SCIENTIFIC ARCHIVES OF DENTAL SCIENCES

Volume 1 Issue 1 November 2018

Research Article

A Case-Control Study to Investigate an Association between Lung Cancer Patients and Periodontal Disease

Nikolaos Andreas Chrysanthakopoulos*

Dental Surgeon, Resident in Maxillofacial and Oral Surgery, 401 General Military Hospital of Athens and Department of Pathological Anatomy, Medical School, University of Athens, Athens, Greece

***Corresponding Author:** Nikolaos Andreas Chrysanthakopoulos, Dental Surgeon, Resident in Maxillofacial and Oral Surgery, 401 General Military Hospital of Athens and Department of Pathological Anatomy, Medical School, University of Athens, Athens, Greece.

Received: September 15, 2018; **Published**: October 12, 2018

Abstract

Aim: The aim of the current case-control study was to ascertain if individuals suffering from lung cancer show any difference s in periodontal disease severity compared to non-cancer individuals..

Methods: 172 individuals with lung cancer and 318 matching controls were selected. The measurements used to diagnose periodontal disease included Probing Pocket Depth (PPD), Clinical Attachment Loss (CAL) and Bleeding on Probing (POB). The control group was selected from the same city population with patients and their selection was based on patients' social environment. Chi-square test and multiple logistic regression analysis model were used to evaluate the data.

Results: Patients with lung cancer showed a significantly high number of periodontal manifestations compared with controls. Lung cancer patients, had worst periodontal indices among all the indices examined such as PPD ($p = 0.000$), CAL ($p = 0.028$) and BOP ($p = 0.010$) after adjustment for smoking and socio-economic status.

Conclusions: Smoking and periodontal disease indices examined were found statistically significant with difference between cancer and non-lung cancer patients.

Keywords: Lung Cancer; Periodontal Disease; Adults

Introduction

Lung cancer (LC) consists of leading cause of cancer-related deaths in both genders worldwide and causes the second highest number of deaths in Europe after cardiovascular disease [1]. The main cause for the mentioned high mortality is the lack of reliable bio-markers that could lead to early diagnosis and treatment. In addition a low proportion of individuals, merely 15%, stay alive 5 years after the initial diagnosis and the main reason is that the majority of LC patients are presented with advanced stages at the time of initial diagnosis, whereas initial diagnosis made at localized early stage increases the 5-year survival rate significantly [2].

LC affects the patients' life quality because of its severe symptoms and clinical signs and provision of the proper treatment, such as radiotherapy, chemotherapy and surgical therapy that can lead to serious side-effects.

Etiological and risk factors of LC are environmental and genetics factors such as male gender, advanced age, cigarette smoking, family history of cancer and genetic pre-disposition, prior pulmonary diseases such as Chronic Obstructive Pulmonary Disease (COPD), etc. Only a part of LC incidence can be explained by the mentioned factors, whereas other possible etiological or risk factors still remain unknown [3].

Periodontal disease (PD) is the most common chronic progressive and destructive disease worldwide and affects one or more of periodontal tissue structures [4] and can lead to systemic effects and several systemic health problems such as cardio-vascular and atherosclerotic diseases, respiratory diseases, allergies, diabetes mellitus, etc [5].

Several investigators have examined the possible role of PD as an etiological or risk factor in cancer development in several loca-

tions such as in the oral tissues, stomach, oesophagus, lungs and pancreas [6-11], with conflicting outcomes, even after controlling for possible known and unknown potential confounders such as smoking status, socioeconomic level, etc. In contrast to the mentioned reports, few studies have investigated the periodontal health status or the oral conditions in patients who suffered from LC or other types of cancer, e.g. gastric cancer [12].

It has been suggested that oral and periodontal lesions in cancer patients could be attributed to psychological burden mainly and to a lesser extent to factors such as abnormalities in patients' nutrition or alterations regarding the quantity/quality of saliva, or abnormalities in the microbiological and immunological balance parameters in the oral cavity that could be affected because of the chemotherapy, radiotherapy or targeted treatment [13,14]. Individuals who suffer from the cancer that is characterized by extremely poor prognosis, such as LC or gastric cancer it possibility of periodontal tissue destruction is much higher than non-cancer individuals [12].

