Is septal deviation associated with headache? A nationwide 10-year follow-up cohort study

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Abstract
To investigate the potential relationship between septal deviation (SD) and headache using nationwide representative cohort sample data.

This study used a nationwide cohort sample from the Korean National Health Insurance Service database. The cohort sample was composed of 1 million patients, which is obtained by propensity score matching from 2002 to 2013. There were 9171 individuals in the SD group and 28243 in the control or no SD group. The Kaplan–Meier survival analysis, the log-rank test, and Cox proportional hazard regression analysis were used to calculate the incidence, survival curve, and hazard ratio of headache for each group.

There were no statistically significant differences in sex (P = .7708), age (P = .991), residential area (P = .9626), or socioeconomic status (P = .9982) between the 2 groups. The survival curve between SD and control or no SD showed a statistically significant difference. The adjusted hazard ratio for headache incidence during the 10-year follow-up period of the SD group was 1.37 (95% CI: 1.31-1.43).

This cohort study suggests that SD is associated with headache. Therefore, these findings suggest that septoplasty can be considered as 1 of the treatment option in SD patients with headache.

Abbreviations: HR = hazard ratio, KNHIS-NSC = Korea National Health Insurance Service-National Sample Cohort, non-SD = control or no septal deviation, SD = septal deviation.

Keywords: deviated nasal septum, headache, septal deviation

1. Introduction
Septoplasty is a method of surgical correction of deviated nasal septum, which is 1 of the most common surgery in ear nose throat. The septic deviation and inferior turbinate hypertrophy are the predominant conditions that can cause nasal obstruction. These septoplasty has been known as a common treatment for nasal obstruction with turbinoplasty.\(^1\)

Although septoplasty is an effective surgical procedure for nasal obstruction, current literature on its efficacy is rare and often inconclusive. (2) Some literature reports that the prevalence of septal deviation (SD) is approximately 80%, however, among these patients, few patients complain of nasal obstruction until some events such as trauma or upper respiratory tract infection occurs.\(^2\)

So what about the relationship between SD and headache?

When the nasal septum is deviated, the septum on the convex side touches the mucosa of the peripheral nasal wall of the inferior turbinate or middle turbinate, or the lateral nasal wall of the nasal septum. This mucosal contact point may cause pain along the end of the sensory nerve.\(^3\) It is reported that in such rhinogenic headaches, surgical treatment is more effective than medical treatment;\(^4-6\) however, the occurrence of these headaches may not be reduced even with surgical treatment.\(^7,8\)

In this regards, it will be interesting to conduct a nationwide cohort study of the association between headaches and SD.

2. Methods
2.1. Database
This study passed the Institutional Review Board of Chonbuk National University Hospital (IRB number 2019-04-010). Since the patient’s individual information is not included in this study, informed consent from patient was waived. The Korea National Health Insurance Service-National Sample Cohort (KNHIS-NSC) database is anonymized and stores the resident registration data.
number of each individual in place of the unique identification number. In addition, KNHS-NSC includes information such as a patient’s age, sex, income, residential area, medical expenses, and so on, and related diagnostic codes, medical history, prescription history, and prescription details. This database includes almost all Koreans in the country, and the code for the disease (Korean Classification of Diseases) is based on the International Classification of Diseases, Tenth Revision. Around 1 million individuals were randomly selected in a cohort based on this database, representing a total population of 50 million.

2.2. SD population

Patients who were diagnosed with a deviated nasal septum (code J342) between January 1, 2002 and 31 December 2003 were included in the study population. To improve the accuracy of diagnosis, patients were limited to those who had undergone nasal examination by endoscopy (procedure codes: E7560, E7550, E7540, E7530).

Exclusion criteria were as follows: Patients undergoing functional endoscopic sinus surgery, septoplasty, or turbinoplasty between January 1, 2002 and December 31, 2003.

2.3. Control (non-SD) population

Subjects with similar age, sex, residential area, and economic status as the SD cohort, again from January 1, 2002 to December 31, 2003, were selected as a control group through 1:3 propensity score matching. The matching ratio was adjusted by applying the hybrid system in the same way so that the assignment ratios were not the same for all treatment groups. The index for the control group was patients not having code J342, that is, patients without SD disease.

