The prevalence and factors associate with vocal nodules in general population
Cross-sectional epidemiological study

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Abstract
The purpose of this study was to analyze the prevalence of vocal nodules and to identify factors related with an increased risk for vocal nodules.

This study was conducted using data from the Korean National Health and Nutrition Examination Survey 2008 to 2011. The subjects consisted of 19,636 men and women aged ≥19 years. Related factors such as age, marital status, incomes, and education level were assessed in individual interviews, and health-related behaviors including smoking, alcohol, and activity were assessed with self-administered questionnaires. Also, examination survey such as laryngoscopy examination, basic physical examination, and blood sampling was conducted.

The prevalence of vocal nodules was 1.31% (n = 258). Among variable factors, age, education level, and voice disorder were related with the presence of vocal nodules (P < 0.05). Other factors including sex, alcohol, smoking, physical activities, hypertension, obesity, waist circumference and metabolic syndrome, hypercholesterolemia, serum calcium, and vitamin D did not show any meaningful relationship with the presence of vocal nodules.

This result may help reduce the incidence of vocal nodules and offer proper management for patients with vocal nodules, and may also facilitate efficient allocation of public health resources.

Abbreviations: BMI = body mass index, KNHANES = Korean National Health and Nutrition Examination Survey, OR = odds ratio, WC = waist circumference.

Keywords: age, education, general population, prevalence, vocal nodules, voice

1. Introduction
A vocal nodule is a benign mucosal lesion on the vocal fold and frequent meet on general population.[1] Vocal nodules are typically located at the midpoint of the membranous vocal fold, which is the point of maximal amplitude during the mucosal wave, and thus, the section subjected to the most phono traumatic force.[2] The cause of vocal nodules is generally laryngeal trauma due to chronic vocal abuse or misuse. Laryngeal trauma initially causes localized edema or submucosal hemorrhage on the vocal fold.[2]

Previous studies of vocal nodules have been conducted on patients with a deviant voice.[2,3] Thus, each study had a different result, and these results were not representative of the general population. For example, the incidence and formation of vocal nodules were different in each study and risk factor was not clear. Even though the related factor such as smoking or alcohol drinking was not defined with relationship of vocal nodule. Therefore, research is needed to investigate the actual prevalence and related factor of vocal nodules.

Epidemiologic studies of the sociodemographic factors related to vocal nodules in the nationwide surveys are rare. This present study was undertaken to determine the national prevalence of vocal nodules in South Korea based on survey data obtained from the 2008 to 2011 Korean National Health and Nutrition Examination Survey (KNHANES) and to investigate related factors.[4–6] The results may help reduce the incidence of vocal nodules and offer proper management for patients with vocal nodules, and may also facilitate efficient allocation of public health resources.

2. Patients and methods

2.1. Study population
This study was conducted using data from the KNHANES 2008 to 2011. Each year 10,000 to 12,000 individuals in 4600
of the membranous vocal fold, usually less well-defined than a polyp, which often extends anteriorly and posteriorly along the membranous and subepithelial layers of the vocal fold. Subepithelial nodules include subepithelial fibrosis at the midpoint of the membranous vocal fold, usually less well-defined than a polyp. Vocal nodules can be bilateral and approximately symmetrical or, more rarely, unilateral.

2.2. Laryngoscopy examination

A 4-mm 70°-angled rigid endoscope with a CCD camera was used for the laryngeal examinations. The laryngoscopy examination findings were classified as 12 types of laryngeal disease: vocal nodules, vocal polyp, vocal cyst, laryngitis, Reinke edema (diffuse polyposis), vocal fold palsy, sulcus vocalis, epiglottic cyst, contact granuloma, laryngeal papilloma, hyperkeratosis, and laryngeal. The diagnosis of laryngeal lesions was made using a disease decision protocol developed by the Epidemiologic Survey Committee of the Korean Otolaryngologic Society.

The diagnosis of vocal nodules was broadly consistent with those in the current literature. Typical features of vocal nodules include subepithelial fibrous thickening at the midpoint of the membranous vocal fold, usually less well-defined than a polyp, which often extends anteriorly and posteriorly along the vibratory margin. Vocal nodules can be bilateral and approximately symmetrical or, more rarely, unilateral.

