A laryngeal disorders prediction model based on cluster analysis and regression analysis

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Abstract
This study provided the baseline for establishing policies for community health promotion programs to propose the clusters of multiple health risk factors and identify the risks of laryngeal disorders according to the clusters by using the national level survey representing the South Korean population. This study targeted 5941 people who completed the 5th Korean National Health and Nutrition Examination Survey. The independent variables were age, sex, smoking, high-risk drinking, education level, occupation, household income, and self-reported voice problems. The identify cluster relationship with laryngeal disorders by conducting 2-way cluster analysis and multinomial logit analysis. The prevalence of laryngeal disorder was 6.7%. The results of analysis, 3 clusters were automatically extracted. Multinomial logistic regression analysis showed that sociodemographic factors, health risk behaviors, and health status clusters were significantly related to the risk of laryngeal disorders. The males who were smoking, high-risk drinking, college graduate and above, high income, and non-manual workers had a higher risk of laryngeal disorders than females who were non-smokers, non-drinkers, 60 years old and older, economically inactive, and high school graduate. The results of this study suggested that it may be effective to classify population according to sociodemographic and health behaviors and develop health education materials and health promotion program accordingly in order to prevent laryngeal disorders.

Abbreviations: 5th KNHANES = 5th Korean National Health and Nutrition Examination Survey, AUDIT = Alcohol Use Disorder Identification Test, BIC = Bayesian inference criterion, OR = odds ratio.

Keywords: cluster analysis, dysphonia, laryngeal disorders, multiple health risk factors, risk factors, voice disorder

1. Introduction
Lifestyle is important to prevent the occurrence or recurrence of laryngeal disorders. Health risk behaviors such as smoking and drinking may cause laryngeal disorders such as glottic cancer or laryngeal leukoplakia by drying the mucous membrane of vocal cords to induce inflammation.[1,2] Moreover, if the mucous membrane of vocal cords is chronically stimulated (e.g., misuse or abuse of vocal cords, and inappropriate vocalization habit stimulating it), it is difficult to permanently recover the laryngeal disorders caused by them.[3] It has been reported that the recurrence rate of the laryngeal disorder is approximately 75%, even the surgical treatment and rehabilitation are successfully conducted.[4] Therefore, it is necessary to prepare systematic preventive measures at the national level in addition to the management at the personal level in order to prevent laryngeal disorders and maintain healthy voice. Additionally, it is necessary for healthcare professionals to help the patients change their health risk behaviors as well as to treat the diseases in order to prevent laryngeal disorders successfully.[5]

Prevention is a long-standing health policy to slow the outbreak of a disease or prevent the outbreak of it that increases the cost of healthcare. In the United States, it is estimated that the social costs (e.g., unemployment and medical cost) of teachers associated with laryngeal issues is $2.5 billion annually.[6] Moreover, it has been reported that the cost of laryngeal disorders could be up to 3% of gross national product in the United States.[7] Therefore, speech pathologists are not only interested in developing the treatment for the laryngeal disorder but also in preventing the severe diseases such as laryngeal cancer by inducing healthy lifestyle by altering health risk behavior and conducting secondary prevention measures such as screening programs. They are also interested in tertiary prevention measures, which indicate the efforts for preventing complications. Particularly, many studies have continuously evaluated the risk factors of laryngeal disorders for the past 2 decades because the best strategy to prevent them is to help patients have healthy lifestyle.[8–10] These studies have reported that occupation, gender, the misuse and abuse of voice, excessive smoking and drinking, caffeine, noise environment, gastric acid reflux, external wound in the tunica mucosa laryngis, and upper airway infection are the major health risk factors of laryngeal disorders.[11–15] Among them, some lifestyle factors such as smoking and drinking can be changed. Therefore, it is possible to prevent laryngeal disorders or delay the deterioration of symptoms by altering the lifestyle of an individual. It has been reported recently that health risk behaviors are highly correlated and constitute a cluster.[16] For example, it is known that smoking and drinking are highly correlated.
the effects of health risk behaviors on health status are synergistic rather than additive.\(^{[18]}\) Furthermore, Byeon and Lee\(^{[11]}\) showed that the elderly who smoked and drank alcohol had a higher risk of laryngeal disorders than those who only smoked or only drank. Therefore, in order to effectively prevent the occurrence and recurrence of laryngeal disorders, it is necessary to understand the cluster of health behaviors and try to change the behaviors of each cluster. To achieve this goal, first of all, it is necessary to identify health behavior clusters of the population.