2.4. Follow-up

The patients (SD group) and control or no SD (non-SD group) were examined by follow-up for 10 years from January 1, 2004 to December 31, 2013 to determine whether the primary end point, headache, occurred. Considering that it is difficult to include a rhinogenic headache when evaluating the patients, we considered a broad headache syndrome by including G43 (migraine), G44 (headache), or R51 (other headache). Follow-up was based on the duration of headache. The difference between the date of the first SD diagnosis and the date of headache was calculated as the time period until the headache occurred.

2.5. Outcome variables and statistical analysis

Our study divided the population between January 1, 2002 and December 31, 2003 into the SD group and the non-SD group, and checked the occurrence of headache in each group for 10 years thereafter. The detailed age, sex, residential area, and socioeconomic status of each group was obtained from the KNHS-NSC database. The sex of the patient was male or female, and the hazard ratio (HR) of the female was calculated based on the male. Patients were divided into 4 groups: those younger than 20 years, those aged 20 to 40, those aged 40 to 60, and those aged 60 or older. The residential areas were divided into 3 groups (Metropolitan, Urban and Rural). The socioeconomic status was divided into 3 groups of low (less than 30 quartile), middle (30–70 quartile), and high (70 quartile and above).

Data analysis was conducted between January and April 2019. The Kaplan–Meier survival curve was used for univariate survival analysis, and the log-rank test was used to compare the differences between the SD and non-SD groups. Multivariate survival analysis used Cox proportional hazard regression analysis to examine the relationships with other variables. All statistical analyses were performed using R version 3.5.3 and STATA version 14.

3. Results

3.1. Baseline demographics

The basic demographic information is summarized in Table 1. There were 9171 individuals in the SD group and 28243 in the non-SD group. There were no statistically significant differences in sex (P = .7708), age (P = .991), residential area (P = .9626), or socioeconomic status (P = .9982) between the 2 groups. Therefore, we obtained the control group (non-SD) through appropriate propensity score matching from these statistics.

3.2. Incidence rate and HR for headaches

The incidence rate for headache per 1000 person-years over the 10-year follow-up period was calculated for each category in the SD and non-SD groups and the results are shown in Table 2. The incidence rates for headache were 24.5 and 33.8 per 1000 person-years in the non-SD and SD groups, respectively. The adjusted HR for the SD group was 1.37 (95% CI: 1.31-1.43), compared to the non-SD group.

The incidence rates for headache were 22.6 and 34.5 per 1000 person-years in the male and female groups, respectively. The adjusted HR for the female group was 1.58 (95% CI: 1.52-1.64), compared to the male group.

The incidence rates for headache were 21.5, 23.9, 29.4 and 34.7 per 1000 person-years in the groups <20, 20 to 40, 40 to 60, and over 60 years old, respectively. The adjusted HR for the groups 20 to 40, 40 to 60, and over 60 years old were 1.09 (95% CI: 1.02-1.17), 1.39 (95% CI: 1.29-1.49) and 1.67 (95% CI: 1.53-1.81), respectively, compared to the group <20 years old.

Table 1

| Variable                              | Control (non-SD) group (n = 28243) | Study (SD) group (n = 9171) | Chi squared | P- value |
|---------------------------------------|-----------------------------------|----------------------------|-------------|----------|
| Sex                                   | Male                              | Female                    |             |          |
|                                       | 18582                             | 9661                      | 0.0849      | .7708    |
| Age, yr                               |                                   |                           |             |          |
|                                       | 20                                | 20-40                     | 40-60       | >60      |
|                                       | 2876                              | 12724                     | 10054       | 2589     | 0.1072 | .991 |
| Residential area                      | Metropolitan                      | Urban                     | Rural       |          |
|                                       | 8619                              | 6545                      | 13079       | 0.0763  | .9626 |
| Socioeconomic status                  | <30 (low)                         | 30-70 (middle)            | >70 (high)  |          |
|                                       | 2681                              | 11977                     | 13585       | 0.0036  | .9982 |

SD = septal deviation.
The incidence rates for headache were 24.0, 28.1 and 27.4 per 1000 person-years in the metropolitan, urban and rural groups, respectively. The adjusted HR for the urban and rural groups were 1.22 (95% CI: 1.16–1.29) and 1.17 (95% CI: 1.12–1.22), respectively, compared to the metropolitan group.