The current research was performed to assess the possible differences in periodontal health status between LC patients diagnosed by histological examinations and the non-cancer patients.

Materials and Methods

Sample of the study

A total of 490 individuals, 306 males and 184 females, aged 49 - 80 years were selected from a private medical and a dental practice enrolled in the study. Participants included in the study filled up a medical and dental health questionnaire and underwent an oral clinical examination.

The current report was carried out between March and September 2018.

Selection criteria

172 individuals, 100 males and 72 females who were suffering from various LC and consented to participate in the study were selected. LC diagnosis was confirmed by the histopathological examination. 318 non-cancer individuals were selected as the control group.

Cases and controls, were selected from the same city population in an effort to avoid or eliminate possible selection biases. In addition, the selection of healthy individuals was based on LC patients' environment, such as colleagues, friends, etc. and both groups, cases and controls, were matched regarding epidemiological aspects such as gender, age and smoking status in an effort to control potential confounders.

It has been shown that epidemiological variables such as age [15], smoking history [16] and gender [17] act as covariates [18] and are involved in PD pathogenesis.

For the study those individuals were selected for case and control group who met determined criteria of established periodontitis [19], should have at least a mean of 20 natural teeth, ought not to be treated for any type of PD during a period of the previous six months and ought not to be received anti-inflammatory medication, antibiotics or other systemic medication for a period of the previous six weeks in order to be enrolled in the study. The mentioned selection criteria might have effects on periodontal tissues [20].

Individuals who suffered from cardiovascular diseases, diabetes mellitus, liver cirrhosis, rheumatoid arthritis, patients that were treated with immuno-suppressive medicines or those who received medication for the mentioned conditions or glucocorticoids were excluded from the study protocol in an effort to eliminate potential effects by known and unknown confounders.

LC patients with advanced disease under treatment, recurrent disease, distant metastases, lung metastases due to a different initial location diagnosed with other type of cancer which was located in the region of head-neck-thorax-carcinogenesis field theory [21]-were excluded from the study. Those conditions could have potential effects on the periodontal tissues.

Patients who suffered from types of cancer that smoking is an etiological factor such as oral cavity, nose, sinuses, larynx, etc., or hospital patients suffered from the mentioned types of cancer, were also excluded from the study protocol. In addition, cases should undergo the oral clinical examination before giving of any medical treatment i.e. surgery, radiotherapy or chemotherapy as those conditions could also have potential effects on the periodontal tissues and consequently in the intraexaminer variance.

Oral examination

The periodontal indices examined and recorded were Probing Pocket Depth (PPD), Clinical Attachment Loss (CAL) and Bleeding on Probing (BOP). Permanent teeth of all the participants of the study were clinically examined whereas remaining roots and 3rd molars were excluded. William's 12 PCP probe (PCP 10-SE, Hu-Friedy Mfg. Co. Inc., Chicago, IL, USA) was used at six sites per tooth (mesio-facial, facial, distofacial, mesio-lingual, lingual and disto-lingual) by a calibrated dentist.

As mentioned six sites per tooth were examined to assess the periodontal indices, PPD, CAL, BOP. In case where the tooth cervix was destructed by abrasion, erosion, decay or any other lesion, or the Cement-Enamel Junction (CEJ) was covered by a filling or prosthetic restoration its location was recorded by extrapolating the CEJ location from the adjacent teeth, whereas no record was recorded in case was not visible.

PPD was coded as [22]: score 0: moderate pockets, 4 - 6.0 mm and score 1: advanced pockets, > 6.0 mm.

CAL severity was coded as [23]: core 0: mild/moderate, 0.0 - 5.0 mm of attachment loss, and score 1: severe, ≥ 6.0 mm of attachment loss. The mentioned records was approximated to the immediate full millimetre.

BOP presence/absence was coded as: score 0: BOP absence, and score1: BOP presence, and was recorded as positive if it occurred within 15 seconds of probing.