Although many studies have evaluated the effects of an individual risk factor on laryngeal disorders, only a few studies have examined the distribution and characteristics of multiple health risk factors in a local population.\(^{[19,20]}\) Byeon and Lee\(^{[11]}\) identified the multiple health risk factors of laryngeal disorders by using the number of health risk behaviors. However, even though it is an effective way to assess the health status, it has a limitation to classify clusters based on the rule of thumb of researchers, not based on the actual phenomenon. Therefore, this method is inappropriate to provide information regarding the intervention for enhancing health status. It is critical to understand how the health risk behaviors of subjects are clustered in order to prevent the diseases and change the health risk behaviors of patients. However, to the best of our knowledge, no study has identified multiple health risk factor clusters and examined the association between these clusters and laryngeal disorders. This study provided the baseline for establishing policies for community health promotion programs to propose the clusters of multiple health risk factors and identify the risks of laryngeal disorders according to the clusters by using the national level survey representing the South Korean population.

2. Methods

2.1. Data source and participants

This is a secondary data analysis study, which analyzed the raw data of the 5th Korean National Health and Nutrition Examination Survey (5th KNHANES), which is the representative epidemiological data of the Republic of Korea conducted between 2010 and 2012. The 5th KNHANES is a nationwide cross-sectional survey conducted by Korean-CDC using a rolling sampling design that is based on a complex, stratified multistage probability cluster survey of non-institutionalized population in the Republic of Korea. The subjects of this survey were adults (19–60 years old), who participated in the 5th KNHANES and participated in a health interview, a urinary cotinine test, and a laryngoscope examination.\(^{[11]}\) The survey conformed to the principles outlined in the Declaration of Helsinki and received clearance from the Institutional Review Board of the Korean Center for Disease Control and Prevention (Korean-CDC, No. 2010-02CON-21-C) and Honam university (No. 1041223–201801-HR-40). The survey procedures were designed to protect participant privacy by allowing anonymous and voluntary participation. Participants were given identification numbers and guaranteed anonymity. After the survey had been fully explained and all participants had provided written informed consent (both directly and from their parents or legal guardians), participants completed a survey. The sampling methods of the KNHANES are described in detail elsewhere.\(^{[21]}\)

Briefly, the 5th KNHANES was conducted on 31,596 people from 11,400 households, and the participation rate was 80.9\% (\(n = 25,553\)).

This study targeted 6904 people who completed both the health survey and laryngoscope examinations. Among them, 963 persons whose laryngoscopic findings could not be interpreted as laryngeal disorders were excluded from the study, and 5941 persons (2559 man, 3382 women) were analyzed (Fig. 1).

3. Measurement

The independent variables were age (19–39, 40–60), sex (male, female), smoking (non-smoking, past smoking, current smoking), high-risk drinking (yes, no), education level (under elementary school graduation, middle school graduation, high school graduation, college graduation, or higher), occupation (economically inactive person, non-manual worker, and manual worker), monthly average household income (quartiles), and self-reported voice problems (yes, no). High-risk drinking was defined as Alcohol Use Disorder Identification Test (AUDIT).\(^{[22]}\) The AUDIT is a screening tool developed by the World Health Organization (WHO) to assess alcohol consumption, drinking behaviors, and alcohol-related problems. AUDIT,\(^{[22]}\) which means higher levels of binge drinking, is defined as high-risk drinking with 12 points or more on the total score and 12 points or more on the total score. Occupations classified based on the 6th Korean Standard Classification of Occupations\(^{[23]}\) were reclassified into economically inactive (unemployed person, homemaker), non-manual (managers & professionals, clerical support workers, service & sales workers), and manual (skilled agricultural & forestry & fishery workers, craft & plant machine operators and assemblers, and unskilled laborer) occupations.