2.3. Survey of selected factors

Related factors such as age, sex, marital status, incomes, and education level were assessed with basic individual interviews. Income was divided into lower, low middle, upper middle, and upper quartiles using the formula as follows: (household income)/ (the square root of the number of household members). Education level was divided into 4 categories in accordance with the final graduated school level as follows: elementary, middle, high, and college.

Health-related behaviors such as stress, alcohol, smoking, physical activities, and voice disorder were assessed with self-administered questionnaires. The participants who usually felt a “very much” or “much” stress in daily life were classified “yes” in stress questionnaire. Alcohol consumption was divided into no alcohol consumption and from zone 1 to zone 4 using Alcohol Use Disorders Identification Test (AUDIT) score as follows: zone 1 (AUDIT score <7), zone 2 (AUDIT score 8–15), zone 3 (AUDIT score 16–19), and zone 4 (AUDIT score >20). Smoking status was divided into 3 groups as follows: no smoking, past smoking, and present smoking. Physical activities were categorized into high, middle and walk activity. The category “high activity” means the faction of vigorous physical activity (exercise that causes shortness of breath or very difficult, per 10 minutes in 1 time, more than a total of 20 minutes in 1 day, 3 days a week or more, during recent 1 week) The category “middle activity” means the fraction of moderate physical activity (exercise that cause shortness of breath slightly or a little bit difficult, per 10 minutes in 1 time, more than a total of 30 minutes in 1 day, 5 days a week or more, during recent 1 week) The category “walk activity” means the fraction of walking physical activity per 10 minutes in 1 time, more than a total of 30 minutes in 1 day, 5 days a week or more, during recent 1 week. Moreover, voice disorder was confirmed whether or not the current experience of their voice change.

Basic examination of body status was conducted about weight, height, waist circumference, and blood pressure. Also, related factors such as anemia, triglyceride, high-density lipoprotein (HDL), hypercholesterolemia, serum calcium, serum vitamin D, and glucose level were assessed with blood sampling. Obesity was divided 3 groups, which was based on the criteria for the Asia-Pacific region of BMI: low (BMI <18.5), normal (BMI 18.5–25), and high (BMI >25). Metabolic syndrome (syndrome X) was diagnosed when satisfying the 3 criteria among the 5 following conditions: increased blood pressure, waist circumference above 90cm (male) or 85cm (female), excess triglyceride >150mg/dL, low HDL below 40mg/dl (male) or 30mg/dl (female), and fasting glucose above 110mg/dL or diabetes. Serum calcium and serum vitamin D in blood sampling were also selected and analyzed.

2.4. Statistical analysis

The univariate associations between the presence of vocal nodules and potential factors were assessed. The correlations between vocal nodules and age were analyzed with the Student t
test. Also, the correlation between vocal nodules and other factors except age was assessed with Fisher exact test. Stepwise logistic regression was then performed separately for multivariate model outcomes, including predictors associated with P values no greater than 0.30 in univariate analyses and keeping predictors with P values no greater than 0.15 in the multivariable model. All models were sorted with Akaike information criterion (AIC)\[^8\]; goodness of fit for each model was determined with the Hosmer–Lemeshow test.\[^9\] The model with the lowest AIC was considered to have the best fit. The data in this study produced several models with similar low AIC values. Our final model was chosen on the basis of clinical relevance, and not all variables reached a P value of 0.05 or less. Results are reported as odds ratios (ORs) with associated 95% confidence intervals (CIs). We considered a 2-sided P value of less than 0.05 to indicate statistical significance.

3. Results

3.1. Patient characteristics

The survey participants were ≥19 years of age (n = 19,636). Of the participants, 8461 were men and 11,175 were women, with a male-to-female ratio of 1:1.32. Of them, 385 (1.96%) had laryngeal disease and vocal nodules were seen in 258 participants (1.31%).

3.2. Prevalence of vocal nodules

The prevalence of vocal nodules in the population after weighting was 0.99% in 2008, 1.72% in 2009, 1.71% in 2010, and 1.21% in 2011 (Table 1).

