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치주염과 구강편평상피세포암의
연관성에 대한 병원
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Association of periodontitis and
oral squamous cell carcinoma:
a hospital cancer case-cohort
control study

2018년 2월

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- Abstract -

Association of periodontitis and oral squamous cell carcinoma: a hospital cancer case-cohort control study

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Objectives : The association between periodontitis and oral squamous cell carcinoma (OSCC) in large cases with cohort controls have yet to be evaluated. The aim of this study was to investigate the association of periodontitis with OSCC across the tumor location and tumor-node-metastasis (TNM) stage among Koreans.

Methods : Among 424 participants, OSCC cases (n=146) were recruited from Seoul National University dental hospital and controls (n=278) matched to age, sex and smoking of cases were selected from Yangpyeong health and periodontal cohort in Korea. OSCC was diagnosed through tissue biopsy and radiographs such as computed tomography and magnetic resonance imaging. The location and TNM stage were classified after the surgery. Periodontitis was defined by alveolar bone loss using panoramic

radiograph following the 5th European guideline. Alcohol intake, education, physical activity, obesity by body mass index, hypertension by blood pressure, diabetes by plasma glucose, and hypercholesterolemia by plasma cholesterol were considered as confounders. Information about age, sex, smoking, alcohol intake, education, and physical activity was obtained through interview. Body mass index and blood pressure were through physical examination. Pre-operative glucose and cholesterol were obtained through laboratory tests. Bivariate analysis was applied using Fisher's exact chi-square test. Multivariable conditional logistic regression models were applied to evaluate the adjusted association of periodontitis with OSCC after controlling for confounders. Subgroup analyses by age, sex and smoking were explored by OSCC and periodontitis.

Results : Participants with periodontitis is 3.7 times more likely to have OSCC (adjusted odds ratio [aOR]=3.66, 95% confidence interval=1.46-9.23) as compared to participants without periodontitis. The differences in periodontitis was not statistically significant across TNM stages of OSCC ($p>0.05$) nor its location ($p>0.05$). The link was highlighted among males (aOR=6.55) and elders over 60 (aOR=4.98).

Conclusion : Our data showed that periodontitis was independently associated with OSCC. Thus periodontitis could be a risk factor of OSCC.

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Keywords: Oral squamous cell carcinoma; periodontitis; tumor location; TNM stage; epidemiology

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I. Introduction

Oral squamous cell carcinoma (OSCC) is known to be the most common oral malignant lesion¹. The Korea National Cancer Incidence Database showed that the crude prevalence rates of lip, oral cavity and pharynx per 100,000 in both sexes are reported to be 38.8 (52.2 in men and 25.3 in women) and the age-standardized prevalence rate per 100,000 in both sexes was 25.0 (35.5 in men and 154.8 in women) as of January 1, 2015². The percentage of oral cancer (OC) in the total cancer count is relatively small, however, the life-threatening characteristic of oral cancer is practically important to the overall wellness of people.

Commonly known risk factors of OC include tobacco and alcohol³. Other risk factors include human papilloma virus (HPV)⁴, Epstein-Barr virus and Cytomegalovirus⁵, systemic diseases such as diabetes⁶, metabolic syndrome⁷, and chronic inflammation and infection⁸.

Periodontitis, a chronic inflammation being the 6th most prevalent disease worldwide with the global burden increased by 57.3% from 1990 to 2010, has been linked to carcinogenesis⁹. However, association between periodontitis and OSCC is still controversial. From 1990 until the August 2018, 18 articles have been reported on the association between oral health status and head and neck cancer. Out of 18 articles, 15 articles have shown positive association¹⁰⁻²⁴ while the other three papers have shown no association²⁵⁻²⁷. Hitherto, there are five meta-analysis papers reported from 2013 until August 2018 reporting on positive

association (OR of 2.0–3.21) between periodontal disease and head and neck cancer. There were high heterogeneity in these meta-analysis papers due to differences in assessment methods for periodontitis, tumor sites (oral cavity, tongue, head and neck, and oropharyngeal), geographical differences, lack of potential confounders like important risk factors and systemic health diseases, and the selection of controls. To overcome these limitations, we considered a hospital OSCC case and cohort control study encompassing sufficient number of cases from the hospital and controls matched to age, sex and smoking of cases from the community health cohort. This hospital case and cohort control study could reduce the risk of a false-negative finding due to hospital controls and increase the precision of the estimates. Moreover, we applied the definite assessment method for periodontitis using panoramic radiograph for reducing the information bias due to the misclassification. Also confounders including alcohol intake, education, physical activity, obesity, diabetes, hypertension and hypercholesterolemia were considered to reduce a false-positive findings due to under adjustment. Especially, no result was published on the adjusted association of periodontitis with OSCC according to the location of tumor and tumor-node-metastasis (TNM) stages in Korea.

Taking these into consideration, the aims of our hospital OSCC cases and cohort controls matched to age, sex and smoking of cases study was to evaluate the hypothesis that periodontitis is associated with OSCC among Koreans adjusted for confounding variables. Also the stratified associations by age, sex and smoking were evaluated. Moreover, we explored whether periodontitis is associated with OSCC according to the location of

tumor and tumor-node-metastasis (TNM) stages.

II. Materials and methods

Study design

This study follows the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines. This observational hospital case and cohort control study was cross-sectionally evaluated. The data set for this study was obtained from OSCC cases in the Seoul National University hospital and controls in the Yangpyeong health cohort. The ratio between OSCC cases and controls was decided as 1:2 due to difficulty in recruiting OSCC cancer cases.

Ethical considerations

All participants provided an informed consent statement voluntarily. The ethical approval for this study was reviewed and granted by Seoul National University Dental Hospital Institutional Review Boards (ERI17014).

Sample size estimation

Sample size was estimated by using chi-square test based on alpha error at 0.05 and beta error at 0.2. In the pilot study, proportion of periodontitis in controls (P1) was 0.3 and that in cases (P2) was 0.6. The estimated ratio between the cases and controls was set at 1:2. The estimated sample size was 93 (31 cases and 62 controls). Since one confounder increase sample size by 10%, 10 confounders increased the sample size by 100% to 186 (62 cases and 124 controls). In consideration of stratified

analysis using binary variable, total sample size became the double to 372 with 124 cases and 248 controls.

Selection of participants

Hospital OSCC cases were patients from Seoul National University Dental Hospital (SNUDH) from 2015 until 2017. The inclusion criteria for cases with final diagnosis of OSCC are as follows: 1) agreed to be participants voluntarily, 2) scheduled for surgery, 3) no pregnancy, and 4) no inflammatory diseases of the oral and maxillofacial region as well as auto-immune disorders and/or infectious diseases. Controls matched to age, sex, and smoking were randomly selected from Yangpyeong (YP) health and dental cohort that is a part of Korean Genome Epidemiologic Study (KoGES), supported by the Korea Centers for Disease Control and Prevention since 2010. For hospital OSCC cases, 153 patients satisfied the inclusion criteria but only 146 OSCC cases had age, sex, and smoking matching controls that were selected from YP cohort. Out of 146 cases, 132 OSCC cases were matched with controls in a 1:2 ratio, and 14 OSCC cases in a 1:1 ratio. As a result, 278 controls were selected. Finally, total of 424 participants with 146 cases and 278 controls, were included in this hospital case and cohort control study for final analyses.

Assessment of oral squamous cell carcinoma

Initial diagnosis of OSCC (International Classification of Diseases for Oncology [ICD-0] codes C02.0-C06.9) was through oral examination on the first visit by a single oral and maxillofacial cancer surgeon (JH Lee) and also radiographs

including panoramic radiograph, enhanced computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography - computed tomography (PET-CT) confirmed the initial diagnosis by SNUDH radiologist and histological tissue biopsy made the final diagnosis by SNUDH pathologist. Information on the location of tumor and TNM stage²⁸ were obtained from the gross biopsy of tumor after the surgery. In this study, carcinoma in situ were also noted as stage 0. According to the location, OSCC was classified into tongue (C02.0–C02.9), floor of the mouth (C04–C04.9), hard palate (C05.0–C05.9), buccal mucosa (C06.0), retromolar trigone (C06.2), alveolar ridge (C06.8–C06.9)²⁹.

Assessment of Periodontitis

Radiographic alveolar bone loss (RABL) of each natural tooth was assessed by two trained dentists (YJ Shin, HW Choung) using the panoramic radiograph (Orthopantomograph OP100, GE Healthcare, Finland). RABL, a definitive measure of periodontitis, was assessed and recorded by measuring the mesial and distal of the remaining teeth from the cemento–enamel junction (CEJ) of the tooth up to the highest point of the proximal alveolar bone crest. All mesial and distal part of the natural teeth, except the 3rd molars, were measured. Classification was categorized following the guidelines from the 5th European workshop in Periodontology as: “Normal” if there is presence of proximal bone loss < 3mm in < 2 non-adjacent teeth, “Incipient” if there is presence of proximal bone loss of ≥ 3 mm in ≥ 2 non-adjacent teeth, “Severe” if there is presence of proximal bone loss of ≥ 5 mm in $\geq 30\%$ of teeth present³⁰. Periodontitis was dichotomized

into periodontitis group for incipient and severe periodontitis and non-periodontitis group for normal.

Assessment of confounders

We included demographic and health-related behavioral factors and systemic factors^{14,31} in the analysis to eliminate the impact of confounders.

All participants were interviewed and screened in person by trained personnel for demographic information such as age and sex, health-related behavioral variables such as smoking, alcohol intake, education level, physical activity, and medical history of systemic diseases (diabetes, hypertension and hypercholesterolemia). Other health-related behavioral variables such as body mass index (BMI), systolic and diastolic blood pressure were through physical examination, and pre-operative fasting plasma glucose (FPG) and fasting total cholesterol (FTC) were obtained through serum laboratory tests.