Health questionnaire

Cases and controls completed a medical/dental health questionnaire that included epidemiological variables such as: gender, age, smoking status (current/ previous smokers and never smokers), educational and socio-economic level and data that concerned their medical history with reference to the mentioned conditions and medication under use of the respondent.

A randomly selected sample that consisted of 100 individuals (20%) was re-examined clinically by the same dentist after 3 weeks to assess the intra-examiner variance and no differences were found between 1st and 2nd clinical examinations (Cohen's Kappa= 0.97).

The current case-control study could not be reviewed and approved by authorized Greek committees (Greek Dental Associations, Ministry of Health, etc.) as it was not an experimental one. The performance of the study was in full accordance with the World Medical Association Declaration of Helsinki. Cases and controls who accepted the invitation to participate in the study protocol and signed an informed consent form were selected.

Statistical analysis

The following variables were coded as1: male gender, current/former smokers, individuals with high educational (graduated from University/College) and socio- economic (income/monthly ≥ 1,000 €) level.

Univariate analysis was used to assess the association between the independent indices examined and LC separately. Finally, a multivariate regression statistical model was used to assess the relationships between LC as a dependent index and the independent ones that were recorded after the performance by the Enter method.

Adjusted Odds Ratios (OR's) and 95% Confidence Interval (CI) were recorded as well. The independent indices were included to Wald method in order to assess gradually the indices that showed significant associations with the dependent one.

Cohran's and Mantel-Haenszel's method was performed to control the possible confounders, in an effort to avoid biased secondary associations.

Statistical analysis was performed using the statistical package of SPSS ver.19.0. A p value less than 5% (P< 0.05) was considered to be statistically significant.

Results

Cases and controls showed a mean age of 67,2 years (± 4.2).

Table 1 presents the results after performing of the mentioned model. All the variables examined, except for age and educational level were found statistically significant different between cases and controls. The same table also presents unadjusted OR's and 95% CI.

Enter method of the regression analysis model showed that smoking and the indices of PD were significantly different between cases and controls (Table 2). Table 2 also presents adjusted OR's with 95% CI. The final step, Wald method, (5a) confirmed the mentioned associations.

After using the Cohran's and Mantel-Haenszel's method for adjusting known confounders such as smoking and socioeconomic status the same associations were recorded (Table 3).

Variables	Cases (no) (%)	Controls (no) (%)	p-value	Odds Ratio (OR)	95% Confidence Interval (CI)
Gender					
Males	100 (58.1)	142 (44.7)			
Females	72 (41.9)	176 (55.3)	0.044*	1.72	1.01 - 2.93
Age (years)					
50 - 59	26 (15.1)	56 (17.6)			
60 - 69	76 (44.2)	106 (33.3)			
70 - 79	56 (32.6)	116 (36.5)	0.359	-	-
80	14 (8.1)	40 (12.6)			
Socio-economic level					
Low	76 (44.2)	184 (57.9)	0.041*	0.58	0.34 - 0.98
High	96 (55.8)	134 (42.1)			
Educational level					
Low	52 (29.9)	122 (38.0)	0.204	0.70	0.40 - 1.22
High	120 (70.1)	196 (62.0)			
Smoking					
No	66 (38.4)	178 (56.0)	0.129	0.58	0.29 - 1.18
Yes	106 (61.6)	140 (44.0)			
Periodontal pockets					
Depth 0 - 4,0 mm	56 (32.6)	202 (63.5)	0.000*	0.28	0.16 - 0.48
Depth ≥ 5,0 mm	116 (67.4)	116 (36.5)			
CAL					
Mild/Moderate 0 - 5,0 mm	66 (38.4)	188 (59.1)	0.002*	0.43	0.25 - 0.74
Severe ≥ 6,0 mm	106 (61.6)	130 (40.9)			
BOP					
No	60 (34.9)	176 (55.3)	0.002*	0.43	0.25 - 0.74
Yes	112 (65.1)	142 (44.7)			

Table 1: *Univariate analysis of cases and controls regarding each independent variable examined*