3.3. Presence of vocal nodules and related factors

In the result of the associations between the presence of vocal nodules and related factors, age, education level, and vocal disorder were significantly correlated with the presence of vocal nodules (P < 0.05). Other factors including sex, marital status, income, alcohol, smoking, stress, physical activities, anemia, diabetes, hypercholesterolemia, hypertension, obesity, waist circumference and metabolic syndrome, serum calcium, and serum vitamin D were not significantly correlated with the presence of vocal nodules (P > 0.05). In the multiple logistic regression model, age was significantly correlated with the presence of vocal nodules (OR 0.975, 95% CI 0.97–1.00, P = 0.025). Also, education level was positively correlated with the presence of vocal nodules (persons graduated high school: OR 1.80, 95% CI 1.00–3.22, P = 0.048; persons graduated college: OR 2.56, 95% CI 1.41–4.67, P = 0.002). The incidence of vocal nodules was high in relatively young participants than in older participants, and in those of high education level, especially in those who completed college. Income was correlated with the presence of vocal nodules in univariate analysis, but finally did not show meaningful results in multivariate model.

4. Discussion

Vocal nodules are common among the general population; with a lifetime prevalence reported at 2.29% to 16.9% of the population are currently experiencing voice problems.\[^12,7,10\] However, the majority of previous studies concerning vocal nodules has involved specific occupation (almost teachers) or patients complained of voice disorders. Because of this limitation, known prevalence of vocal nodules was relatively highly detected unlike prevalence of vocal nodules in the general population. The data of our study were taken from randomly selected large number of subjects in the general population. Thus, the prevalence of vocal nodules in our study was 1.31%, which is relatively lower than other studies. However, it was important that this point was actual prevalence of vocal nodules. The factors related with the presence of vocal nodules in our study were age, education level, and voice disorder. These factors were significantly correlated with the presence of vocal nodules in the multivariate analysis (P < 0.05).

Our study was a larger-scale study on the prevalence and factors related with vocal nodules in individuals aged ≥19 years, and was based on physical examination findings. Vocal nodules have been associated with relatively young age.\[^11,12\] Relatively younger subjects have a greater possibility to overuse or abuse their voice, compared with that of the older age group. High-pitched vibration causes mechanical stress confined to the edge of the vocal folds, which is associated with a predisposition to nodule formation by activating subepithelial fibroblasts leading to excessive collagenous fiber deposition.\[^7\]

Unlike generally known, we found no association between the presence of vocal nodules and sex to be mentioned most previous studies.\[^13\] The prevalence of a voice disorder is generally reported to be higher in females than in males. Also, the rate of benign vocal fold pathology is disproportionately higher in females.\[^14,15\] This result has been explained based on the higher fundamental frequency and consequent increase in collision trauma.\[^16\] In addition, less hyaluronic acid (HA) in the superficial layer of the lamina propria of females is another possible cause.\[^17\] However, in our study, vocal nodules were not related with females, unlike previous studies. This result may have been caused by a different study group. The previous study was performed on patients visiting a clinic, or a specific

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**Table 1**

| Year | No. | Prev. | SE  | No. | Prev. | SE  | No. | Prev. | SE  | No. | Prev. | Total |
|------|-----|-------|-----|-----|-------|-----|-----|-------|-----|-----|-------|-------|
| 2008 | 3141 | 0.99% | (0.23) | 6592 | 1.72% | (0.34) | 5224 | 1.71% | (0.27) | 4679 | 1.21% | (0.22) | 19,636 | 1.31% |