Sex, smoking, alcohol intake, education level, physical activity, obesity, and systemic diseases including diabetes, hypertension and hypercholesterolemia were dichotomized into male and female, until middle school and high school or higher, smoker and non-smoker, drinker and non-drinker, doing physical activity and not doing physical activity, and with and without systemic diseases. Obesity was dichotomized using BMI which was calculated as weight (kg) divided by the square of height (m²) as: no= < 25.0 kg/m² and yes= ≥25.0 kg/m² and above³². Diabetes was validated using the pre-operative glucose level by categorizing FPG into 2 groups according to the diagnostic criteria of American Diabetes Association³³: no= FPG<126mg/dl

and yes= FPG \geq 126mg/dl, taking insulin shots or on anti-diabetic medication and / or diagnosed by the physician. Hypertension was validated using the pre-operative SBP and DBP in mmHg by categorizing into 2 groups according to the criteria of Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) 7th, 2004: no= SBP<140 mmHg or DBP<90mmHg and yes= SBP \geq 140mmHg or DBP \geq 90mmHg or on anti-hypertensive medication³⁴. Hypercholesterolemia was validated using the pre-operative FTC level by categorizing into 2 groups according to the criteria of National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III)³⁵: no=FTC<240 mg/dl and yes= FTC \geq 240mg/dl, or on anti-cholesterol medication.

Statistical analysis

Characteristics of variables were derived by using mean values with standard deviations (\pm SD) for continuous variable (age) and frequency distributions for categorical variables (all other variables) (Table 1). Chi-square and t-tests were used to compare differences in categorical and continuous variables, respectively. For evaluating specific association of periodontitis with OSCC according to the location and TNM stages of cancer, chi-square test was applied among periodontitis, the location and TNM stages of cancer. Multivariable conditional logistic regression models were used to evaluate the association of periodontitis with OSCC conditional on age, sex and smoking by calculating the adjusted odds ratios (aORs) and the associated 95% confidence interval (CI) after controlling for potential confounders such as alcohol intake, education level, physical

activity, obesity, diabetes, hypertension, and hypercholesterolemia. We constructed the final model (Model II) using the dichotomized periodontitis variables (normal versus periodontitis). Age, sex and smoking stratified associations were also analyzed. Statistical significance was set at p-value <0.05. All statistical analyses were performed using SPSS software, version 25.0 (SPSS, Inc. Armonk, NY, USA).

III. Results

Characteristics of participants

The total of 424 participants in this hospital OSCC case-cohort control study consist of 146 (34.43%) hospital OSCC cases (90 men and 56 women with mean age of 63.8) and 278 (65.57%) cohort controls (167 men and 111 women with mean age of 64.4) (Table 1).

OSCC cases compared to controls were more periodontitis patients, less alcohol drinkers, more high school or higher graduates, more diabetic and more hypercholesterolemic ($p < 0.05$).

Distribution of oral squamous cell carcinoma according to its location, TNM stages and periodontitis

The total OSCC cases showed highest prevalence in alveolar ridge (44.5%), followed by tongue (21.2%), buccal mucosa (17.1%), hard palate (6.8%), retromolar trigone (6.2%), and then floor of the mouth (4.1%) (Table 2). Stage IV cancers were the most (39.7%) with carcinoma in situ the least (2.7%) (Table 2).

In terms of TNM stages of OSCC, stage IV showed the biggest proportion of 40.9%, while stage II showed the highest proportion of 44.4% in the non-periodontitis group. However, prevalence of periodontitis was not significantly different across the TNM stages of OSCC (Figure.1-A).

In terms of the location of OSCC, alveolar ridge had the highest number amongst other location (45.3%) in the

periodontitis group, while tongue had the highest number (55.6%) in non-periodontitis group. Tongue cancer showed less prevalence of periodontitis, which was not statistically significant (Figure.1-B).

Association between periodontitis and oral squamous cell carcinoma

Compared to normal participants, those with incipient periodontitis is more likely to have OSCC by 3.5 times (aOR=3.46 95% CI=1.35-8.90) and those with severe periodontitis is more likely to have OSCC by 4.1 times (aOR=4.07, 95% CI=1.50-11.03), which shows the significant dose-response relationship (trend $p=0.003$) (Table 3, Model I). Those with periodontitis encompassing incipient and severe periodontitis also showed significant association with OSCC (aOR=3.66, 95% CI=1.46-9.23) (Table 3, Model II).

Stratified association between periodontitis (normal versus incipient and severe) and oral squamous cell carcinoma

There is an effect modification by age, sex and smoking on the association of periodontitis with OSCC. The link was more highlighted among males (aOR=6.5, 95% CI=1.12-38.22) and elders aged more than 60 years (aOR=5.0, 95% CI=1.37-18.11), but less highlighted among non-smokers (aOR=3.2, 95% CI=1.07-9.37) (Table 4).

IV. Discussion

This hospital OSCC case and cohort control study showed that those with periodontitis as compared to those without periodontitis is 3.7 times more likely to have OSCC among Koreans. Our results conformed to previous studies which showed the positive association of periodontitis with OC. Moreover, there is an effect modification of age, sex, and smoking. The link in our data was highlighted showing prevalence of 5 times among those over 60 years and 6.5 times in males. A previous study also showed predilection of the link in older adults and in males¹⁴.

Our data showed that prevalence of periodontitis was high in OSCC but not different across TNM staging of OSCC, which suggests that periodontal inflammation could have a critical role in the initiation of cancer, but not in the progression of OSCC. Some previous studies reported that OSCC was usually detected in advanced stages¹⁴. The discrepancies between our and previous results indicate further studies for clarification.

The novelties of this study compared to previous reports are as follows. Firstly, hospital cases catered OSCC among Koreans while the cohort controls were from the general Korean population, which reduced the bias associated with error resulting from the hospital controls. Secondly, despite the rarity among cancers, sufficient number of cases were recruited, which reduced the uncertainty due to small numbers. Thirdly, the controls were selected by matching the well-known risk factors such as age, sex and smoking of cases, which adjusted the influence of these risk factors on the association. Fourthly, periodontitis was

assessed using panoramic radiograph, which reduced the information bias due to the misclassification of periodontitis. Fifthly, definitive confounders including alcohol intake, education level, physical activity, obesity, diabetes, hypertension and hypercholesterolemia were added in the model for the adjustments. And finally, stratified analyses for the link were done to evaluate the effect modification of age, sex and smoking.

Periodontal disease is a chronic inflammatory disease that is significantly associated with an increased risk in OC²⁶, which is highlighted in OC as compared to those of gastric, pancreatic, lung, prostate, hematologic and other cancers³¹. In addition, deep periodontal pockets have been suggested as a niche for viral infections such as human papillomavirus (HPV)⁴, and Epstein-Barr virus (EBV) and cytomegalovirus⁵. Our data did not include these as confounders which may have led to over-estimation of our results. The mechanism of chronic inflammatory processes including the aforementioned variables in OC should be indicated as a future research.

Chronic inflammation has multifaceted association with OC and it has been first suggested by Virchow during the 19th century³⁷. Poor oral hygiene, pre-malignant lesions such as leukoplakia and lichen planus¹¹ were reported as related factors resulting to chronic inflammation which are associated with head and neck cancer. The connection of chronic inflammation is brought in two ways: through infectious conditions and through activation of oncogenes. Both ways release chemical mediators which induces carcinogenesis⁸. The prevalence rate of periodontitis was 32.0% from Korea National Health and Nutrition Examination Survey (KNHANES IV 2007-2009)³⁸. Due to high prevalence rate of

periodontitis, advantageous effect of periodontal care and therapy which decreases the chance of infection and inflammation will eventually lessen the risk of OC hence, prevention and treatment of periodontitis could also serve as a preventive care for OC. This could be of great clinical relevance. Hence, it is speculated that the risk of OSCC could be ameliorated through the reduction of periodontal inflammation.

Salivary proteomics and blood exosome analysis may be used to identify diagnostic markers in the detection of OSCC in association with chronic periodontitis. Saliva has been an interesting alternative diagnostic fluid that is reproducible and non-invasive although its composition is affected easily by environmental factors³⁹. Salivary molecular biomarkers such as DNA, RNA and protein markers may have the ability to detect OSCC with high sensitivity and specificity that is accessible easily by mass population but handling and storing must be carefully done in saliva collection³⁶. Salivary protein biomarker such as matrix metalloproteinase 9 (MMP-9), an indicator of periodontal disease, was suggested to be evaluated as an indicator for early diagnosis of OC⁴⁰. Further researches must focus on detecting OSCC at an earlier stage through systemic influences such as salivary and serum biomarkers. Moreover, innovative salivary diagnostic tool that is easily accessible to people should be developed.

This study has some limitations. Firstly, a case-control study design has inherent selection bias for controls. However, a case-control study design is the most appropriate study design for cancer research, because oral cancer is a rare disease among other cancers. Secondly, information on other potential risk

factors such as HPV, Epstein-Barr virus and Cytomegalovirus is limited. These limitations could lead to over-estimation of the association. Notwithstanding these limitations, this study is valid enough to evaluate the association of periodontitis with OSCC.

V. Conclusion

Overall, our data showed that periodontitis was independently associated with oral squamous cell carcinoma. Thus, periodontitis could be a risk factor of OSCC and its progress. Moreover, the high risk groups of the link were elders, and males. Thus, the risk of OSCC could be ameliorated by reducing periodontitis.