** p-value: Statistically Significant.*

Variables in the Equation									
		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
								Lower	Upper
Step 1[a]	Gender	,434	,321	,406	1	,341	,813	,501	1,273
	Age	,102	,172	,353	1	,552	,903	,645	1,265
	Socioeconomic	,327	,300	1,192	1	,275	1,387	,771	2,497
	Education	,174	,324	,288	1	,591	1,190	,630	2,248
	Smokstat	,730	,352	8,136	1	,012*	1,878	,840	1,752
	Prodpocdep	1,276	,366	12,173	1	,000*	3,582	1,749	7,334
	Clinattloss	,672	,318	4,474	1	,034*	1,957	1,051	3,647
	Blonprob	,813	,313	6,739	1	,009*	2,256	1,221	4,169
	Constant	2,638	,478	30,429	1	,000	,071		
Step 5[a]	Smokstat	1,056	,313	11,383	1	,001*	2,876	1,557	5,313
	Prodpocdep	1,239	,312	15,776	1	,000*	3,452	1,873	6,362
	Clinattloss	,671	,305	4,851	1	,028*	1,957	1,077	3,557
	Blonprob	,781	,302	6,670	1	,010*	2,184	1,207	3,951
	Constant	2,555	,380	45,091	1	,000	,078		
a. Variable(s) entered on step 1: gender, age, socioeconlev, educlev, smokstat, prodpocdep, clinattloss, blonprob.									

Table 2: *Presentation of correlation between independent variables and lung cancer according to Enter (first step) and Wald (final step) method of multivariate logistic regression analysis model.*

** p-value: Statistically Significant.*

Variables	Exp (B)	95% CI
Probing Pocket Depth (PPD)		
Non-smokers	3.721	0.872 - 6.528
Smokers	5.115	3.012 - 12.127
Clinical Attachment Loss (CAL)		
Non-smokers	1.915	0.902 - 3.389
Smokers	4.519	2.495 - 11.104
Bleeding on Probing (BOP)		
Non-smokers	2.626	0.774 - 4.283
Smokers	4.297	3.486 - 9.152
Probing Pocket Depth (PPD)		
Low socio-economic status	1.470	0.768 - 3.128
High socio-economic status	5.137	2.751 - 10.628
Clinical Attachment Loss (CAL)		
Low socio - economic status	2.166	0.806 - 4.250
High socio - economic status	4.762	2.791 - 11.122
Bleeding on Probing (BOP)		
Low socio - economic status	2.674	1.081 - 4.984
High socio - economic status	4.649	2.043 - 9.047

Table 3: *Application of Cohran's and Mantel - Haenszel's, statistical method for controlling possible confounders.*

Discussion

The purpose of the current research was to investigate a comparison between LC patients and epidemiologically matched healthy individuals regarding several PD indices and not to investigate a possible relationship between PD indices, as etiological or risk factors, and LC development.

Consequently, the current study has certain limitations that should be taken into account during the procedure of results interpreting. It is well known that case-control studies, do not have the reliability of the prospective ones, whereas selection, recall, random biases and the effect of known and unknown confounders are likely higher and could lead to biased secondary associations regarding the variables examined.

Another drawback of those studies that are based on questionnaires is that the participants either could not respond or could give no reliable responses, or could over- or under-estimate their potential medical diseases or disorders. That results to limitations on the study validity.

The decision to be included in the current study older individuals who have at least 20 natural teeth would lead to under-estimate those individuals with previous PD who may have had teeth removed for periodontal reasons.

The results showed no statistically significant difference between cases and controls examined, regarding epidemiological indices of gender, age, educational and socioeconomic level, however, OR's values for socio-economic and educational level were slightly higher in cases group compared with controls (step 1a).

Smoking consists a main risk factor for initiation and progress of PD and LC and [22,24] and often acts as a confounder in researches that examine the possible association between PD and several types of cancer in which smoking is associated with cancer development. The results showed that smoking was statistically significant different between cases and controls.

It is also recorded that LC patients showed significantly higher values in PD as it is expressed by the PPD index, compared with healthy individuals, observation that cannot be confirmed by previous or recent studies as similar studies have not been carried out.