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| Variables                      | Univariate | Multivariate | p   | Univariate | Multivariate | p   |
|-------------------------------|------------|--------------|-----|------------|--------------|-----|
| Age, y (mean)                 | 0.975      | 0.967        | 0.983| 0.000      | 0.99         | 0.97|
| Sex                           |            |              |     |            |              |     |
| Male                          | 1.179      | 0.917        | 1.517| 0.199      |              |     |
| Female                        | 0.780      | 0.530        | 1.171| 0.231      |              |     |
| Table of marital status       |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 0.869      | 0.458        | 0.977| 0.037      | 0.66         | 0.42|
| Income                        |            |              |     |            |              |     |
| Lower                         |            |              |     |            |              |     |
| Lower middle                  | 1.069      | 0.780        | 1.522| 0.616      | 0.95         | 0.63|
| Upper middle                  | 1.044      | 0.744        | 1.464| 0.805      | 0.72         | 0.47|
| Upper                         |            |              |     |            |              |     |
| Education                     |            |              |     |            |              |     |
| Elementary                    |            |              |     |            |              |     |
| Middle                        | 1.425      | 0.781        | 2.598| 0.248      | 0.90         | 0.42|
| High                          | 2.725      | 1.800        | 4.125| 0.000      | 1.80         | 1.00|
| College                       | 3.712      | 2.462        | 5.597| 0.000      | 2.56         | 1.41|
| Alcohol drinking              |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 1.871      | 0.610        | 1.245| 0.449      |              |     |
| Zone 1                        | 1.020      | 0.656        | 1.584| 0.391      |              |     |
| Zone 2                        | 1.392      | 0.770        | 2.515| 0.273      |              |     |
| Zone 4                        | 0.744      | 0.349        | 1.588| 0.445      |              |     |
| Smoking                       |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 0.823      | 0.511        | 1.326| 0.424      |              |     |
| Past                          | 1.001      | 0.605        | 1.654| 0.998      |              |     |
| Present                       | 1.098      | 0.801        | 1.504| 0.563      |              |     |
| Stress                        |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 1.164      | 0.853        | 1.590| 0.338      |              |     |
| Voice disorder                |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 5.650      | 4.289        | 7.444| 0.000      | 7.01         | 4.97|
| Activity                      |            |              |     |            |              |     |
| High activity                 |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 1.023      | 0.683        | 1.532| 0.912      |              |     |
| Middle activity               |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 0.823      | 0.511        | 1.326| 0.424      |              |     |
| Waist activity                |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 0.871      | 0.649        | 1.170| 0.358      |              |     |
| Anemia                        |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 0.930      | 0.565        | 1.533| 0.777      |              |     |
| Diabetes                      |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 1.117      | 0.699        | 1.785| 0.643      |              |     |
| Hypercholesterolemia          |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 1.489      | 1.012        | 2.190| 0.043      | 1.42         | 0.95|
| Hypertension                  |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 1.232      | 0.879        | 1.727| 0.227      |              |     |
| Obesity                       |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 2.182      | 0.803        | 5.929| 0.126      |              |     |
| BMI < 18.5                    |            |              |     |            |              |     |
| BMI < 25.0                    |            |              |     |            |              |     |
| BMI ≥ 25.0                    | 2.505      | 0.910        | 6.393| 0.073      |              |     |
| Waist circumference           |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 1.094      | 0.753        | 1.588| 0.642      |              |     |
| Metabolic syndrome            |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 1.083      | 0.764        | 1.564| 0.627      |              |     |
| Serum calcium                 |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 1.324      | 0.884        | 1.883| 0.174      |              |     |
| <300                          |            |              |     |            |              |     |
| 300–600                       | 1.341      | 0.831        | 2.165| 0.230      |              |     |
| 600–900                       | 1.177      | 0.561        | 2.468| 0.667      |              |     |
| ≥900                          | 1.045      | 0.619        | 1.763| 0.869      |              |     |
| ≥1200                         |            |              |     |            |              |     |
| Serum vitamin D               |            |              |     |            |              |     |
| No                            |            |              |     |            |              |     |
| Yes                           | 0.810      | 0.570        | 1.150| 0.238      |              |     |
| <20                           |            |              |     |            |              |     |
| 20–30                         | 0.563      | 0.246        | 1.292| 0.176      |              |     |
| ≥30                           |            |              |     |            |              |     |

Bold value indicates a statistically significant results.
occupation group, for example, teacher and student, whereas our study population was selected randomly in the general population and the survey was conducted on a large scale. In our study, the prevalence of vocal nodules was not different between men and women.