The dependent variables were determined by the presence of a laryngeal disorder (yes or no). The laryngoscope examination was conducted by trained medical staffs at a mobile examination center. The endoscopic laryngeal examination was performed to detect the presence of laryngeal diseases and it was carried out by an otolaryngologist with a 70° endoscope on female adults. The laryngeal examinations were conducted upon the collaboration with Korean Society of Otorhinolaryngology-Head and Neck Surgery, which offered technical advice and highly trained otolaryngologists. The laryngeal disorders identified from laryngoscopic examination included vocal nodules, vocal polyp, intracordial cyst, Reinke edema, laryngeal granuloma, sulcus vocalis, laryngeal keratosis, laryngitis, laryngeal papilloma, and suspected malignant neoplasm of the larynx.

4. Statistical analysis

This study aimed to analyze multiple health risk factors and sociodemographic factors and identify their relationship with laryngeal disorders by conducting 2-way cluster analysis and multinomial logit analysis. Hierarchical cluster analysis and K-means cluster analysis have been widely used in cluster analysis traditionally.\(^{[24]}\) However, the hierarchical cluster analysis requires a large amount of computation time to process a large amount of data. On the other hand, the K-means cluster analysis is highly affected by an outlier and needs to have the predetermined number of clusters, which are disadvantages, although it takes a little computation time. However, the 2-way cluster analysis has an advantage of using continuous variables and categorical variables in combination, and it is also useful for processing a large amount of data because it requires only 1 data processing.\(^{[25]}\) When both continuous variables and categorical
variables are present, the 2-way cluster analysis uses the log-likelihood distance. The basic procedure of the 2-way cluster analysis is as follows. The first step is to create multiple pre-clusters by analyzing each individual. At this time, depending on the size of the distance of a case, it is either included in the pre-cluster or forms a new pre-cluster. In the second step, after completing the pre-cluster step, a hierarchical cluster analysis is conducted.

This study used the method of determining the number of clusters automatically based on the Schwartz's Bayesian inference criterion (BIC). Multinomial logistic regression analysis was performed to identify the relationship between the extracted clusters and laryngeal disorders and presented the odds ratio (OR) and 95% confidence interval. The regression model of this study included all confounding variables.

5. Results
5.1. General characteristics of subjects

The general characteristics of all subjects (5941 people) were examined (Table 1). The mean age was 41.1 years (standard deviation = 10.9), 56.9% of subjects were women and 43.1% for men. The majority of subjects were high school graduates (40.8%), non-manual workers (44.9%), and non-smokers (58.3%). The prevalence of laryngeal disorder was 6.7%.

5.2. Cluster characteristics of sociodemographic factors, health risk behavior, health status

BIC-based 2-way cluster analysis was performed using 9 variables including sociodemographic factors, health risk behaviors, and health status. As a result, 3 clusters were automatically extracted (Table 2, Fig. 2). The characteristics of each cluster are shown in Table 3. The cluster 1 is the smallest cluster. It is composed of males between 40 and 59 years old, who were college graduate and above, non-manual workers. They were smoking and high-risk drinking. They fell in the high household income class (4 out of 4 quartiles) without being aware of voice problem. It accounted for 19.1% of all subjects. The cluster 3 was the second largest cluster. It was composed of economically inactive females between 19 and 39 years old, who were college graduate and above. They did not smoke or drink alcohol. Their household income was medium-high (3 out of 4 quartiles) without being aware of voice problem. It accounted for 39.7% of the total subjects. The cluster 2 was the largest. It was composed of economically inactive females more than 60 years old, who were high school graduates. They did not smoke or

Table 1
The general characteristics of the subjects.