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Appendix 1 : Tables and Figure

Table I. Characteristics of variables according to oral squamous cell carcinoma cases and cohort controls (N=424)

Variable	Cancer Case (n=146)	Cohort Control (n=278)	p-value
Periodontitis[*], n (%)			<0.001
Normal	9 (6.2)	60 (21.6)	
Incipient	91 (62.3)	143 (51.4)	
Severe	46 (31.5)	75 (27.0)	
			<0.001
Normal	9 (6.2)	60 (21.6)	
Incipient and Severe	137 (93.8)	218 (78.4)	
Age, mean±SD	63.76 ± 10.662	64.38 ± 10.244	0.557
Sex, n (%)			0.834
Male	90 (61.6)	167 (60.1)	
Female	56 (38.4)	111 (39.9)	
Smoking[†], n (%)			0.918
No	80 (54.8)	155 (55.8)	
Yes	66 (45.2)	123 (44.2)	
Alcohol intake[‡], n (%)			<0.001
No	92 (63.0)	109 (39.2)	
Yes	54 (37.0)	169 (60.8)	
Education level, n (%)			<0.001
Middle school	46 (31.5)	177 (63.7)	
High school or higher	100 (68.5)	101 (36.3)	
Physical activity[§], n (%)			0.123
No	108 (74.0)	185 (66.5)	
Yes	38 (26.0)	93 (33.5)	
Obesity, n (%)			0.239
No	101 (69.2)	176 (63.3)	
Yes	45 (30.8)	102 (36.7)	
Diabetes[¶], n (%)			0.009
No	118 (80.8)	251 (90.3)	
Yes	28 (19.2)	27 (9.7)	

Hypertension[#], n (%)			0.080
No	55 (37.7)	130 (46.8)	
Yes	91 (62.3)	148 (53.2)	
Hypercholesterolemia^{**}, n (%)			0.029
No	124 (84.9)	256 (92.1)	
Yes	22 (15.1)	22 (7.9)	

The ratio between cancer cases and controls matched for age, sex and smoking was 1:2 except for 14 cases for 1:1.

Bold denotes statistical significance ($p < 0.05$)

*Periodontitis: 3 groups: Normal= presence of proximal bone loss $< 3\text{mm}$ in < 2 non-adjacent teeth Incipient=presence of proximal bone loss of $\geq 3\text{mm}$ in ≥ 2 non-adjacent teeth, Severe=presence of proximal bone loss of $\geq 5\text{mm}$ in $\geq 30\%$ of teeth present.

† Smoking: No=never smoked, Yes=past smoker and currently smoking.

‡ Alcohol intake: No=never drank, Yes=past drinker and currently drinking.

§ Physical activity: No=no exercise Yes=any form of exercise more than 30 minutes daily.

|| Obesity: Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m^2): No= $< 25.0 \text{ kg/m}^2$, Yes= $\geq 25.0 \text{ kg/m}^2$ and above.

¶ Diabetes: No= Fasting Plasma Glucose (FPG) $< 126\text{mg/dl}$, Yes= FPG $\geq 126\text{mg/dl}$, taking insulin shots or on anti-diabetic medication and / or diagnosed by the physician

#Hypertension: No= Systolic Blood Pressure (SBP) $< 140 \text{ mmHg}$ or Diastolic Blood Pressure (DBP) $< 90\text{mmHg}$, Yes= SBP $\geq 140\text{mmHg}$ or DBP $\geq 90\text{mmHg}$ or on anti-hypertensive medication

**Hypercholesterolemia: No=Fasting Total Cholesterol (FTC) $< 240 \text{ mg/dl}$ and Yes= FTC $\geq 240\text{mg/dl}$

Table 2. Distribution of oral squamous cell carcinoma according to its location, TNM stage and periodontitis (N=146)

Periodontitis Location	N (%) *	TNM stage, n (%) [†]				
		0	I	II	III	IV
Total	146 (100)	4 (2.7)	31 (21.2)	41 (28.1)	12 (8.2)	58 (39.7)
Alveolar ridge	65 (44.5)	1 (1.5)	8 (12.3)	20 (30.8)	4 (6.2)	32 (49.2)
Tongue	31 (21.2)	2 (6.5)	8 (25.8)	12 (38.7)	2 (6.5)	7 (22.6)
Buccal mucosa	25 (17.1)	1 (4.0)	7 (28.0)	12 (38.7)	2 (6.5)	7 (22.6)
Retromolar trigone	9 (6.2)	0 (0)	1 (11.1)	1 (11.1)	0 (0)	7 (77.8)
Hard palate	10 (6.8)	0 (0)	3 (30.0)	3 (30.0)	0 (0)	7 (77.8)
Floor of the mouth	6 (4.1)	0 (0)	4 (66.7)	1 (16.7)	0 (0)	1 (16.7)
Non-periodontitis	9 (100)	2 (22.2)	1 (11.1)	4 (44.4)	0 (0)	2 (22.2)
Alveolar ridge	3 (33.3)	0 (0)	0 (0)	2 (66.7)	0 (0)	1 (33.3)
Tongue	5 (55.6)	2 (40.0)	1 (20.0)	1 (20.0)	0 (0)	1 (20.0)
Buccal mucosa	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Retromolar trigone	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hard palate	1 (11.1)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
Floor of the mouth	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Periodontitis[‡]	137 (100)	2 (1.5)	30 (21.9)	37 (27.0)	12 (8.8)	56 (40.9)
Alveolar ridge	62 (45.3)	1 (1.6)	8 (12.9)	18 (29.0)	4 (6.5)	31 (50.0)
Tongue	26 (19.0)	0 (0)	7 (26.9)	11 (42.3)	2 (7.7)	6 (23.1)
Buccal mucosa	25 (18.2)	1 (4.0)	7 (28.0)	4 (16.0)	6 (24.0)	7 (28.0)
Retromolar trigone	9 (6.6)	0 (0)	1 (11.1)	1 (11.1)	0 (0)	7 (77.8)
Hard palate	9 (6.6)	0 (0)	3 (33.3)	2 (22.2)	0 (0)	4 (44.4)
Floor of the mouth	6 (4.4)	0 (0)	4 (66.7)	1 (16.7)	0 (0)	1 (16.7)

* column %

† row %

‡ Periodontitis: incipient and severe periodontitis

Table 3. Adjusted association between periodontitis and oral squamous cell carcinoma (N=424)

Variable	Adjusted odds ratio (95% confidence interval)	
	Model I	Model II
Periodontitis, n (%)		
Normal	1	
Incipient	3.463 (1.348-8.895)	
Severe	4.066 (1.499-11.026)	
Trend-p	0.003	
Normal		1
Incipient and severe		3.664 (1.455-9.226)
Alcohol intake, n (%)		
No	1	1
Yes	0.317 (0.181-0.557)	0.313 (0.178-0.549)
Education level, n (%)		
Middle school	1	1
High school or higher	5.225 (2.832-9.639)	5.136 (2.797-9.431)
Physical activity, n (%)		
No	1	1
Yes	0.550 (0.315-0.962)	0.557 (0.319-0.970)
Obesity, n (%)		
No	1	1
Yes	0.732 (0.436-1.230)	0.718 (0.430-1.199)
Diabetes, n (%)		
No	1	1
Yes	2.515 (1.221-5.180)	2.518 (1.227-5.164)
Hypertension, n (%)		
No	1	1
Yes	1.532 (.900-2.608)	1.532 (0.900-2.609)
Hypercholesterolemia, n (%)		
No	1	1
Yes	1.939 (0.860-4.374)	1.908 (0.851-4.277)

Bold denotes statistical significance ($p < 0.05$)

* Model I: Adjusted association of periodontitis (three groups) by multivariable conditional logistic regression model, conditional on age, sex

and smoking, adjusted for alcohol intake, education level, physical activity, obesity, diabetes, hypertension, hypercholesterolemia.
Model II: Adjusted association of periodontitis (two groups) by multivariable conditional logistic regression model same as Model I.

Table 4. Age, sex, and smoking stratified association of periodontitis with oral squamous cell carcinoma

Subgroup	N	Adjusted odds ratio (95% confidence interval)	
		Non-periodontitis	Periodontitis*
Age			
60 years old and below	173	1	4.107 (0.831-20.299)
More than 60 years	251	1	4.979 (1.369-18.106)
Sex			
Male	257	1	6.545 (1.121-38.220)
Female	167	1	2.756 (0.926-8.197)
Smoking			
No	235	1	3.173 (1.074-9.373)
Yes	189	1	4.738 (0.728-30.834)

Multivariable conditional logistic regression model, conditional on age, sex and smoking, adjusted for variables in Table 3.

*Periodontitis: incipient and severe periodontitis

Bold denotes OR>3.664 and statistical significance of $p<0.05$.

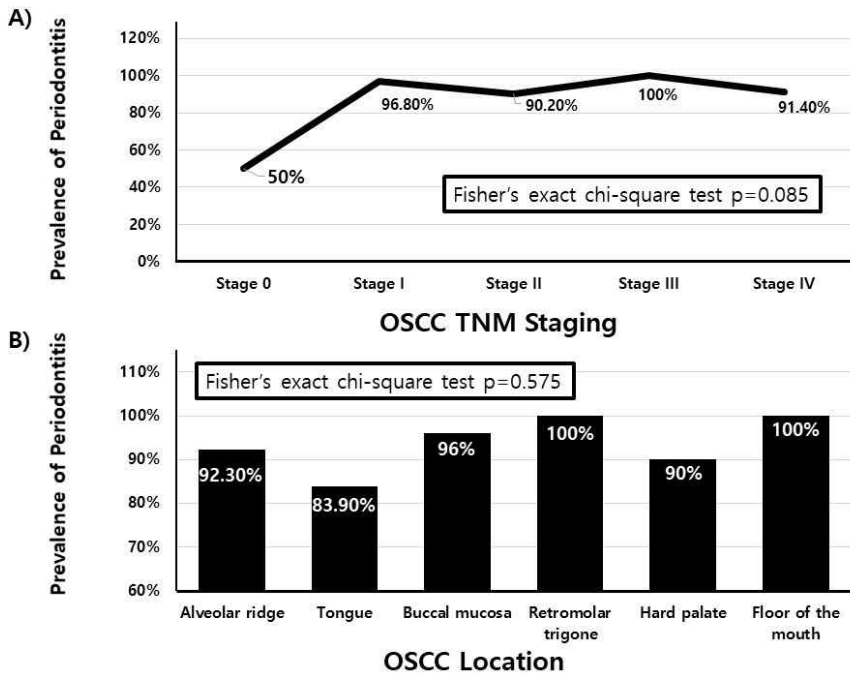


Figure 1. Prevalence of periodontitis across A) TNM staging of oral squamous cell carcinoma and B) its location.

