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#### Availability of Data and Material

The datasets generated or analyzed during the current study are available in the Korea National Health and Nutrition Examination Survey website [https://knhanes.kdca.go.kr].

#### Conflicts of Interest

Younghee Choe, a contributing editor of the Korean Journal of Helicobacter and Upper Gastrointestinal Research, was not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

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# Association Between Oral Health and Gastric Cancer in Korean Adults

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**Objectives:** Poor oral hygiene is known to be associated with gastric cancer, but this remains controversial. In this study, we investigated the association between oral health and gastric cancer in Korean adults using data from the Korea National Health and Nutrition Examination Survey. Methods: We analyzed data of 79501 patients with gastric cancer and 41856805 individuals without gastric cancer (control group) using the 7th and 8th Korea National Health and Nutrition Examination Survey (2016–2019) records. Layer and colony variables and weights were used for the complex sample design. We performed logistic regression analysis of complex samples to analyze factors that affect gastric cancer development. Results: Patients with gastric cancer were older and had a higher prevalence of hypertension, hyperlipidemia, and diabetes and a higher rate of current smoking and alcohol consumption than individuals without gastric cancer (p<0.001). Regarding oral health-related factors, the prevalence of very uncomfortable chewing difficulty was significantly higher in patients with gastric cancer (14.4% vs. 3.6%, p<0.001). On multivariate analysis of factors associated with gastric cancer, chewing difficulty showed the highest odds ratio (5.351, 95% confidence interval 2.128–8.982). Patients with very uncomfortable chewing difficulty had high rates of previous dental nerve treatment, gum disease treatment, tooth extraction or intraoral surgery, and prosthetic repair (p<0.001). Conclusions: Oral health-related chewing difficulties were associated with gastric cancer, which may be attributable to poor oral hygiene and degradation of oral microbiota. Patients at risk of gastric cancer warrant timely medical interventions to address their oral health and chewing difficulties.

**Keywords** Oral health; Chewing difficulty; Gastric cancer; Korea National Health and Nutrition Examination Survey.

## INTRODUCTION

Based on the World Health Organization records, cancer was the leading cause of death among people aged 30-70 in 183 countries worldwide in 2019. The increasing importance of cancer as a primary cause of death is partially established by the significant decrease in mortality rates associated with stroke and coronary heart disease compared with those asso-

ciated with cancer in many countries globally.1 Gastric cancer is widely prevalent and was ranked the fifth most common cancer worldwide in 2020.2 The cancer survival rate in Korea has significantly increased owing to early detection facilitated by the National Cancer Screening Program. However, based on the Korea Central Cancer Registry data, gastric cancer was the fourth most common new cancer in 2021, following thyroid, colon, and lung cancers.<sup>3</sup> Gastric cancer is significantly associated with individual genetic predisposition as well as environmental factors, such as Helicobacter pylori infection and diet including consumption of excessive salt, salt-preserved foods, and nitroso compounds; therefore, identification of the causative factors can reduce gastric cancer incidence and mortality. However, considering the current incidence of gastric cancer, some issues remain unclear even after control of known risk factors. For example, smoking is a significant risk factor for gastric cancer in high-income areas; however, it fails to adequately account for the high incidence of gastric cancer even in regions where smoking is uncommon.<sup>5</sup> Furthermore, H. pylori infection, a well-established risk factor for gastric cancer, is associated with only a relatively modest increase in risk in areas with high infection rates and high gastric cancer incidence.5 These findings suggest that the etiology of gastric cancer may be associated with risk factors that currently remain unidentified.

Meanwhile, bacterial colonization in the oral cavity increases the risk of dental caries. Oral-origin gastric microbiota may be associated with gastric cancer development, and the possibility of an interaction between oral microbiota and H. pylori has been suggested.<sup>6</sup> Additionally, poor oral hygiene and H. pylori in the oral cavity are associated with dental caries.<sup>7-9</sup> Some reports suggest that poor oral hygiene is associated with an increased risk of gastric cancer,7,10-13 although others do not report a significant association.14-17 A domestic study did not observe any association between gastric neoplastic lesions, including adenomas and oral health.<sup>18</sup> However, this was a smallscale, single-center retrospective study. In contrast, a recent Korean study using the National Health Insurance Service-National Sample Cohort reported that individuals with a history of chronic periodontitis may be at risk of developing gastric cancer.19

Therefore, we investigated the association between oral health and gastric cancer in Korean adults using data from the Korea National Health and Nutrition Examination Survey (KNHANES), which serves as a useful indicator of the health status of Korean adults.