Statistically significant difference was observed regarding CAL between LC patients and healthy individuals, observation that is in accordance with the higher severity of PD as it is expressed by the PPD index. Similar findings have not been reported by other investigators regarding that index due to the reason that was mentioned.

BOP was another PD index that was found to be statistically significantly different between cases and controls, and consists a critical index of periodontal tissues examination and PD diagnosis and the most valid and reliable index of PD activity [25].

Those observations regarding the PD indices examined, recorded after controlling potential confounders such as smoking, and socio-economic status (Table 3).

In the literature few studies have been performed regarding the oral conditions or periodontal health status in patients who suffered from various types of cancer. In one previous report was found that head and neck cancer patients showed poor oral health at the time of diagnosis after using dental caries and PD indices as parameters for assessing oral conditions and periodontal health status [26]. Another report that examined the periodontal condition in gastric cancer patients reported that smoking, gingival inflammation, and CAL were statistically significantly different between gastric cancer patients and healthy individuals [12]. A similar prospective cross-sectional study showed that oral or oropharyngeal cancer, patients showed PPD 6.00 mm or greater of 76% of the patients assessed, whereas only 10% in the health group showed the same severity of disease. The important observation was that an association was recorded between cancer and more severe PD regardless of the dental health status and oral hygiene [27].

The only report that examined the oral health status in LC patients was focused on LC patients who had undergone chemotherapy and used different indices to examine the oral health status such as DMFT, OHI-S, etc. However, it was found that LC patients with good oral hygiene showed a lower incidence of oral mucositis during the cycles of chemotherapy, whereas the use of chemotherapy agents showed a deleterious effect on the condition of the oral mucosa of LC patients [14].

According to the results it is clear that PD appears to be increased in LC patients and more severe and generalized than in healthy individuals, a clinical sign that concerns all the PD indices examined and would suggest clinical implications for the treatment and management of PD in LC patients.

It has been suggested that the initiation and development of PD and cancer is associated with chronic inflammatory reaction and possible abnormalities in the cellular signaling pathways. Consequently, any type of PD treatment, conservative or surgery could eliminate the levels of biomarkers and mediators that are involved and promote a disturbed chronic inflammatory reaction, giving importance to the application of a strict oral care program and preventive dentistry of LC patients [28].

Conclusions

In conclusion, PD as expressed by indices such as PPD, CAL and BOP was found statistically different in LC patients compared with non-cancer individuals.

Bibliography

1. Ferlay J, Autier P, Boniol M, et al. Estimates of the cancer incidence and mortality in Europe in 2006. Ann Oncol. 2007;18(3):581-592.

2. Tyczynski JE, Bray F, Maxwell Parkin D. Lung cancer in Europe in 2000:epidemiology, prevention, and early detection. The Lancet Oncology. 2003;4(1):45-55.

3. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. CA: A Cancer Journal for Clinicians. 2008;58(2):71-96.

4. Papapanou PN. Periodontal diseases: epidemiology. Ann Periodontol. 1996;1(1):1-36.

5. Holmstrup P, Poulsen AH, Andersen L, Skuldbøl T, Fiehn NE. Oral infections and systemic diseases. Dent Clin North Am. 2003;47(3):575-598.

6. Michaud DS, Joshipura K, Giovannucci E, Fuchs CS. A prospective study of periodontal disease and pancreatic cancer in US male health professionals. J Natl Cancer Inst. 2007;99(2):171-175.

7. Stolzenberg-Solomon RZ, Dodd KW, Blaser MJ, Virtamo J, Taylor PR, Albanes D. Tooth loss, pancreatic cancer, and Helicobacter pylori. Am J Clin Nutr. 2003;78(1):176-181.

8. Hujoel PP, Drangsholt M, Spiekerman C, Weiss NS. An exploration of the periodontitis-cancer association. Ann Epidemiol. 2003;13(5):312-316.

9. Abnet CC, Qiao YL, Mark SD, Dong ZW, Taylor PR, Dawsey SM. Prospective study of tooth loss and incident esophageal and gastric cancers in China. Canc Caus Contr. 2001;12(9):847-854.