Appendix 2 : Raw data

Raw data for Table 1

```

CROSSTABS
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  /FORMAT=AVALUE TABLES
  /STATISTICS=CHISQ
  /CELLS=COUNT ROW COLUMN TOTAL
  /COUNT ROUND CELL.

```

Crosstabs

Case Processing Summary

	Valid		Cases Missing		Total	
	N	Percent	N	Percent	N	Percent
Perio_EU_3G * case=1 control=0	424	100.0%	0	0.0%	424	100.0%

Perio_EU_3G * case=1 control=0 Crosstabulation

Perio_EU_3G			case=1 control=0		Total	
			control	case		
normal	Count		60	9	69	
		% within Perio_EU_3G	87.0%	13.0%	100.0%	
		% within case=1 control=0	21.6%	6.2%	16.3%	
		% of Total	14.2%	2.1%	16.3%	
	incipient	Count		143	91	234
			% within Perio_EU_3G	61.1%	38.9%	100.0%
			% within case=1 control=0	51.4%	62.3%	55.2%
			% of Total	33.7%	21.5%	55.2%
	severe	Count		75	46	121
			% within Perio_EU_3G	62.0%	38.0%	100.0%
			% within case=1 control=0	27.0%	31.5%	28.5%
			% of Total	17.7%	10.8%	28.5%
Total	Count		278	146	424	
		% within Perio_EU_3G	65.6%	34.4%	100.0%	
		% within case=1 control=0	100.0%	100.0%	100.0%	
		% of Total	65.6%	34.4%	100.0%	

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	16.729 ^a	2	.000
Likelihood Ratio	19.105	2	.000
Linear-by-Linear Association	8.774	1	.003
N of Valid Cases	424		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 23.76.

CROSSTABS

/TABLES=Perio_EU_2G BY cancer

/FORMAT=AVALUE TABLES

/STATISTICS=CHISQ

/CELLS=COUNT ROW COLUMN TOTAL

/COUNT ROUND CELL.

Crosstabs

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Perio_EU_2G * case=1 control=0	424	100.0%	0	0.0%	424	100.0%

Perio_EU_2G * case=1 control=0 Crosstabulation

			case=1 control=0		Total
			control	case	
Perio_EU_2G	.00	Count	60	9	69
		% within Perio_EU_2G	87.0%	13.0%	100.0%
		% within case=1 control=0	21.6%	6.2%	16.3%
		% of Total	14.2%	2.1%	16.3%
1.00	Count	Count	218	137	355
		% within Perio_EU_2G	61.4%	38.6%	100.0%
		% within case=1 control=0	78.4%	93.8%	83.7%
		% of Total	51.4%	32.3%	83.7%
Total	Count	Count	278	146	424
		% within Perio_EU_2G	65.6%	34.4%	100.0%
		% within case=1 control=0	100.0%	100.0%	100.0%
		% of Total	65.6%	34.4%	100.0%

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	16.702 ^a	1	.000		
Continuity Correction ^b	15.589	1	.000		
Likelihood Ratio	19.079	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	16.662	1	.000		
N of Valid Cases	424				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 23.76.

b. Computed only for a 2x2 table

```
T-TEST GROUPS=cancer(0 1)
/MISSING=ANALYSIS
/VARIABLES=cst_age
/CRITERIA=C1(.95).
```

T-Test

[DataSet1] C:\Users\USER\Desktop\HMP_9 논문\18July20_ANA_HMP9_30\4. 18Sept07_case_control_For ANA_n=424.sav

Group Statistics

	case=1 control=0	N	Mean	Std. Deviation	Std. Error
					Mean
Age (연령)	control	278	64.38	10.244	.614
	case	146	63.76	10.662	.882

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means				95% Confidence Interval of the Difference		
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Age (연령)	Equal variances assumed	.386	.534	.588	422	.557	.625	1.062	-1.463	2.712
	Equal variances not assumed			.581	284.648	.562	.625	1.075	-1.492	2.741

```

CROSSTABS
  /TABLES=cs1_sex BY cancer
  /FORMAT=AVALUE TABLES
  /STATISTICS=CHISQ
  /CELLS=COUNT ROW COLUMN TOTAL
  /COUNT ROUND CELL.

```

Crosstabs

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
성별 * case=1 control=0	424	100.0%	0	0.0%	424	100.0%

성별 * case=1 control=0 Crosstabulation

	성별		case=1 control=0		Total
			control	case	
male	Count		167	90	257
	% within 성별		65.0%	35.0%	100.0%
	% within case=1 control=0		60.1%	61.6%	60.6%
	% of Total		39.4%	21.2%	60.6%
female	Count		111	56	167
	% within 성별		66.5%	33.5%	100.0%
	% within case=1 control=0		39.9%	38.4%	39.4%
	% of Total		26.2%	13.2%	39.4%
Total	Count		278	146	424
	% within 성별		65.6%	34.4%	100.0%
	% within case=1 control=0		100.0%	100.0%	100.0%
	% of Total		65.6%	34.4%	100.0%

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.099 ^a	1	.753		
Continuity Correction ^b	.044	1	.834		
Likelihood Ratio	.099	1	.753		
Fisher's Exact Test				.834	.418
Linear-by-Linear Association	.099	1	.753		
N of Valid Cases	424				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 57.50.

b. Computed only for a 2x2 table

CROSSTABS

/TABLES=SMOKING_2G BY cancer

/FORMAT=AVALUE TABLES

/STATISTICS=CHISQ

/CELLS=COUNT ROW COLUMN TOTAL

/COUNT ROUND CELL.

Crosstabs

Case Processing Summary

	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
평생흡연 여부 * case=1 control=0	424	100.0%	0	0.0%	424	100.0%

평생흡연 여부 * case=1 control=0 Crosstabulation

			case=1 control=0		Total
			control	case	
평생흡연 여부	no	Count	155	80	235
		% within 평생흡연 여부	66.0%	34.0%	100.0%
		% within case=1 control=0	55.8%	54.8%	55.4%
		% of Total	36.6%	18.9%	55.4%
yes	yes	Count	123	66	189
		% within 평생흡연 여부	65.1%	34.9%	100.0%
		% within case=1 control=0	44.2%	45.2%	44.6%
		% of Total	29.0%	15.6%	44.6%
Total	Total	Count	278	146	424
		% within 평생흡연 여부	65.6%	34.4%	100.0%
		% within case=1 control=0	100.0%	100.0%	100.0%
		% of Total	65.6%	34.4%	100.0%

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Pearson Chi-Square	.036 ^a	1	.850		
Continuity Correction ^b	.007	1	.931		
Likelihood Ratio	.036	1	.850		
Fisher's Exact Test				.918	.465
Linear-by-Linear Association	.036	1	.850		
N of Valid Cases	424				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 65.08.

b. Computed only for a 2x2 table.

CROSSTABS

/TABLES=DRINK_2G BY cancer

/FORMAT=AVALUE TABLES

/STATISTICS=CHISQ

/CELLS=COUNT ROW COLUMN TOTAL

/COUNT ROUND CELL.

Crosstabs

Case Processing Summary

	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
DRINK_2G * case=1 control=0	424	100.0%	0	0.0%	424	100.0%

DRINK_2G * case=1 control=0 Crosstabulation

		case=1 control=0		Total	
		control	case		
DRINK_2G	no	Count	109	92	201
		% within DRINK_2G	54.2%	45.8%	100.0%
		% within case=1 control=0	39.2%	63.0%	47.4%
		% of Total	25.7%	21.7%	47.4%
	yes	Count	169	54	223
		% within DRINK_2G	75.8%	24.2%	100.0%
		% within case=1 control=0	60.8%	37.0%	52.6%
		% of Total	39.9%	12.7%	52.6%
Total		Count	278	146	424
		% within DRINK_2G	65.6%	34.4%	100.0%
		% within case=1 control=0	100.0%	100.0%	100.0%
		% of Total	65.6%	34.4%	100.0%

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Pearson Chi-Square	21.757 ^a	1	.000		
Continuity Correction ^b	20.813	1	.000		
Likelihood Ratio	21.915	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	21.706	1	.000		
N of Valid Cases	424				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 69.21.

b. Computed only for a 2x2 table

```

CROSSTABS
  /TABLES=Edu_2G BY cancer
  /FORMAT=AVALUE TABLES
  /STATISTICS=CHISQ
  /CELLS=COUNT ROW COLUMN TOTAL
  /COUNT ROUND CELL.

```

Crosstabs

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
학력 2G * case=1 control=0	424	100.0%	0	0.0%	424	100.0%

학력 2G * case=1 control=0 Crosstabulation

		case=1 control=0		Total	
		control	case		
학력 2G	중졸이하	Count	177	46	223
		% within 학력 2G	79.4%	20.6%	100.0%
		% within case=1 control=0	63.7%	31.5%	52.6%
		% of Total	41.7%	10.8%	52.6%
고졸이상	Count	101	100	201	
		% within 학력 2G	50.2%	49.8%	100.0%
		% within case=1 control=0	36.3%	68.5%	47.4%
		% of Total	23.8%	23.6%	47.4%
Total	Count	278	146	424	
		% within 학력 2G	65.6%	34.4%	100.0%
		% within case=1 control=0	100.0%	100.0%	100.0%
		% of Total	65.6%	34.4%	100.0%

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Pearson Chi-Square	39.715 ^a	1	.000		
Continuity Correction ^b	38.436	1	.000		
Likelihood Ratio	40.357	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	39.621	1	.000		
N of Valid Cases	424				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 69.21.

b. Computed only for a 2x2 table

CROSSTABS
 /TABLES=Exer_2G BY cancer
 /FORMAT=AVALUE TABLES
 /STATISTICS=CHISQ
 /CELLS=COUNT ROW COLUMN TOTAL
 /COUNT ROUND CELL.