We found that subjective perception of a voice disorder was significantly higher in individuals with vocal nodules. This result shows that voice discomfort is strongly correlated with vocal mucosal lesions, particularly vocal nodules. Thus, vocal mucosal lesions must be treated to improve quality of life in subjects with voice disorders.

Interestingly, we found that the subjects of graduate high school and college showed high prevalence of vocal nodules. In the previous study, occupation such as teacher had more voice disorders as a result of voice overuse. In our study, we found an association between vocal nodules and a relatively high education level. Based on this results, we think, it is possible to discover the relationship between occupation with relatively more voice use and the prevalence of vocal nodules. Because specific occupation with voice overuse or abuse, for example, teacher, was needed high level education. However, in KNHANES data, occupation was not finely classified. Although teaching is an educational service according to the Korean Standard Classification of Occupations (Sixth Version, Korean National Statistical Office, 2007), in this survey, teaching was classified as an office and administrative occupation, along with public servant and general office worker. This classification of teaching as an office and administrative occupation explained the lack of an association with voice nodules in the present study. Although we found no association between vocal nodules and occupation, individuals with significant occupational voice demands, such as teachers, are at the greatest risk for developing voice problems. A number of studies have considered the association between voice disorders and occupational factors. Some reported that over 30% to 38% of teachers quit their jobs or have trouble with teaching because of voice problems.

Also, other factors such as marital status, alcohol consumption, smoking, stress, physical activities, anemia, waist circumference, diabetes, hypercholesterolemia, hypertension, metabolic syndrome, serum calcium, and serum vitamin D did not show a significant correlation with vocal nodules. However, these results showed some differences when compared with previous studies using similar KNHANES data. Joo et al. had reported about analysis of the factors associated with chronic laryngitis. They showed that chronic laryngitis was related with age, sex, smoking, income, education level, waist circumference, and body mass index (BMI). Although this study selected a limited disease—vocal nodules—it could not show associations with factors mentioned above. In other words, this difference could be observed that vocal nodules were related only with voice abuse or misuse, and not with other factors. And in another study which analyzed similar data, Hah et al. had proposed the related factors with vocal nodules as follows: BMI, education level, allergic rhinitis. These contents did not match the results of our study. These differences may be due to the factors used in the statistical analysis. We think that our result was more reliable for the following reasons. This study considered only the factors related with vocal nodules. And next, it included most of the factors that can affect the occurrence of vocal nodules compared with previous studies.

Generally known, the environmental factors such as smoking and alcohol consumption were related to a vocal disorder such as Reinke edema, but relationship between smoking, alcohol consumption, and vocal nodules was not detected. From this result, it can be assumed that environmental factors were not affected with vocal nodules, except for factors which directly caused trauma of vocal fold. Each factor of metabolic syndrome is as follows: hypertension, diabetes, hypercholesterolemia, and waist circumference did not show a significant correlation with prevalence of vocal nodules. And metabolic syndrome was also not related with prevalence of vocal nodules. Other factors such as anemia, serum calcium, and serum vitamin D did not show a significant correlation with prevalence of vocal nodules. This result showed that the presence of vocal nodules that are not associated with physical condition significantly.

Also known, voice misuse or overuse was a major cause of vocal nodules. And this fact was repeated in our study. Significant related factors were all associated with voice use. Relative young people had more chance to use voice because of more needs for social activities. Also, persons with high education level were required more voice use for the same reason.

The results of this large epidemiological study provide valuable information regarding the prevalence of vocal nodules and specific data regarding associated factors. Our study showed that to prevent vocal nodules, it is important to reduce voice misuse or overuse. This result suggests potential ways to counsel patients with vocal nodules and prevent their development.

5. Conclusions

The results of this study had high reliability because this study was performed targeting a large number of participants that was selected randomly in public. The prevalence of vocal nodules was 1.31%. Vocal nodules were strongly associated with age, education level, and voice disorder. This result can be explained the cause of vocal nodules by extrinsic differences in voice use and environmental factors, including differences in phonetic demand and this study will facilitate efficient allocation of public health resources.

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