## **METHODS**

## Study design and data source

This cross-sectional study utilized data from the 7th and 8th KNHANES performed between 2016 and 2019. The KNHANES is a nationally representative survey that obtains information regarding the health and nutritional status of Korean citizens. In this study, we focused on adults diagnosed with gastric cancer, and our dataset included 79501 patients.

## Participants and sample selection

Study participants were selected from the KNHANES records based on current diagnosis of gastric cancer. The inclusion criteria were adults aged ≥18 years who were diagnosed with gastric cancer at the time of the survey. The control group consisted of individuals from the same dataset but without gastric cancer; the study included 41856805 participants.

#### Variables and data collection

The key variables analyzed in this study included demographic information (age and sex), health-related factors (body mass index [BMI], hypertension, hyperlipidemia, and diabetes), specific oral health indicators (chewing difficulties, oral health perception, and a history of dental treatments, among other variables) (Supplementary Table 1 in the online-only Data Supplement), and data regarding lifestyle practices, such as smoking and alcohol consumption. Current smoking was defined as having smoked at least 100 cigarettes in one's lifetime and currently continuing to smoke, and alcohol consumption was defined as consumption of alcohol more than once a month.

## Complex sample design and weights

Considering the complex sample design of the KNHANES, layer and colony variables and sample weights were used to ensure accurate representativeness of the sample and account for the stratified multistage clustered probability design of the survey.

#### Statistical analysis

We performed univariate and multivariate logistic regression analysis. Univariate analysis was performed to determine the association between each variable and gastric cancer, and multivariate logistic regression was used to control for potential confounders and determine the independent effect of oral health factors on gastric cancer. Therefore, multiple logistic regression analysis was performed to adjust meaningful variables observed on univariate analysis. Odds ratios (OR) and 95% confidence intervals (CI) were calculated to quantify the

strength of associations. All statistical tests were two-tailed, and a p-value < 0.05 was considered statistically significant. All statistical analyses were performed using the IBM SPSS Statistics software, ver. 25.0 (IBM Corp., Armonk, NY, USA).

#### **Ethics statement**

This study was approved by the Review Board of Kangwon National University Hospital (approval number: KNUH-2023-11-005). Informed consent was not required owing to the retrospective nature of the study.

## **RESULTS**

## Demographic and health-related characteristics

Our analysis revealed significant demographic and healthrelated differences between individuals with and without gastric cancer. Patients with gastric cancer were older (mean age 62.6 years vs. 47.7 years, p<0.001) (Table 1). Although not statistically significant, there was a tendency for there to be more men in the gastric cancer group (52.8% vs. 49.7%, p=0.098). We observed no significant intergroup difference in BMI between the two groups (22.0 kg/m<sup>2</sup> vs. 24.0 kg/m<sup>2</sup>, p=0.086). However, prevalence of hypertension (32.5% vs. 19.0%, p< 0.001), hyperlipidemia (19.9% vs. 12.8%, p<0.001), and diabetes (20.0% vs. 7.6%, p<0.001) was higher in the gastric cancer group. We observed significant differences in lifestyle factors such as current smoking (53.0% vs. 40.6%, p<0.001) and alcohol consumption rates (51.1% vs. 22.2%, p<0.001).

#### Oral health-related factors

With regard to oral health, the prevalence of very uncomfortable chewing difficulty was higher in patients with gastric cancer than in the control group (14.4% vs. 3.6%, p<0.001) (Table 1). We also observed significant differences in oral healthrelated variables, specifically in the rates of dental nerve treatment (15.9% vs. 12.5%, p<0.001), treatment for gum disease (16.5% vs. 12.5%, p<0.001), tooth extraction or intraoral surgery (14.7% vs. 9.9%, p<0.001), and creation or repair of dental prostheses (21.3% vs. 15.4%, p<0.001). Although statistically nonsignificant, self-perceived poor oral condition (poor or very poor) (8.0% vs. 7.4%, p=0.078), history of toothache in the preceding year (31.5% vs. 30.2%, p=0.060), and reasons for activity limitations (dental and oral issues) (1.1% vs. 0.1%, p=0.055) were more frequent in the gastric cancer group.