Crosstabs

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
몸에 힘이 날 정도의 운동을 규칙적으로 하십니까? * case=1 control=0	424	100.0%	0	0.0%	424	100.0%

몸에 힘이 날 정도의 운동을 규칙적으로 하십니까? * case=1 control=0

Crosstabulation

		case=1 control=0		Total	
		control	case		
몸에 힘이 날 정도의 운동을 규칙적으로 하십니까?	1	Count	185	108	293
		% within 몸에 힘이 날 정도의 운동을 규칙적으로 하십니까?	63.1%	36.9%	100.0%
		% within case=1 control=0	66.5%	74.0%	69.1%
		% of Total	43.6%	25.5%	69.1%
2	Count	93	38	131	
	% within 몸에 힘이 날 정도의 운동을 규칙적으로 하십니까?	71.0%	29.0%	100.0%	
	% within case=1 control=0	33.5%	26.0%	30.9%	
	% of Total	21.9%	9.0%	30.9%	
Total	Count	278	146	424	
	% within 몸에 힘이 날 정도의 운동을 규칙적으로 하십니까?	65.6%	34.4%	100.0%	
	% within case=1 control=0	100.0%	100.0%	100.0%	
	% of Total	65.6%	34.4%	100.0%	

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.472 ^a	1	.116		
Continuity Correction ^b	2.137	1	.144		
Likelihood Ratio	2.513	1	.113		
Fisher's Exact Test				.123	.071
Linear-by-Linear Association	2.467	1	.116		
N of Valid Cases	424				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 45.11.

b. Computed only for a 2x2 table

CROSSTABS

/TABLES=BMI_2G BY cancer
 /FORMAT=AVALUE TABLES
 /STATISTICS=CHISQ
 /CELLS=COUNT ROW COLUMN TOTAL
 /COUNT ROUND CELL.

Crosstabs

Case Processing Summary

	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
BMI_2G * case=1 control=0	424	100.0%	0	0.0%	424	100.0%

BMI_2G * case=1 control=0 Crosstabulation

		case=1 control=0		Total	
		control	case		
BMI_2G	1.00	Count	176	101	277
		% within BMI_2G	63.5%	36.5%	100.0%
		% within case=1 control=0	63.3%	69.2%	65.3%
		% of Total	41.5%	23.8%	65.3%
2.00	Count	102	45	147	
	% within BMI_2G	69.4%	30.6%	100.0%	
	% within case=1 control=0	36.7%	30.8%	34.7%	
	% of Total	24.1%	10.6%	34.7%	
Total	Count	278	146	424	
	% within BMI_2G	65.6%	34.4%	100.0%	
	% within case=1 control=0	100.0%	100.0%	100.0%	
	% of Total	65.6%	34.4%	100.0%	

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Pearson Chi-Square	1.456 ^a	1	.228		
Continuity Correction ^b	1.208	1	.272		
Likelihood Ratio	1.469	1	.225		
Fisher's Exact Test				.239	.136
Linear-by-Linear Association	1.452	1	.228		
N of Valid Cases	424				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 50.62.

b. Computed only for a 2x2 table

CROSSTABS

/TABLES=Diabetes_2G BY cancer

/FORMAT=AVALUE TABLES

/STATISTICS=CHISQ

/CELLS=COUNT ROW COLUMN TOTAL

/COUNT ROUND CELL.

Crosstabs

Case Processing Summary

	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
당뇨혈당126 * case=1 control=0	424	100.0%	0	0.0%	424	100.0%

당뇨혈당126 * case=1 control=0 Crosstabulation

			case=1 control=0		Total
			control	case	
당뇨혈당126	no	Count	251	118	369
		% within 당뇨혈당126	68.0%	32.0%	100.0%
		% within case=1 control=0	90.3%	80.8%	87.0%
		% of Total	59.2%	27.8%	87.0%
	yes	Count	27	28	55
		% within 당뇨혈당126	49.1%	50.9%	100.0%
		% within case=1 control=0	9.7%	19.2%	13.0%
		% of Total	6.4%	6.6%	13.0%
Total	Count	278	146	424	
	% within 당뇨혈당126	65.6%	34.4%	100.0%	
	% within case=1 control=0	100.0%	100.0%	100.0%	
	% of Total	65.6%	34.4%	100.0%	

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Pearson Chi-Square	7.598 ^a	1	.006		
Continuity Correction ^b	6.783	1	.009		
Likelihood Ratio	7.267	1	.007		
Fisher's Exact Test				.009	.005
Linear-by-Linear Association	7.580	1	.006		
N of Valid Cases	424				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 18.94.

b. Computed only for a 2x2 table

```

CROSSTABS
  /TABLES=Hypertension BY cancer
  /FORMAT=AVALUE TABLES
  /STATISTICS=CHISQ
  /CELLS=COUNT ROW COLUMN TOTAL
  /COUNT ROUND CELL.

```

Crosstabs

Case Processing Summary

	Valid		Cases Missing		Total	
	N	Percent	N	Percent	N	Percent
고혈압-SBP140,DBP90,약복용 * case=1 control=0	424	100.0%	0	0.0%	424	100.0%

고혈압-SBP140,DBP90,약복용 * case=1 control=0 Crosstabulation

			case=1 control=0		Total
			control	case	
고혈압-SBP140,DBP90,약복용	No	Count	130	55	185
		% within 고혈압-SBP140, DBP90,약복용	70.3%	29.7%	100.0%
		% within case=1 control=0	46.8%	37.7%	43.6%
		% of Total	30.7%	13.0%	43.6%
	Yes	Count	148	91	239
		% within 고혈압-SBP140, DBP90,약복용	61.9%	38.1%	100.0%
		% within case=1 control=0	53.2%	62.3%	56.4%
		% of Total	34.9%	21.5%	56.4%
Total	Count	278	146	424	
	% within 고혈압-SBP140, DBP90,약복용	65.6%	34.4%	100.0%	
	% within case=1 control=0	100.0%	100.0%	100.0%	
	% of Total	65.6%	34.4%	100.0%	

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.217 ^a	1	.073		
Continuity Correction ^b	2.858	1	.091		
Likelihood Ratio	3.239	1	.072		
Fisher's Exact Test				.080	.045
Linear-by-Linear Association	3.209	1	.073		
N of Valid Cases	424				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 63.70.

b. Computed only for a 2x2 table

CROSSTABS

/TABLES=Hypercholesterol_2G BY cancer
 /FORMAT=AVALUE TABLES
 /STATISTICS=CHISQ
 /CELLS=COUNT ROW COLUMN TOTAL
 /COUNT ROUND CELL.

Crosstabs

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Hypercholesterol240이상 * case=1 control=0	424	100.0%	0	0.0%	424	100.0%

Hypercholesterol240이상 * case=1 control=0 Crosstabulation

			case=1 control=0		Total
			control	case	
Hypercholesterol240이상	no	Count	256	124	380
		% within Hypercholesterol240이상	67.4%	32.6%	100.0%
		% within case=1 control=0	92.1%	84.9%	89.6%
		% of Total	60.4%	29.2%	89.6%
	yes	Count	22	22	44
		% within Hypercholesterol240이상	50.0%	50.0%	100.0%
		% within case=1 control=0	7.9%	15.1%	10.4%
		% of Total	5.2%	5.2%	10.4%
Total	Count	278	146	424	
	% within Hypercholesterol240이상	65.6%	34.4%	100.0%	
	% within case=1 control=0	100.0%	100.0%	100.0%	
	% of Total	65.6%	34.4%	100.0%	

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	5.269 ^a	1	.022		
Continuity Correction ^b	4.528	1	.033		
Likelihood Ratio	5.037	1	.025		
Fisher's Exact Test				.029	.018
Linear-by-Linear Association	5.257	1	.022		
N of Valid Cases	424				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 15.15.

b. Computed only for a 2x2 table

Raw data for Table 2

```

CROSSTABS
  /TABLES=csi_cancer_loc BY csi_cancer_stage
  /FORMAT=AVALUE TABLES
  /CELLS=COUNT ROW COLUMN TOTAL
  /COUNT ROUND CELL.
  
