

Increased risk of sialolithiasis in smokers: A nested case-control study using a national health screening

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Abstract

Objectives

The purpose of this study was to evaluate the relationships among tobacco smoking, drinking alcohol, obesity and sialolithiasis in a Korean population.

Methods

The Korean National Health Insurance Service-Health Screening Cohort, which includes patients ≥ 40 years old, was assessed from 2002 to 2013. 947 sialolithiasis participants were matched with 3,788 control subjects at a ratio of 1:4 with respect to age group, sex, income group, region of residence, hypertension, diabetes, and dyslipidemia. We analyzed participants' previous histories of smoking (current or past smokers compared to nonsmokers) and alcohol consumption (≥ 1 time per week compared to < 1 time per week) in the sialolithiasis and control groups. Obesity was measured using body mass index (BMI, kg/m^2), which was categorized as < 18.5 (underweight), ≥ 18.5 and < 23 (normal), ≥ 23 and < 25 (overweight), ≥ 25 and < 30 (obese I), and ≥ 30 (obese II). Crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using conditional logistic regression analyses.

Results

The rate of smoking was higher in the sialolithiasis group (32.4% [307/947]) than in the control group (29.1% [1,103/3,788], $P = 0.047$). The adjusted OR of smoking for sialolithiasis was 1.31 (95% CI = 1.08-1.59, $P = 0.006$). Alcohol consumption and obesity were not statistically significantly related to sialolithiasis.

Conclusion

The odds of smoking were increased in sialolithiasis patients compared with the control subjects in ≥ 40 years old population.

Introduction

Sialolithiasis, which is the presence of a salivary duct stone, is the most common cause of major salivary gland swelling and pain in the ipsilateral salivary gland, which typically at the time of eating [1, 2]. The annual incidence of sialolithiasis is 5.5/100,000 in Denmark [3] and 2.7-5.9/100,000 in England [4, 5] based on hospital data. The incidence rate was increased to 7.3-14.1/100,000 from 2.05-3.98/100,000 in children (younger than 20 years old) in a Danish population-based study [6]. However, there are no reports on the incidence rate of sialolithiasis in Korea. The submandibular glands are the most commonly affected glands (80%–90%), followed by the parotid glands (5%–20%) and the sublingual glands (very rare) [1, 2, 7]. The predominant prevalence in the submandibular gland is because Wharton's duct has a longer course and a larger diameter than Stenson's duct; thus, saliva flows against gravity and has a

more viscous composition with higher calcium and mucin content in this gland than in other salivary glands [8, 9].

The exact pathogenesis of stone formation in the salivary gland remains unclear. It is generally accepted that reduced saliva flow leads to an accumulation of salivary stones [10]. The retrograde theory suggests that food substances or bacteria in the oral cavity may ascend the salivary ducts and act as a nidus for further calcification [11]. Smoking and alcohol consumption were the most commonly performed social habits in patients with sialolithiasis. The association of sialolithiasis with smoking has been reported in several previous studies [1, 9, 10, 12, 13]. However, we could not find any study evaluating the correlation between alcohol consumption and sialolithiasis.

As the clinician, we know that poor oral hygiene affects sialolithiasis [14]. However, few studies reported the association between sialolithiasis and alcohol consumption/obesity [15, 16]. The aim of this study was to identify the predisposing factors associated with ialolithiasis in a nationwide population-based cohort study using data from the Korean National Health Insurance Service-Health Screening Cohort (NHIS-HEALS). In this study, we estimated the odds ratios (ORs) of smoking, alcohol consumption and obesity in sialolithiasis patients compared to participants in a 1:4 matched control group.

Materials And Methods

Study Population and Data Collection

The Ethics Committee of Hallym University (2017-1102) approved the use of these data. The study was exempted from the need for written informed consent by the institutional review board.