| Characteristics                                      | n (%)   |
|------------------------------------------------------|---------|
| Age, Mean ± SD                                       | 41.1 ± 10.9 |
| Gender                                               |         |
| Male                                                 | 2559 (43.1) |
| Female                                               | 3382 (56.9) |
| Income for households                                |         |
| 1st quartile                                         | 479 (8.2) |
| 2nd quartile                                         | 1546 (26.4) |
| 3rd quartile                                         | 1877 (31.6) |
| 4th quartile                                         | 1945 (32.7) |
| Education level                                      |         |
| Under elementary school graduation                   | 472 (8.7) |
| Middle school graduation                             | 534 (9.6) |
| High school graduation                               | 2214 (40.8) |
| College graduation or higher                         | 2207 (40.7) |
| Occupation                                           |         |
| Economically inactive person                         | 1765 (32.6) |
| Non-manual worker                                    | 2429 (44.9) |
| Manual worker                                        | 1213 (22.4) |
| High-risk drinking                                   |         |
| Yes                                                  | 1828 (36.7) |
| Smoking                                              |         |
| Non - smoking                                        | 3167 (58.3) |
| Past smoking                                         | 932 (17.2) |
| Current smoking                                      | 1332 (24.5) |
| Self-reported voice problems                         |         |
| Yes                                                  | 406 (6.8) |
| Laryngeal disorders                                  |         |
| Yes                                                  | 397 (6.7) |
high-risk drink. Their household income was high (4 out of 4 quartiles) without being aware of voice problem. They accounted for 41.2%.

5.3. The relationship between laryngeal disorders and the clusters of sociodemographic factors, health risk behaviors, and health status

Chi-square test was used to identify the difference in the prevalence of laryngeal disorders according to the cluster of sociodemographic factors, health risk behaviors, and health status (Table 4). There was no significant difference between clusters ($P = 0.094$).

Multinomial logistic regression analysis was conducted to evaluate the independent relation between laryngeal disorders and sociodemographic factors, health risk behaviors, and health status clusters and the results of this analysis is presented in Table 5. This study designated the cluster 1 (college graduate or above males between 40 and 59 years old, non-manual workers, currently smoking and high-risk drinking, falling in the 4 out of 4 quartiles, without being aware of laryngeal disorders) as a reference category. The analysis results showed that sociodemographic factors, health risk behaviors, and health status clusters were significantly related to the risk of laryngeal disorders. The cluster 2 had 31% less risks (significantly less) of laryngeal disorders than the cluster 1 (OR=0.69, 95% CI=0.51–0.94, $P < .05$).

6. Discussion

This study identified the clusters of sociodemographic factors, health risk behaviors, and health status, and confirmed the association with laryngeal disorders according to the clusters by using the national epidemiological data representing Korean adults aged 19 years or older. When the trends of the 3 clusters derived from this study were evaluated, the health risk behavior cluster such as smoking and high-risk drinking was only found in males between 40 and 59 years old. The group had high
household income and these males were college graduate and above and non-manual workers. This cluster can be explained by 3 possibilities.

First, the difference of clusters was caused by the difference in the lifestyle between employed males and economically inactive females (e.g., homemakers). While females were mostly in charge of housework and took care of family members, employed males were highly affected by the workplace environment in developing or maintaining health behaviors. Many previous studies have shown that work environment influences health risk behaviors. Kim and Shon[26] analyzed the health risk behaviors of 4747 South Korean adult males (≥20 years old) and reported that full-time employers with higher education level had more frequent health risk behaviors and more alcohol consumption. They argued that the results implied that males with white-collar jobs and higher education level experienced higher tension and had a more intense response to stress from workplace culture and workload than others.[26] Moreover, the inverse correlation between smoking cessation and occupational stress suggested the possibility of a cluster between the occupation and health risk behaviors.[27]

Second, gender differences in preventive health behaviors may have affected the formation of a cluster of health risk behaviors only in men. The preventive health behaviors include the exposure to disease and damage, and active behaviors detecting and preventing diseases. It has been reported that males generally tend to commit health risk behaviors (e.g., smoking and drinking) more frequent than females, and conduct preventative actions less.[28] At the same time, females try to avoid health risk behaviors more than males and take preventative actions more.[29] Park[29] investigated the cluster of health risk behaviors (e.g., smoking, excessive drinking, insufficient exercise, overweight, hyper-/hypomnia, skipping breakfast, and frequent snacks) of 14,833 people (8925 males and 5908 females), who participated in the KNHANES. They revealed that 21.1% of males had more than 4 health risk behaviors at the same time but only 6.5% of females had more than 4 health risk behaviors at the same time. The study supported the results of this study, which found a health risk behavior cluster only in males.