## Logistic regression analysis

Table 2 shows the results of univariate and multivariate logistic regression analyses of factors associated with gastric

Table 1. Baseline characteristics of participants

Variable	Gastric cancer (n=79501)	Non-gastric cancer (n=41856805)	<i>p</i> -value
Age (yr)	62.6±1.9	47.7±0.2	< 0.001
Sex, male	52.8	49.7	0.098
Body mass index (kg/m²)	22.0±0.4	24.0±0.1	0.086
Hypertension	32.5	19.0	< 0.001
Hyperlipidemia	19.9	12.8	< 0.001
Diabetes	20.0	7.6	< 0.001
Current smoking*	53.0	40.6	< 0.001
Alcohol consumption <sup>†</sup>	51.1	22.2	< 0.001
Chewing difficulties (very uncomfortable)	14.4	3.6	< 0.001
Self-perceived oral condition (poor or very poor)	8.0	7.4	0.078
History of one or more permanent tooth decay	96.5	97.8	0.086
Current permanent tooth decay	18.9	24.8	0.968
History of toothache in the preceding year	31.5	30.2	0.060
Reasons for activity limitations (dental and oral issues)	1.1	0.1	0.055
Dental nerve treatment	15.9	12.5	< 0.001
Treatment for gum disease	16.5	12.5	< 0.001
Treatment for simple cavities	15.7	15.5	0.806
Tooth extraction or intraoral surgery	14.7	9.9	< 0.001
Creation or repair of dental prostheses	21.3	15.4	< 0.001
Oral examination in the preceding year	38.1	36.0	0.501

Data are presented as mean±standard deviation or percentage.

<sup>\*</sup>Current smoking refers to having smoked at least 100 cigarettes in one's lifetime and currently continuing to smoke; †Alcohol consumption refers to consumption of alcohol more than once a month.

cancer. We investigated the effects of age, sex (male), hypertension, diabetes, hyperlipidemia, current smoking, alcohol consumption, and oral health indicators, such as chewing difficulties, and self-perceived oral condition on gastric cancer. Age, sex, hypertension, diabetes, alcohol consumption, and chewing difficulties showed a trend (p<0.06) on univariate analysis and were subjected to multivariate analysis. On multivariate analysis, the OR for chewing difficulties was significantly higher in the gastric cancer group (OR 5.351, 95% CI 2.128-8.982, p<0.001) (Table 2). Other factors such as age (OR 1.258, 95% CI 1.005–1.480, p<0.001), hypertension (OR 1.488, 95% CI 1.108-3.155, p<0.001), and diabetes (OR 1.830, 95% CI 1.125–3.721, p<0.001) were also significantly associated with gastric cancer.

## Dental health treatment history

Patients with very uncomfortable chewing difficulties had a significantly higher rate of previous dental nerve treatment (5.7% vs. 3.1%, p<0.001), gum disease treatment (6.8% vs. 2.8%, p<0.001), tooth extraction or intraoral surgery (7.4% vs. 2.9%, p<0.001), and prosthetic repair (6.4% vs. 2.7%, p<0.001) compared with individuals without these issues (Table 3).