This national cohort study relied on data from the Korean NHIS-HEALS [17]. The Korean NHIS selects ~ 10% of random samples ($n = \sim 515,000$) directly from the entire population who underwent health evaluations from 2002 through 2013 ($n = \sim 5,150,000$). Age- and sex-specific distributions of the cohort population have been described online [18]. The details of the methods used to perform these procedures are provided by the National Health Insurance Sharing Service [19].

All insured Koreans who are at least 40 years old and their dependents undergo no-cost biannual health evaluations. Each examinee must complete a standard questionnaire for this health evaluation program [20]. Because all Korean citizens are recognized by a 13-digit resident registration number from birth to death, exact population statistics can be determined using this database. It is mandatory for all Koreans to enroll in the NHIS. All Korean hospitals and clinics use the 13-digit resident registration number to register individual patients in the medical insurance system. Therefore, the risk of overlapping medical records is minimal, even if a patient moves from one place to another. Moreover, all medical treatments in Korea can be tracked without exception using the Korean Health Insurance Review & Assessment (HIRA) system. In Korea, providing notice of death to an administrative entity is legally required before a funeral can be held, and the causes and date of death are recorded by medical doctors on a death certificate.

This cohort database included (i) personal information, (ii) health insurance claim codes (procedures and prescriptions), (iii) diagnostic codes using the International Classification of Disease-10 (ICD-10), (iv) death records from the Korean National Statistical Office (using the Korean Standard Classification of disease), (v) socioeconomic data (residence and income), (vi) medical examination data (vii) health check-up data (body mass index [BMI], alcohol consumption, smoking habits, blood pressure, urinalysis, hemoglobin, fasting glucose, lipid parameters, creatinine, and liver enzymes) for each participant over the period from 2002 to 2013 [19, 20].

Participant Selection

Out of 514,866 cases with 497,931,549 medical claim codes, we included participants who were diagnosed with sialolithiasis (n = 1,037). The sialolithiasis participants were matched 1:4 with participants (control group) who were never diagnosed with sialolithiasis from 2002 through 2013 among this cohort. The control group was selected from the original population (n = 513,829). Subjects were matched by age group, sex, income group, region of residence, and medical history (e.g., hypertension, diabetes, and dyslipidemia). Participants in the control group were sorted using a random number order and selected from top to bottom to prevent selection bias. It was assumed that the matched control participants were involved at the same time as each matched sialolithiasis participant (index date). Therefore, participants in the control group who died before the index date were excluded. Sialolithiasis participants who had no previous history of health evaluations before the index date were excluded (n = 89). One sialolithiasis participant was excluded due to the lack of a matching participant. Finally, 1:4 matching resulted in the inclusion of 947 sialolithiasis participants and 3,788 control participants. We analyzed the previous health evaluation data in the sialolithiasis and control groups after matching (Fig. 1). In this study, we used the latest health evaluation data before the index date.

Variables

Independent variables

Tobacco smoking was categorized based on the current smoking status (nonsmoker or past smoker/current smoker), duration of smoking (nonsmoker, < 20 years, and \geq 20 years), and current number of cigarettes smoked per day (0 cigarettes per day, < 20 cigarettes per day, and \geq 20 cigarettes per day, S1 Table). We selected the current smoking status in this study. We used 'smoking' to define current or past smokers compared to nonsmokers.

Alcohol consumption was evaluated by the frequency of alcohol consumption (< 1 time per week, and \geq 1 time per week) and the amount of alcohol consumed at a time (<1 soju bottle, 1 soju bottle, and > 1 soju bottle, S1 Table). Generally, a bottle of Soju contains 17.5% of alcohol with 360ml. A bottle of soju is same about 3.5 bottles of bear. We selected the frequency of alcohol consumption in this study. We used

'alcohol consumption' to define alcohol consumption ≥ 1 time per week compared to alcohol consumption < 1 time per week.

