values in the lateral maxillary area and in the frontal mandibular area. Most patients presented missing teeth in the lateral mandibular region, a fact also confirmed on the ortopantomographs.

The risk factors for oral cancer include smoking, alcohol consumption and poor nutrition [19], family history [19,20], low socioeconomic status [19,20], certain viral infections such as infections with the human papilloma virus [19,20] and poor oral hygiene [21]. 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 the colonization of bacterial colonies and disturbing the balance in the sulcus. These microorganisms implicated in the genesis of periodontitis lead to the destruction of the profound and superficial periodontium, generating friability in the local tissues and blood vessels.

These bacteria along with their by products and inflammatory cytokines pass into the saliva and the blood stream. Thus, oral microorganisms may be implicated in the etiology of oral cancer [22].

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 tumors [16,17]. It is known that smoking, alcohol consumption and betel quid chewing have a synergic effect: in Taiwan, those who combine all these three habits exhibit a 123-fold incidence of oral cavity cancer than those who do not have any of the habits. Alcohol consumption did not represent a significant factor in our study, the association between ABL and HNSCC in the two groups being similar: alcohol users (OR 4.45) and non alcohol users (OR 4.31).

Overall, periodontal history was not associated in a significant manner with tumor 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 tumors in comparison with patients who did not have a periodontitis history (32.8% versus 11.5%, $p=0.038$).

CONCLUSION

Our study suggests that chronic periodontitis is a risk factor for HNSCC. These results have implications for practical and safe strategies for prevention, diagnosis, and treatment of HNSCC. With a good periodontal therapy plan, not only do patients have a lower risk of developing oral cavity carcinoma, but also improve their quality of life.

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