## **DISCUSSION**

Based on analysis of the KNHANES data, we observed a significant association between poor oral health, specifically chewing difficulty and the prevalence of gastric cancer among Korean adults, in addition to known risk factors such as old age, hypertension, and diabetes. These results align with emerging research trends that have reported an association between oral health issues and various types of cancers. 20-23 However, a recent meta-analysis that analyzed periodontitis and gastrointestinal (GI) cancers observed no association between periodontitis and the risk of colorectal, gastric, or esophageal cancer.<sup>24</sup> In particular, Western studies have reported no correlation between oral health indicators such as tooth loss and upper GI cancer; however, this result may vary depending on differences in underlying risk factors for gastric cancer in the populations investigated. 14-17 In this regard, a meta-analysis of the associa-

Table 2. Logistic regression analysis of factors associated with gastric cancer

Variable	Univariate analysis		Multivariate analysis	
variable -	OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value
Age	1.024 (1.001-1.047)	< 0.001	1.258 (1.005–1.480)	< 0.001
Sex, male	1.392 (0.660-2.935)	0.051	1.422 (0.868-2.352)	0.059
Hypertension	2.049 (1.045-3.053)	< 0.001	1.488 (1.108-3.155)	< 0.001
Diabetes	2.917 (2.547-3.316)	< 0.001	1.830 (1.125-3.721)	< 0.001
Hyperlipidemia	1.252 (0.628-3.496)	0.955		
Current smoking*	1.851 (0.513-6.680)	0.955		
Alcohol consumption <sup>†</sup>	1.897 (0.998-4.414)	0.058	2.412 (0.845-5.985)	0.070
Chewing difficulties (very uncomfortable)	3.756 (3.302-4.102)	< 0.001	5.351 (2.128-8.982)	< 0.001
Self-perceived oral condition (poor or very poor)	1.140 (0.270-4.812)	0.066		
History of one or more permanent tooth decay	0.650 (0.101-4.030)	0.088		
Current permanent tooth decay	0.705 (0.289-1.721)	0.968		
History of toothache in the preceding year	1.124 (0.656-2.849)	0.078		
Reasons for activity limitations (dental and oral issues)	2.186 (0.300-18.826)	0.531		
Oral examination in the preceding year	0.853 (0.152-4.654)	0.712		

<sup>\*</sup>Current smoking refers to having smoked at least 100 cigarettes in one's lifetime and currently continuing to smoke; †Alcohol consumption refers to consumption of alcohol more than once a month.

Table 3. Association between chewing difficulties and dental health treatment

Dental health treatment	Chewing difficulties (very uncomfortable)	Others (without chewing difficulties)	<i>p</i> -value
Dental nerve treatment	5.7	3.1	< 0.001
Treatment for gum disease	6.8	2.8	< 0.001
Treatment for simple cavities	3.5	3.8	0.085
Tooth extraction or intraoral surgery	7.4	2.9	< 0.001
Creation or repair of dental prostheses	6.4	2.7	< 0.001

Data are presented as percentage.

CI, confidence interval; OR, odds ratio.

tion between tooth loss and gastric cancer revealed a stronger correlation in Asian than in European or American populations.25 In addition, some related studies have included cancers other than gastric cancer, and these studies differ in their design and statistical analysis methods.14-17

Among studies on oral health and cancer, few have specifically addressed functional aspects, such as chewing difficulties and cancer. A history of periodontal disease and tooth loss was associated with the risk of esophageal and gastric adenocarcinoma.26 Tooth loss was associated with chewing difficulties,27 and a recent history of dental treatment was associated with chewing difficulties among older adults.<sup>28</sup> A longitudinal study showed that chewing difficulties were more likely to occur in individuals with tooth loss than in those without tooth loss.<sup>29</sup> Chewing, oral food transport, and swallowing are continuous processes.<sup>30</sup> The process of chewing affects the timing of food movement and initiation of swallowing.<sup>31</sup> The chewing ability can be evaluated with regard to "masticatory performance," which is defined as the percentage of food particle size distribution when chewed a certain number of times. 32 Changes in masticatory performance were associated with non-ulcerative functional dyspepsia.<sup>33</sup> Dyspepsia is also one of the symptoms of gastric cancer, and symptoms of early-stage cancer may be indistinguishable from those of benign dyspepsia.<sup>34</sup> The clear correlation observed between poor oral health, specifically between chewing difficulties and gastric cancer is a novel aspect of this study.