Obesity was measured using BMI (kg/m^2) and was categorized as < 18.5 (underweight), ≥ 18.5 and < 23 (normal), ≥ 23 and < 25 (overweight), ≥ 25 and < 30 (obese I), and ≥ 30 (obese II) following the WPRO 2000 guidelines [21].

Covariate analysis

The age groups were classified using 5-year age intervals: 40-44, 45-49, 50-54, ..., and 85+ years old. A total of 10 age groups were designated. The income groups were initially divided into 41 classes according to the premium (one health aid class, 20 self-employment health insurance classes, and 20 employment health insurance classes). These groups were recategorized into 5 classes (class 1 [lowest income]-5 [highest income]). The region of residence was divided into 16 areas according to administrative district. These regions were regrouped into urban (Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan) and rural (Gyeonggi, Gangwon, Chungcheongbuk, Chungcheongnam, Jeollabuk, Jeollanam, Gyeongsangbuk, Gyeongsangnam, and Jeju) areas.

The participants' prior medical histories were evaluated using ICD-10 codes. To ensure an accurate diagnosis, hypertension (I10 and I15), diabetes (E10-E14), and dyslipidemia (E78) were regarded as present if a participant was treated ≥ 2 times.

Dependent variable

Sialolithiasis was diagnosed based on the ICD-10 code K115.

Statistical Analyses

Chi-square tests were used to compare the general characteristics between the sialolithiasis and control groups.

To analyze the ORs of smoking, drinking alcohol, and obesity on sialolithiasis, conditional logistic regression analysis was used. In this analysis, a crude (simple), adjusted model (adjusted model for obesity, smoking status, and frequency of alcohol consumption) was used, and 95% confidence intervals (CIs) were calculated. In these analyses, age group, sex, income group, region of residence, hypertension, diabetes, and dyslipidemia were stratified.

For the subgroup analyses, we divided the participants by age and sex (< 60 years old, ≥ 60 years old; men and women). Division of the age groups was determined by the median value of all the participants.

Two-tailed analyses were conducted, and P values less than 0.05 were considered to indicate significance. The results were statistically analyzed using SPSS v. 22.0 (IBM, Armonk, NY, USA).

Results

The rate of tobacco smoking was higher in the sialolithiasis group (32.4% [307/947]) than in the control group (29.1% [1,103/3,788], $P = 0.047$, Table 1). Alcohol consumption and obesity were not different between the sialolithiasis and control groups. The general characteristics (age, sex, income, region of residence, hypertension, diabetes, and dyslipidemia) of the participants were the same due to the matching procedure ($P = 1.000$).

The adjusted OR of smoking for sialolithiasis was 1.31 (95% CI = 1.08-1.59, $P = 0.006$, Table 2). The adjusted ORs of alcohol consumption and obesity for sialolithiasis did not reach statistical significance.

In subgroup analyses performed according to age and sex, the adjusted OR of smoking reached statistical significance in participants < 60 years old and in men (Table 3).

Discussion

In our study, the rate of smoking was higher in the sialolithiasis group (32.4%) than in the control group (29.1%), and the adjusted OR of smoking was significantly higher in the sialolithiasis group than in the control group (adjusted OR = 1.31, 95% CI = 1.08-1.59). However, the rates of alcohol consumption and obesity did not differ between the sialolithiasis and control groups. We found the similar results when analyzed these factors according to duration of smoking and amount alcohol intake (S3 table). Similar to our findings, a history of smoking has been reported as a predisposing factor for sialolithiasis in the general population (adjusted OR = 1.21, 95% CI = 1.02-1.44, $P = 0.028$) [22]. The stone size has been reported to be much larger in current smokers than in ex-smokers (12.4 mm vs. 7.5 mm, $P = 0.03$) [13].