```

Crosstabs

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
종양의 위치 (원발병소의) * 암의병기	146	34.4%	.278	65.6%	424	100.0%

종양의 위치 (원발병소의) * 암의병기 Crosstabulation

			암의병기					Total
			0	1	2	3	4	
종양의 위치 (원발병소의)	Floor of the mouth	Count	0	4	1	0	1	6
		% within 종양의 위치 (원발병소의)	0.0%	66.7%	16.7%	0.0%	16.7%	100.0%
		% within 암의병기	0.0%	12.9%	2.4%	0.0%	1.7%	4.1%
		% of Total	0.0%	2.7%	0.7%	0.0%	0.7%	4.1%
	Tongue	Count	2	8	12	2	7	31
		% within 종양의 위치 (원발병소의)	6.5%	25.8%	38.7%	6.5%	22.6%	100.0%
		% within 암의병기	50.0%	25.8%	29.3%	16.7%	12.1%	21.2%
		% of Total	1.4%	5.5%	8.2%	1.4%	4.8%	21.2%
	Buccal mucosa	Count	1	7	4	6	7	25
		% within 종양의 위치 (원발병소의)	4.0%	28.0%	16.0%	24.0%	28.0%	100.0%
		% within 암의병기	25.0%	22.6%	9.8%	50.0%	12.1%	17.1%
		% of Total	0.7%	4.8%	2.7%	4.1%	4.8%	17.1%
	Alveolar ridge	Count	1	8	20	4	32	65
		% within 종양의 위치 (원발병소의)	1.5%	12.3%	30.8%	6.2%	49.2%	100.0%
		% within 암의병기	25.0%	25.8%	48.8%	33.3%	55.2%	44.5%
		% of Total	0.7%	5.5%	13.7%	2.7%	21.9%	44.5%
	Hard palate	Count	0	3	3	0	4	10
		% within 종양의 위치 (원발병소의)	0.0%	30.0%	30.0%	0.0%	40.0%	100.0%
		% within 암의병기	0.0%	9.7%	7.3%	0.0%	6.9%	6.8%
		% of Total	0.0%	2.1%	2.1%	0.0%	2.7%	6.8%
Retromolar trigone	Count	0	1	1	0	7	9	
	% within 종양의 위치 (원발병소의)	0.0%	11.1%	11.1%	0.0%	77.8%	100.0%	
	% within 암의병기	0.0%	3.2%	2.4%	0.0%	12.1%	6.2%	
	% of Total	0.0%	0.7%	0.7%	0.0%	4.8%	6.2%	
Total	Count	4	31	41	12	58	146	
	% within 종양의 위치 (원발병소의)	2.7%	21.2%	28.1%	8.2%	39.7%	100.0%	
	% within 암의병기	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
	% of Total	2.7%	21.2%	28.1%	8.2%	39.7%	100.0%	

SORT CASES BY Perio_EU_2G.
 SPLIT FILE LAYERED BY Perio_EU_2G.

CROSSTABS
 /TABLES=cs1_cancer_loc BY cs1_cancer_stage /FORMAT=AVALUE TABLES
 /STATISTICS=CHISQ
 /CELLS=COUNT ROW COLUMN TOTAL
 /COUNT ROUND CELL.

Crosstabs

Case Processing Summary

Perio_EU_2G		Valid		Cases Missing		Total	
		N	Percent	N	Percent	N	Percent
.00	종양의 위치 (원발병소의) * 암의병기	9	13.0%	60	87.0%	69	100.0%
1.00	종양의 위치 (원발병소의) * 암의병기	137	38.6%	218	61.4%	355	100.0%

Chi-Square Tests

Perio_EU_2G		Value	df	Asymptotic Significance (2-sided)
.00	Pearson Chi-Square	4.500 ^a	6	.609
	Likelihood Ratio	5.774	6	.449
	N of Valid Cases	9		
1.00	Pearson Chi-Square	33.314 ^b	20	.031
	Likelihood Ratio	32.271	20	.040
	N of Valid Cases	137		

a. 12 cells (100.0%) have expected count less than 5. The minimum expected count is .11.

b. 20 cells (66.7%) have expected count less than 5. The minimum expected count is .09.

중양의 위치 (원발병소의) * 양의병기 Crosstabulation

Perlo_EU_2G				양의병기					Total	
				0	1	2	3	4	Total	
.00	중양의 위치 (원발병소의)	Tongue	Count	2	1	1		1	5	
			% within 중양의 위치 (원발병소의)	40.0%	20.0%	20.0%		20.0%	100.0%	
			% within 양의병기	100.0%	100.0%	25.0%		50.0%	55.6%	
			% of Total	22.2%	11.1%	11.1%		11.1%	55.6%	
		Alveolar ridge	Count	0	0	2		1	3	
			% within 중양의 위치 (원발병소의)	0.0%	0.0%	66.7%		33.3%	100.0%	
			% within 양의병기	0.0%	0.0%	50.0%		50.0%	33.3%	
			% of Total	0.0%	0.0%	22.2%		11.1%	33.3%	
		Hard palate	Count	0	0	1		0	1	
			% within 중양의 위치 (원발병소의)	0.0%	0.0%	100.0%		0.0%	100.0%	
			% within 양의병기	0.0%	0.0%	25.0%		0.0%	11.1%	
			% of Total	0.0%	0.0%	11.1%		0.0%	11.1%	
		Total		Count	2	1	4		2	9
				% within 중양의 위치 (원발병소의)	22.2%	11.1%	44.4%		22.2%	100.0%
		% within 양의병기	100.0%	100.0%	100.0%		100.0%	100.0%		
		% of Total	22.2%	11.1%	44.4%		22.2%	100.0%		
1.00	중양의 위치 (원발병소의)	Floor of the mouth	Count	0	4	1	0	1	6	
			% within 중양의 위치 (원발병소의)	0.0%	66.7%	16.7%	0.0%	16.7%	100.0%	
			% within 양의병기	0.0%	13.3%	2.7%	0.0%	1.8%	4.4%	
			% of Total	0.0%	2.9%	0.7%	0.0%	0.7%	4.4%	
		Tongue	Count	0	7	11	2	6	26	
			% within 중양의 위치 (원발병소의)	0.0%	26.9%	42.3%	7.7%	23.1%	100.0%	
			% within 양의병기	0.0%	23.3%	29.7%	16.7%	10.7%	19.0%	
			% of Total	0.0%	5.1%	8.0%	1.5%	4.4%	19.0%	
		Buccal mucosa	Count	1	7	4	6	7	25	
			% within 중양의 위치 (원발병소의)	4.0%	28.0%	16.0%	24.0%	28.0%	100.0%	
			% within 양의병기	50.0%	23.3%	10.8%	50.0%	12.5%	18.2%	
			% of Total	0.7%	5.1%	2.9%	4.4%	5.1%	18.2%	
		Alveolar ridge	Count	1	8	18	4	31	62	
			% within 중양의 위치 (원발병소의)	1.6%	12.9%	29.0%	6.5%	50.0%	100.0%	
			% within 양의병기	50.0%	26.7%	48.6%	33.3%	55.4%	45.3%	
			% of Total	0.7%	5.8%	13.1%	2.9%	22.6%	45.3%	
		Hard palate	Count	0	3	2	0	4	9	
			% within 중양의 위치 (원발병소의)	0.0%	33.3%	22.2%	0.0%	44.4%	100.0%	
			% within 양의병기	0.0%	10.0%	5.4%	0.0%	7.1%	6.6%	
			% of Total	0.0%	2.2%	1.5%	0.0%	2.9%	6.6%	
		Retromolar trigone	Count	0	1	1	0	7	9	
			% within 중양의 위치 (원발병소의)	0.0%	11.1%	11.1%	0.0%	77.8%	100.0%	
			% within 양의병기	0.0%	3.3%	2.7%	0.0%	12.5%	6.6%	
			% of Total	0.0%	0.7%	0.7%	0.0%	5.1%	6.6%	
		Total		Count	2	30	37	12	56	137
				% within 중양의 위치 (원발병소의)	1.5%	21.9%	27.0%	8.8%	40.9%	100.0%
				% within 양의병기	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
				% of Total	1.5%	21.9%	27.0%	8.8%	40.9%	100.0%

Raw data for Table 3

```

RECODE Time (ELSE=1).
EXECUTE.
COXREG time
  /STATUS=cancer(1)
  /STRATA=perio_stratum
  /CONTRAST (Perio_EU_3G)=Indicator(1)
  /METHOD=ENTER Perio_EU_3G DRINK_2G Exer_2G Hypertension Diabetes_2G BMI_2G
    Hypercholesterol_2G Edu_2G
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).

```

Cox Regression

Case Processing Summary

		N	Percent
Cases available in analysis	Event ^a	146	34.4%
	Censored	278	65.6%
	Total	424	100.0%
Cases dropped	Cases with missing values	0	0.0%
	Cases with negative time	0	0.0%
	Censored cases before the earliest event in a stratum	0	0.0%
	Total	0	0.0%
Total		424	100.0%

a. Dependent Variable: Time

Categorical Variable Codings^a

		Frequency	(1)	(2)
Perio_EU_3G ^b	.00=normal	69	0	0
	1.00=incipient	234	1	0
	2.00=seere	121	0	1

a. Category variable: Perio_EU_3G

b. Indicator Parameter Coding

Block 1: Method = Enter

Omnibus Tests of Model Coefficients^a

-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
213.176	83.569	9	.000	96.266	9	.000	96.266	9	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
Perio_EU_3G			7.917	2	.019			
Perio_EU_3G(1)	1.242	.481	6.657	1	.010	3.463	1.348	8.895
Perio_EU_3G(2)	1.403	.509	7.593	1	.006	4.066	1.499	11.026
DRINK_2G	-1.149	.287	15.994	1	.000	.317	.181	.557
몸에 땀이 날 정도의 운동을 규칙적으로 하시니까?	-.597	.285	4.401	1	.036	.550	.315	.962
고혈압-SBP140,DBP90, 약복용	.426	.271	2.467	1	.116	1.532	.900	2.608
당노혈당126	.922	.369	6.264	1	.012	2.515	1.221	5.180
BMI_2G	-.312	.265	1.388	1	.239	.732	.436	1.230
Hypercholesterol240이상	.662	.415	2.548	1	.110	1.939	.860	4.374
학력 2G	1.653	.312	27.999	1	.000	5.225	2.832	9.639

Covariate Means

	Mean
Perio_EU_3G(1)	.552
Perio_EU_3G(2)	.285
DRINK_2G	1.526
몸에 땀이 날 정도의 운동을 규칙적으로 하시니까?	1.309
고혈압-SBP140,DBP90, 약복용	.564
당노혈당126	.130
BMI_2G	1.347
Hypercholesterol240이상	.104
학력 2G	1.474

```

RECODE Time (ELSE=1).
EXECUTE.
COXREG time
  /STATUS=cancer(1)
  /STRATA=perio_stratum
  /CONTRAST (Perio_EU_2G)=Indicator(1)
  /METHOD=ENTER Perio_EU_2G DRINK_2G Exer_2G Hypertension Diabetes_2G BMI_2G
    Hypercholesterol_2G Edu_2G
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).