We observed that patients with gastric cancer were usually older, had a higher incidence of comorbidities such as hypertension and diabetes, and tended to be male, although this was not statistically significant. These demographic and health characteristics align with findings in the existing literature that describes risk factors for gastric cancer. Although there was no significant association in logistic regression analysis, the significant differences in current smoking status and alcohol consumption between the gastric cancer and non-gastric cancer groups also align with the fact that smoking and alcohol consumption are known risk factors for gastric cancer. 35,36

The association between poor oral health and gastric cancer can be explained by the following hypotheses. Poor oral hygiene favors bacterial colonization of the oral cavity, with a consequent increase in the nitrosamine (a carcinogen) levels that can potentially trigger development of gastric cancer. 19-21 Oral bacteria such as Streptococcus mutans may produce carcinogenic metabolites, which convert nitrates into nitrites.<sup>37</sup> Consequently, elevated nitrosamine levels may affect the incidence of gastric cancer. Furthermore, poor oral hygiene facilitates the proliferation of anaerobic bacteria, specifically, Porphyromonas gingivalis and Treponema denticola, in the oral cavity, leading to chronic inflammation such as periodontal disease. 7,10,18 Inflammatory molecules, such as interleukin (IL)-1, IL-6, and tumor necrosis factor-α are released in periodontal diseases such as periodontitis, which can promote the development and progression of gastric cancer. 38,39 In addition, patients with dental caries may develop H. pylori infection in the dental pulp, resulting in systemic H. pylori infection. 6-9

We also observed that patients with very uncomfortable chewing difficulties had higher rates of previous dental nerve treatment, gum disease treatment, tooth extraction or intraoral surgery, and prosthetic repair. This finding indicates that the physical manifestations of poor oral health, such as chewing difficulties, may represent clear and easily measurable markers of underlying pathogenetic contributors to cancer risk.

In light of these findings, considering oral health as a potential factor in gastric cancer screening and prevention strategies is necessary. The integration of oral health checkups into routine medical evaluation for individuals at risk for gastric cancer may be a proactive approach to identify and minimize this risk. Additionally, public health initiatives to improve oral hygiene and to address common dental issues may be beneficial in reducing the incidence of gastric cancer, particularly in high-risk populations.

Our study has some limitations. First, analysis of the KNHANES data showed that the number of patients diagnosed with gastric cancer was significantly smaller than that of patients without this diagnosis. Therefore, the generalizability of our results is debatable. Second, this study utilized data from the 7th and 8th KNHANES; therefore, we cannot ignore the possibility of unmeasured confounders that remained unaddressed, which may limit the applicability of the findings to other demographic groups. In particular, several previous studies have reported an association between oral disease and gastric cancer in terms of H. pylori and microbiota, as well as socioeconomic factors such as education and income. 6-9 However, the KNHANES data do not contain detailed information on various essential aspects, including H. pylori infection status, gastric cancer stage, histological differentiation, family history, and genetic and socioeconomic data. Therefore, our analysis did not adequately address the issue of missing data. Third, the KNHANES is a cross-sectional survey; therefore, establishing a causal association using this data is difficult. Further research and in-depth analyses are warranted to conclusively establish a correlation between gastric cancer and oral health.

In conclusion, this study enhances our understanding of the complex interplay between oral health issues, such as chewing difficulties, and gastric cancer. It emphasizes the potential of addressing poor oral health as a modifiable risk factor for gastric cancer, advocating a comprehensive approach to cancer prevention. Further research is necessary to gain deeper insight into the exact biological mechanisms underlying the association and to investigate the effectiveness of oral health interventions to reduce the risk of gastric cancer.

#### **Supplementary Materials**

The online-only Data Supplement is available with this article at https://doi.org/10.7704/kjhugr.2024.0045.

#### **Authors' Contribution**

Conceptualization: Sang Hoon Lee, Sung Chul Park. Data curation: Sang Hoon Lee, Hyunseok Cho. Formal analysis: Hyunseok Cho. Investigation: Sang Hoon Lee, Hyunseok Cho, Sung Chul Park. Supervision: Sang Hoon Kim, Seung Young Kim, Han Jo Jeon, Sang Pyo Lee, Younghee Choe. Validation: all authors. Writing-original draft: Sang Hoon Lee, Hyunseok Cho. Writing-review & editing: Sung Chul Park. Approval of the final manuscript: all authors.

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