Tobacco smoking can cause oral cavity inflammation [23]. Because the salivary duct opens to the oral cavity, inflammation in the oral cavity can be transmitted into the salivary duct and cause ductal swelling and narrowing. Decreased salivary duct diameter can induce salivary stasis and cause precipitation of salivary stones. Salivary stones and ductal inflammation increase the occurrence of sialolithiasis. After formation of salivary duct stones, bacteria can ascend the duct more easily from the mouth and proliferate on the surface of the stones, contributing to further development of sialolithiasis [10]. Moreover, long-term smoking decreases salivary flow and thus decreases antimicrobial proteins, including IgA, α -amylase and lysozyme, which are important for oral mucosal immunity [24, 25]. Therefore, a vicious cycle accelerating the formation of salivary gland stones ensues.

In this study, alcohol consumption and obesity were not different between the sialolithiasis and control groups. Similar to tobacco smoking, alcohol consumption plays an important role in oral health. However, there have been no previous reports on the association between alcohol intake and sialolithiasis. Because sialolithiasis can be promoted by oral cavity inflammation, we presumed that alcohol intake might be associated with sialolithiasis. Generally, the association between alcohol consumption and inflammation is known to depend on the amount of alcohol intake. The influence of lower to moderate alcohol intake on health outcomes is controversial; however, excessive alcohol intake is connected with worse outcomes

[26]. In particular, light to moderate drinking has shown protective effects against cardiovascular disease, and this amount was defined as daily consumption of a 5 to 6 oz glass of red wine [27]. In our data, we did not compare the amounts of alcohol consumed but the frequency of alcohol consumption (< 1 time per week, ≥ 1 time per week). Moreover, the small number of participants might not have been enough to reach statistical significance.

Obesity is known as a state of abnormal immune activity and increased susceptibility to inflammatory diseases, such as diabetes, airway inflammation, cardiovascular disease and fatty liver disease [28]. Therefore, we hypothesized that obesity might be related to sialolithiasis. However, comparison among the 5 groups divided by BMI did not show any difference. Additional analyses according to sex and age with these groups did not show any differences. There are no previous reports regarding obesity and sialolithiasis. Some study reported that the salivary flow is not decreased in obese patients compared to nonobese patients. However, the activity of salivary enzymes, such as lipase and α -amylase, which break down nutrients, was much higher in the obese group [29]. Therefore, although obesity can be considered chronic inflammation that can cause salivary stone formation, a normal amount of salivary flow and enzymes with high activity can disturb salivary stone formation.

This study has several benefits. In contrast to hospital-based studies, we used participants from a large representative nationwide population who underwent health screening examinations. We analyzed the ORs of tobacco smoking, alcohol intake and obesity based on BMI in the sialolithiasis group and compared them to the ORs in a well-matched control group. The control group was randomly selected and matched by age group, sex, income group, region of residence, and medical history (e.g., hypertension, diabetes, and dyslipidemia) to prevent selection bias. Moreover, we used an adjusted logistic regression model to minimize confounders.

This study has several limitations. First, we used patient claim codes from the HIRA database to confirm which individuals were diagnosed with sialolithiasis. This data may indicate the incidence of sialolithiasis. Second, the participants self-reported their health status and habits, and self-reporting can be biased. Third, we could not evaluate the amount of alcohol consumed, which has an important effect on oral health. Fourth, we did not have data from patients who were younger than 40 years old because the health screening examinations were performed in individuals older than 40 years old. Fifth, the number of sialolithiasis participants was relatively small because of the low incidence rate of this disease. Finally, we could not find the association between women and smoking. The low rates of smoking in women compared to men might affect this (S2 Table).

Conclusion

Tobacco smoking showed a positive association with sialolithiasis in ≥ 40 years old population. However, the association of alcohol consumption and obesity with sialolithiasis did not reach statistical significance.

Declarations

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Compliance with ethical standards

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Conflict of Interest: The authors declare that they have no conflict of interest.