Third, it could be also possible that the health risk behavior cluster was only found in the male because the underestimation of females affected the results in the process of surveying health risk behaviors. In other words, it could be because males tend to externalize (or reveal) their health risk behaviors, while women tend to internalize the problem.[30] Also, in the socio-cultural context, it could be because the Confucian and patriarchal culture of Korea is generous for males to choose a dangerous lifestyle, but not generous for women to choose it. In the Republic of Korea, females tend to hide their health risk behaviors because of the social image that smoking women tend to be sexually promiscuous, which does not apply to smoking men.[31,32] When the difference in smoking rate between genders was evaluated using self-reporting and urine cotinine test, women hid smoking behaviors 6 times more than men.[33] These results support the possibility the health risk behaviors were underestimated for females in the health risk behavior survey and explained why the health risk behavior cluster was found only in males. In summary, the health risk behaviors and the sociodemographic factors are not independent and correlated in the South Korean adults. Therefore, in order to promote health, it will be needed to continuously manage and monitor employed males, who health risk behaviors such as smoking and drinking.

The results of this study showed that sociodemographic factors, health risk behaviors, and health status clusters were significantly related to laryngeal disorders. The males who were smoking, high-risk drinking, college graduate and above, high income, and non-manual workers had a higher risk of laryngeal disorders than females who were non-smokers, non-drinkers, 60 years old and older, economically inactive, and high school graduate. In general, in the case of chronic diseases, the ratio of the health promotion group is lower in the group with lower education level or monthly average household income.[34] However, it has been reported that highly educated non-manual workers such as teachers and announcers have a high risk of laryngeal disorders.[9,35,36] Even after adjusting confounding factors, highly educated non-manual workers not only had a higher risk of being aware of subjective voice problems[37] but also experienced a high risk of laryngeal disorders.[38] Therefore, to prevent laryngeal disorder, it is necessary to support more health promotion projects for highly educated non-manual workers. It is noteworthy that the cluster phenomenon for smoking, drinking, male, non-manual worker, high education, and high household income were found only among males in the Republic of Korea. Therefore, it is necessary to plan customized health promotion projects for these people and to improve health practice such as smoking cessation and appropriate drinking in priority.

This advantage of this study was that this study clustered health risk factors and analyzed the multiple health risk factors of laryngeal disorders. The limitations of the study are as follows. First, due to the characteristics of the national epidemiological survey data, health risk behaviors were evaluated using self-reporting type questionnaire. Therefore, the presence of recall bias is highly possible. Second, because this study is a cross-sectional study, it was not possible to explain the causal relationship between a cluster of variables and the laryngeal disorder, even if the relationship was confirmed. Third, this study did not evaluate causative diseases of laryngeal disorders such as laryngopharyngeal reflux. It is necessary to analyze clusters again including diseases that are related to laryngeal disorders in the future.

### Table 4

| laryngeal disorders | No | Yes | P      |
|---------------------|----|-----|--------|
| Cluster 1           | 92.9 | 7.1 |        |
| Cluster 2           | 94.5 | 5.5 | 0.04   |
| Cluster 3           | 93.8 | 6.2 |        |

The regression model of this study included all confounding variables.

### Table 5

| B       | Wald | P     | OR Low | OR High |
|---------|------|-------|--------|---------|
| Cluster 1 | 1.00 | 1.00  | 1.00   |         |
| Cluster 2 | 5.352 | .021  | .697   | .513    | .946   |
| Cluster 3 | 2.363 | .124  | .792   | .588    | 1.066  |
7. Conclusion

The results of this study suggested that health behaviors such as smoking and drinking tended to be clustered and that individual risk factors of laryngeal disorders are closely related although they seemed independent. Moreover, to prevent laryngeal disorders, it is suggested that it may be effective to classify population according to sociodemographic and health behaviors and develop health education materials and health promotion program accordingly in order to prevent laryngeal disorders.

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