10. Rosenquist K, Wennerberg J, Schildt EB, Bladstrom A, Goran Hansson B, Andersson G. Oral status, oral infections and some lifestyle factors as risk factors for oral and oropharyngeal squamous cell carcinoma. A population-based case-control study in southern Sweden. Acta Otolaryngol. 2005;125(12):1327-1336.

11. Michaud DS, Liu Y, Meyer M, Giovannucci E, Joshipura K. Periodontal disease, tooth loss, and cancer risk in male health professionals:a prospective cohort study. Lancet Oncol. 2008;9(6):550-558.

12. Chrysanthakopoulos NA, Oikonomou AA. A case-control study of the periodontal condition in gastric cancer patients. Stomatological Dis Sci. 2017;1:55-61.

13. Pearman T. Psychological factors in lung cancer: quality of life, economic impact, and survivorship implications. J Psychosoc Oncol. 2008;26(1):69-80.

14. Dyszkiewicz Konwinska M, Mehr K, Owecka M, Kulczyk T. Oral Health Status in Patients Undergoing Chemotherapy for Lung Cancer. Open J Dent Oral Med. 2014;2(1):17-21.

15. Lavstedt S, Bolin A, Henrikson CO. Proximal alveolar bone loss in a longitudinal radiographic investigation. II. A 10-year follow-up study of an epidemiologic material. Acta Odontol Scand. 1986;44(4):199-205.

16. Tonetti MS, Claffey N. Advances in the progression of periodontitis and proposal of definitions of a periodontitis case and disease progression for use in risk factor research. J Clin Periodontol. 2005;32(6):210-213.

17. Reichert S, Stein J, Gautsch A, Schaller HG, Machulla HK. Gender differences in HLA phenotype frequencies found in German patients with generalized aggressive periodontitis and chronic periodontitis. Oral Microbiol Immunol. 2002;17(6):360-368.

18. Loos BG, John RP, Laine ML. Identification of genetic risk factors for periodontitis and possible mechanisms of action. J Clin Periodontol. 2005;32(S6):159-179.

19. Machtei EE, Christersson LA, Grossi SG, Dunford R, Zambon JJ, Genco RJ. Clinical criteria for the definition of "established periodontitis". J Periodontol. 1992;63(3):206-214.

20. Machuca G, Segura-Egea JJ, Jimenez-Beato G, Lakalle JR, Bullon P. Clinical indicators of periodontal disease in patients with coronary heart disease: A 10 years longitudinal study. Med Oral Patol Oral Cir Bucal. 2012;17(4):e569-574.

21. Rubin H. Fields and field cancerization: the preneoplastic origins of cancer: asymptomatic hyperplastic fields are precursors of neoplasia, and their progression to tumors can be tracked by saturation density in culture. BioEssays. 2011;33(3):224-231.

22. Russell AL. Epidemiology of periodontal disease. Int Dent J. 1967;17(2):282-296.

23. Wiebe CB, Putnins EE. The periodontal disease classification system of the American Academy of Periodontology-an update. J Can Dent Assoc. 2000;66(11):594-597.

24. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of world-wide burden of cancer in 2008:GLOBOCAN 2008. Int J Cancer. 2010;127(12):2893-2917.

25. Lang NP, Joss A, Orsanic T, Gusberti FA, Siegrist BE. Bleeding on probing. A predictor for the progression of periodontal disease? J Clin Periodontol. 1986;13(6):590-596.

26. Critchlow SB, Morgan C, Leung T. The oral health status of pre-treatment head and neck cancer patients. Br Dent J. 2014;216(1):E1.

27. Rezende CP, Ramos MB, Daguíla CH, Dedivitis RA, Rapoport A. Oral health changes in with oral and oropharyngeal cancer. Braz J Otorhinolaryngol. 2008;74(4):596-600.

28. Albandar JM. Epidemiology and risk factors of periodontal disease. Dent Clin North Am. 2005;49(3):517-532.

Volume 1 Issue 1 November 2018