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Figures

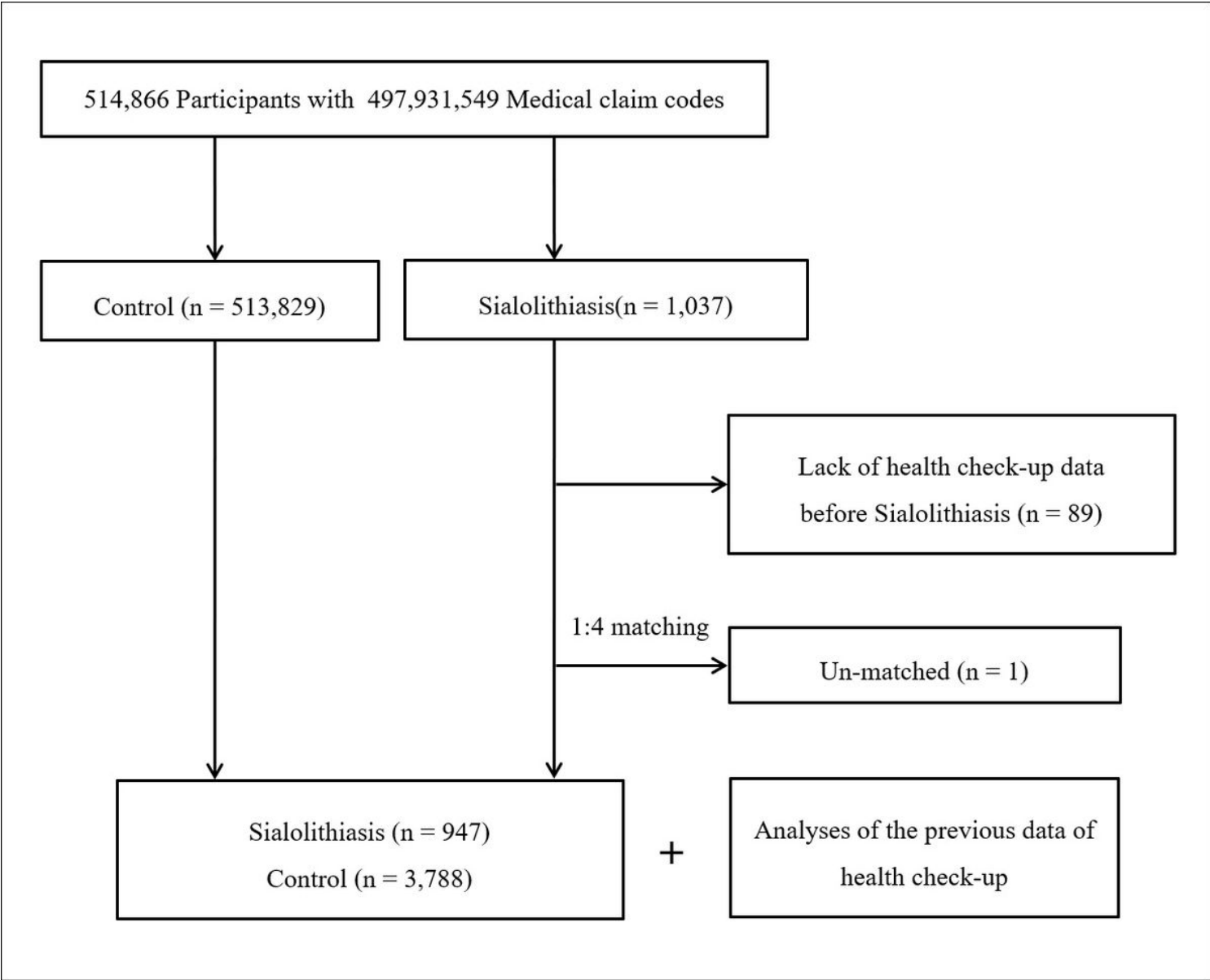


Figure 1

Schematic illustration of the participant selection process used in the present study. Of a total of 514,866 participants, 947 sialolithiasis patients were matched with 3,788 control participants by age, group, sex, income group, region of residence, and past medical history.

Supplementary Files

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