```

Cox Regression

Case Processing Summary

		N	Percent
Cases available in analysis	Event ^a	146	34.4%
	Censored	278	65.6%
	Total	424	100.0%
Cases dropped	Cases with missing values	0	0.0%
	Cases with negative time	0	0.0%
	Censored cases before the earliest event in a stratum	0	0.0%
	Total	0	0.0%
Total		424	100.0%

a. Dependent Variable: Time

Categorical Variable Codings^a

		Frequency	(1)
Perio_EU_2G ^b	.00	69	0
	1.00	355	1

a. Category variable: Perio_EU_2G (Perio_EU_2G)

b. Indicator Parameter Coding

Block 1: Method = Enter

Omnibus Tests of Model Coefficients^a

-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
213.462	83.368	8	.000	95.980	8	.000	95.980	8	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
Perio_EU_2G	1.299	.471	7.598	1	.006	3.664	1.455	9.226
DRINK_2G	-1.163	.287	16.410	1	.000	.313	.178	.549
몸에 힘이 날 정도의 운동을 규칙적으로 하십니까?	-.586	.284	4.271	1	.039	.557	.319	.970
고혈압-SBP140,DBP90, 약복용	.427	.272	2.466	1	.116	1.532	.900	2.609
당뇨혈당126	.923	.367	6.346	1	.012	2.518	1.227	5.164
BMI_2G	-.331	.261	1.605	1	.205	.718	.430	1.199
Hypercholesterol240이상	.646	.412	2.459	1	.117	1.908	.851	4.277
학력 2G	1.636	.310	27.854	1	.000	5.136	2.797	9.431

Covariate Means

	Mean
Perio_EU_2G	.837
DRINK_2G	1.526
몸에 힘이 날 정도의 운동을 규칙적으로 하십니까?	1.309
고혈압-SBP140,DBP90, 약복용	.564
당뇨혈당126	.130
BMI_2G	1.347
Hypercholesterol240이상	.104
학력 2G	1.474

Raw data for Table 4

SPLIT FILE OFF.

SORT CASES BY age_2G60.

SPLIT FILE LAYERED BY age_2G60.

COXREG time

/STATUS=cancer(1)

/STRATA=perio_stratum

/CONTRAST (Perio_EU_2G)=Indicator(1)

/METHOD=ENTER Perio_EU_2G DRINK_2G Edu_2G Hypertension Diabetes_2G

Hypercholesterol_2G Exer_2G BMI_2G

/PRINT=CI(95)

/CRITERIA=PIN(.05) POUT(.10) ITERATE(20).

Cox Regression

Case Processing Summary

age_2G60			N	Percent
1.00	Cases available in analysis	Event ^a	62	35.8%
		Censored	111	64.2%
		Total	173	100.0%
	Cases dropped	Cases with missing values	0	0.0%
		Cases with negative time	0	0.0%
		Censored cases before the earliest event in a stratum	0	0.0%
		Total	0	0.0%
Total		173	100.0%	
2.00	Cases available in analysis	Event ^a	84	33.5%
		Censored	167	66.5%
		Total	251	100.0%
	Cases dropped	Cases with missing values	0	0.0%
		Cases with negative time	0	0.0%
		Censored cases before the earliest event in a stratum	0	0.0%
		Total	0	0.0%
Total		251	100.0%	

Omnibus Tests of Model Coefficients^a

age_2G60	-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
		Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
1.00	64.041	46.508	8	.000	61.645	8	.000	61.645	8	.000
2.00	122.821	52.290	8	.000	60.935	8	.000	60.935	8	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

age_2G60		B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
								Lower	Upper
1.00	Perio_EU_2G	1.413	.815	3.002	1	.083	4.107	.831	20.299
	DRINK_2G	-.728	.551	1.743	1	.187	.483	.164	1.423
	학력 2G	3.076	.846	13.228	1	.000	21.680	4.131	113.776
	고혈압-SBP140,DBP90,약복용	.814	.456	3.183	1	.074	2.257	.923	5.521
	당뇨질환126	1.782	.677	6.925	1	.008	5.942	1.576	22.405
	Hypercholesterol240이상	.522	.769	.460	1	.497	1.685	.373	7.607
	몸에 많이 땀 정도의 운동 을 규칙적으로 하십니까?	-2.304	.670	11.831	1	.001	.100	.027	.371
	BMI_2G	-.879	.459	3.667	1	.056	.415	.169	1.021
2.00	Perio_EU_2G	1.605	.659	5.939	1	.015	4.979	1.369	18.106
	DRINK_2G	-1.668	.389	18.437	1	.000	.189	.088	.404
	학력 2G	1.122	.371	9.166	1	.002	3.071	1.485	6.348
	고혈압-SBP140,DBP90,약복용	-.110	.376	.086	1	.770	.896	.429	1.871
	당뇨질환126	.558	.554	1.012	1	.314	1.747	.589	5.177
	Hypercholesterol240이상	1.565	.639	6.003	1	.014	4.783	1.368	16.731
	몸에 많이 땀 정도의 운동 을 규칙적으로 하십니까?	.421	.384	1.200	1	.273	1.523	.717	3.235
	BMI_2G	-.127	.384	.110	1	.740	.880	.415	1.869

```

SORT CASES BY csl_sex.
SPLIT FILE LAYERED BY csl_sex.

```

```

COXREG time
  /STATUS=cancer(1)
  /STRATA=perio_stratum
  /CONTRAST (Perio_EU_2G)=Indicator(1)
  /METHOD=ENTER Perio_EU_2G DRINK_2G Edu_2G Hypertension Diabetes_2G
    Hypercholesterol_2G Exer_2G BMI_2G
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).

```

Cox Regression

Case Processing Summary

성별			N	Percent
male	Cases available in analysis	Event ^a	90	35.0%
		Censored	167	65.0%
		Total	257	100.0%
	Cases dropped	Cases with missing values	0	0.0%
		Cases with negative time	0	0.0%
		Censored cases before the earliest event in a stratum	0	0.0%
		Total	0	0.0%
	Total		257	100.0%
	female	Cases available in analysis	Event ^a	56
Censored			111	66.5%
Total			167	100.0%
Cases dropped		Cases with missing values	0	0.0%
		Cases with negative time	0	0.0%
		Censored cases before the earliest event in a stratum	0	0.0%
		Total	0	0.0%
Total			167	100.0%

Block 1: Method = Enter

Omnibus Tests of Model Coefficients^a

성별	-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
		Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
male	126.799	51.222	8	.000	60.409	8	.000	60.409	8	.000
female	83.753	34.093	8	.000	38.481	8	.000	38.481	8	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

성별		B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
								Lower	Upper
male	Perio_EU_2G	1.879	.900	4.353	1	.037	6.545	1.121	38.220
	DRINK_2G	-1.331	.370	12.943	1	.000	.264	.128	.546
	학력_2G	1.746	.419	17.399	1	.000	5.732	2.524	13.022
	고혈압-SBP140,DBP90,약복용	.436	.326	1.785	1	.182	1.546	.816	2.931
	당뇨혈당126	.921	.428	4.622	1	.032	2.511	1.085	5.811
	Hypercholesterol240이상	.281	.599	.221	1	.638	1.325	.410	4.282
	몸에 땀이 날 정도의 운동을 규칙적으로 하십니까?	-.454	.361	1.580	1	.209	.635	.313	1.289
	BMI_2G	-.233	.349	.445	1	.505	.792	.400	1.571
female	Perio_EU_2G	1.014	.556	3.321	1	.068	2.756	.926	8.197
	DRINK_2G	-.797	.470	2.874	1	.090	.451	.179	1.132
	학력_2G	1.683	.524	10.321	1	.001	5.381	1.927	15.022
	고혈압-SBP140,DBP90,약복용	.529	.517	1.046	1	.306	1.697	.616	4.674
	당뇨혈당126	1.116	.754	2.193	1	.139	3.054	.697	13.387
	Hypercholesterol240이상	.943	.600	2.472	1	.116	2.568	.793	8.317
	몸에 땀이 날 정도의 운동을 규칙적으로 하십니까?	-.916	.502	3.332	1	.068	.400	.150	1.070
	BMI_2G	-.437	.411	1.132	1	.287	.646	.289	1.445

SORT CASES BY SMOKING_2G.
 SPLIT FILE LAYERED BY SMOKING_2G.

```

COXREG time
  /STATUS=cancer(1)
  /STRATA=perio_stratum
  /CONTRAST (Perio_EU_2G)=Indicator(1)
  /METHOD=ENTER Perio_EU_2G DRINK_2G Edu_2G Hypertension Diabetes_2G
    Hypercholesterol_2G Exer_2G BMI_2G
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
  
```

Cox Regression

Case Processing Summary

평생흡연 여부			N	Percent
no	Cases available in analysis	Event ^a	80	34.0%
		Censored	154	65.5%
		Total	234	99.6%
	Cases dropped	Cases with missing values	0	0.0%
		Cases with negative time	0	0.0%
		Censored cases before the earliest event in a stratum	1	0.4%
		Total	1	0.4%
	Total		235	100.0%
	yes	Cases available in analysis	Event ^a	66
Censored			123	65.1%
Total			189	100.0%
Cases dropped		Cases with missing values	0	0.0%
		Cases with negative time	0	0.0%
		Censored cases before the earliest event in a stratum	0	0.0%
		Total	0	0.0%
Total			189	100.0%

Omnibus Tests of Model Coefficients^a

평생흡연 여부	-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
		Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
no	108.720	54.970	8	.000	62.193	8	.000	62.193	8	.000
yes	98.005	33.884	8	.000	39.714	8	.000	39.714	8	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

평생흡연 여부		B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
								Lower	Upper
no	Perio_EU_2G	1.155	.553	4.366	1	.037	3.173	1.074	9.373
	DRINK_2G	-.648	.386	2.820	1	.093	.523	.246	1.114
	학력_2G	1.878	.448	17.571	1	.000	6.543	2.719	15.748
	고혈압-SBP140,DBP90,약복용	.642	.398	2.605	1	.107	1.901	.871	4.147
	당노혈당126	1.280	.587	4.759	1	.029	3.595	1.139	11.350
	Hypercholesterol240이상	1.236	.588	4.418	1	.036	3.441	1.087	10.891
	몸에 힘이 날 정도의 운동을 규칙적으로 하십니까?	-.726	.413	3.086	1	.079	.484	.215	1.088
BMI_2G	-.426	.360	1.402	1	.236	.653	.323	1.322	
yes	Perio_EU_2G	1.556	.956	2.650	1	.104	4.738	.728	30.834
	DRINK_2G	-1.644	.448	13.442	1	.000	.193	.080	.465
	학력_2G	1.514	.475	10.166	1	.001	4.547	1.792	11.534
	고혈압-SBP140,DBP90,약복용	.453	.395	1.316	1	.251	1.574	.725	3.415
	당노혈당126	.709	.483	2.158	1	.142	2.032	.789	5.234
	Hypercholesterol240이상	-.002	.686	.000	1	.998	.998	.260	3.828
	몸에 힘이 날 정도의 운동을 규칙적으로 하십니까?	-.530	.409	1.680	1	.195	.589	.264	1.312
BMI_2G	-.218	.398	.301	1	.583	.804	.369	1.753	

Raw data for Figure 1

```

CROSSTABS
/TABLES=cs1_cancer_loc BY Perio_EU_incipient
/FORMAT=AVALUE TABLES
/STATISTICS=CHISQ
/CELLS=COUNT ROW COLUMN TOTAL
/COUNT ROUND CELL
/METHOD=EXACT TIMER(5) .

```

Case Processing Summary

	Valid		Cases Missing		Total	
	N	Percent	N	Percent	N	Percent
암의병기 * Perio_EU_incipient	146	100.0%	0	0.0%	146	100.0%

암의병기 * Perio_EU_incipient Crosstabulation

		Perio_EU_incipient		Total
		no	yes	
암의병기 0	Count	2	2	4
	% within 암의병기	50.0%	50.0%	100.0%
	% within Perio_EU_incipient	16.7%	1.5%	2.7%
	% of Total	1.4%	1.4%	2.7%
1	Count	1	30	31
	% within 암의병기	3.2%	96.8%	100.0%
	% within Perio_EU_incipient	8.3%	22.4%	21.2%
	% of Total	0.7%	20.5%	21.2%
2	Count	4	37	41
	% within 암의병기	9.8%	90.2%	100.0%
	% within Perio_EU_incipient	33.3%	27.6%	28.1%
	% of Total	2.7%	25.3%	28.1%
3	Count	0	12	12
	% within 암의병기	0.0%	100.0%	100.0%
	% within Perio_EU_incipient	0.0%	9.0%	8.2%
	% of Total	0.0%	8.2%	8.2%
4	Count	5	53	58
	% within 암의병기	8.6%	91.4%	100.0%
	% within Perio_EU_incipient	41.7%	39.6%	39.7%
	% of Total	3.4%	36.3%	39.7%
Total	Count	12	134	146
	% within 암의병기	8.2%	91.8%	100.0%
	% within Perio_EU_incipient	100.0%	100.0%	100.0%
	% of Total	8.2%	91.8%	100.0%

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	11.496 ^a	4	.022	.033		
Likelihood Ratio	8.293	4	.081	.088		
Fisher's Exact Test	7.416			.085		
Linear-by-Linear Association	.298 ^b	1	.585	.641	.334	.080
N of Valid Cases	146					

a. 6 cells (60.0%) have expected count less than 5. The minimum expected count is .33.

b. The standardized statistic is .546.

```

CROSSTABS
  /TABLES=csl_cancer_stage BY Perio_EU_incipient
  /FORMAT=AVALUE TABLES
  /STATISTICS=CHISQ
  /CELLS=COUNT ROW COLUMN TOTAL
  /COUNT ROUND CELL
  /METHOD=EXACT TIMER(5) .

```

Case Processing Summary

	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
종양의 위치 (원발병소의) Perio_EU_incipient	146	100.0%	0	0.0%	146	100.0%

종양의 위치 (원발병소의) * Perio_EU_incipient Crosstabulation

			Perio_EU_incipient		Total
			no	yes	
종양의 위치 (원발병소의)	Floor of the mouth	Count	0	6	6
		% within 종양의 위치 (원발병소의)	0.0%	100.0%	100.0%
		% within Perio_EU_incipient	0.0%	4.5%	4.1%
		% of Total	0.0%	4.1%	4.1%
	Tongue	Count	5	26	31
		% within 종양의 위치 (원발병소의)	16.1%	83.9%	100.0%
		% within Perio_EU_incipient	41.7%	19.4%	21.2%
		% of Total	3.4%	17.8%	21.2%
	Buccal mucosa	Count	1	24	25
		% within 종양의 위치 (원발병소의)	4.0%	96.0%	100.0%
		% within Perio_EU_incipient	8.3%	17.9%	17.1%
		% of Total	0.7%	16.4%	17.1%
Alveolar ridge	Count	5	60	65	
	% within 종양의 위치 (원발병소의)	7.7%	92.3%	100.0%	
	% within Perio_EU_incipient	41.7%	44.8%	44.5%	
	% of Total	3.4%	41.1%	44.5%	
Hard palate	Count	1	9	10	
	% within 종양의 위치 (원발병소의)	10.0%	90.0%	100.0%	
	% within Perio_EU_incipient	8.3%	6.7%	6.8%	
	% of Total	0.7%	6.2%	6.8%	
Retromolar trigone	Count	0	9	9	
	% within 종양의 위치 (원발병소의)	0.0%	100.0%	100.0%	
	% within Perio_EU_incipient	0.0%	6.7%	6.2%	
	% of Total	0.0%	6.2%	6.2%	
Total	Count	12	134	146	
	% within 종양의 위치 (원발병소의)	8.2%	91.8%	100.0%	
	% within Perio_EU_incipient	100.0%	100.0%	100.0%	
	% of Total	8.2%	91.8%	100.0%	

Chi-Square Tests

	Value	df	Asymptotic Significance (2- sided)	Exact Sig. (2-sided)
Pearson Chi-Square	4.570 ^a	5	.471	.434
Likelihood Ratio	5.409	5	.368	.443
Fisher's Exact Test	3.318			.575
N of Valid Cases	146			

a. 5 cells (41.7%) have expected count less than 5. The minimum expected count is .49.

-국문 초록-

치주염과 구강편평상피세포암의 연관성에 대한 병원 환자-코호트 대조군 연구

신 유 진

서울대학교 대학원

치의학과 구강악안면외과학 전공

(지도 교수: 이 종 호, 김 현 덕)

목적 : 치주염과 구강편평상피세포암 (OSCC)에 대한 대규모 병원 환자-코호트 대조군 연구는 아직 보고되지 않았다. 본 연구의 목적은 한국인에서 치주염의 OSCC 연관성, 특히 종양 위치와 종양-임파절-전이 (tumor-node-metastasis, TNM) 병기별 연관성을 조사하고자 하였다.

연구방법 : 본 연구의 참가자는 총 424명이었다. 그 중 서울대학교 치과병원의 OSCC 환자는 146명이었고, 양평 코호트에서 연령, 성별 및 흡연을 짝짓기한 대조군은 278명 (132쌍은 1:2, 14쌍은 1:1)이었다. OSCC는 방사선 영상들과 조직 생체 검사를 통해 진단하였고, 수술 후 종양 위치와 TNM 병기를 분류하였다. 치주염은 제5차 유

립 치주학회 지침에 따라 파노라마 방사선 사진을 사용하여 치조골 손실로 진단하였다. 알코올 섭취, 교육, 신체 활동, 체질량 지수에 의한 비만, 고혈압, 당뇨병과 고지질증을 혼돈변수로 설정하였다. 면접을 통해 연령, 성별, 흡연율, 음주량, 교육 및 신체 활동에 대한 정보를 얻었고, 신체 검사 및 의사 검진을 통해 체질량 지수와 혈압은 확인하였으며, 혈액검사를 통해 당뇨병과 고지질증 정보를 수집하였다. 치주염의 OSCC에 대한 통계학적 연관성은 조건부 로지스틱 회귀 분석을 사용하여 혼동변수를 보정한 후 치주염의 OSCC에 대한 보정 교차비로 연관성을 평가하였으며, 연령, 성별, 흡연에 따른 층화분석을 추가로 수행하였다. 특히 치주염의 OSCC TNM 병기와 위치에 대한 연관성은 Fisher 's exact chi-square test를 사용하여 검증하였다.

연구결과 : 치주염이 있는 참가자들은 치주염이 없는 참가자들 보다 OSCC 유병자가 될 가능성이 3.7배 높았다 (보정 교차비 [aOR] = 3.66, 95 % 신뢰 구간 = 1.46-9.23). 치주염의 분포는 OSCC의 TNM 병기나 그 위치에 따라 통계적으로 유의한 차이가 없었다 ($p > 0.05$). 치주염의 OSCC에 대한 연관성은 남성 (aOR = 6.55)과 60세 이상 참가자(aOR = 4.98)에서 증가되었다.

결론 : 본 연구는 치주염이 OSCC에 대하여 독립적 연관성이 있음을 보여주었다. 따라서 치주염은 OSCC의 주요한 위험 인자가 될 수 있다.

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주요어 : 구강편평상피세포암, 치주염, 종양위치, TNM병기, 역학

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