The incidence rates for headache were 29.3, 26.4, and 26.1 per 1000 person-years in the socioeconomic groups <30th percentile, 30 to 70th percentile, and >70th percentile, respectively. The adjusted HR for the socioeconomic groups 30 to 70th percentile and >70th percentile, were 0.95 (95% CI: 0.86-1.01) and 0.93 (95% CI: 0.87-0.99), respectively, compared to the <30th percentile group.

3.3. Survival curves of patients in SD and non-SD group

The survival curve between SD and non-SD showed a statistically significant difference. (Fig. 1) We used univariate and multivariate Cox regression models. The univariate Cox regression model is unadjusted HR and the multivariate Cox regression model means adjusted HR. The unadjusted HR for headache incidence during the 10-year follow-up period of the SD group was 1.36 (95% CI: 1.30-1.42). After adjusting the socioeconomic factor (age, sex, household income, residential area), the adjusted HR was 1.37 (95% CI: 1.31-1.43).

4. Discussion

The causes of headache are extremely varied: migraine headache, vascular headache, tension headache, drug-induced headache, and so on, and headache sufferers are often referred to otorhinolaryngology clinics for treatment. Recently, there has been a report that the prevalence of migraine varies according to age and sex. According to 1 study, 1.2 million children and adolescents had a similar prevalence to young men and women, but more migraine headaches occurred in women in their late teens, and migraine headaches were more common as age increased. Another report found that cluster headaches were more common in men than women, but as age increased, the tendency to develop gradually decreased in men and increased in women. Our study showed that women were 1.58 times more likely to have headaches than men and those in their 60s were 1.67 times more likely to have headaches compared to their late teens, indicating that headaches are more likely to occur with age. This is roughly equivalent to reports in previous studies.

SD is a congenital or acquired condition in which the nasal septum is deflected to 1 side. This causes asymmetry of the left and right nasal airflow and can lead to various symptoms including a contact point headache. In this paper, a population-based study was conducted to confirm this with a large sample. To our knowledge, this is the first large sample cohort study regarding SD and headache. The SD group had a higher headache risk compared to the non-SD group, with an adjusted HR of 1.37 and unadjusted HR of 1.36. Regardless of correction, it seems certain that there will be more headache over time in septal development patients.

The strengths of this study are

1. a large number of samples: 9171 in the SD group and 28243 in the non-SD group.
2. We tried to obtain similar power to a randomized controlled trial through propensity score matching even though this cohort study was an observational study.

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Table 2

| Variable     | Study group | Number of cases | Incidence per 1000-person years | HR adjusted | Unadjusted |
|--------------|-------------|----------------|----------------------------------|-------------|------------|
| Group        |             |                |                                  |             |            |
| Non-SD       | 28243       | 7536           | 24.5                             | 1           | 1          |
| SD           | 9171        | 2973           | 33.8                             | 1.37        | 1.36       |
| Sex          |             |                |                                  |             |            |
| Male         | 24600       | 5990           | 22.6                             | 1           | 1          |
| Female       | 12814       | 4619           | 34.5                             | 1.58        | 1.55       |
| Age, yr      |             |                |                                  |             |            |
| <20          | 3813        | 907            | 21.5                             | 1           | 1          |
| 20–40        | 16840       | 4312           | 23.9                             | 1.09        | 1.10       |
| 40–60        | 13324       | 4079           | 29.4                             | 1.39        | 1.37       |
| 60           | 3437        | 1211           | 34.7                             | 1.67        | 1.63       |
| Residential area |       |                |                                  |             |            |
| Metropolitan | 11430       | 2948           | 24.0                             | 1           | 1          |
| Urban        | 8672        | 2560           | 28.1                             | 1.22        | 1.18       |
| Rural        | 17312       | 5001           | 27.4                             | 1.17        | 1.15       |
| Economic status |          |                |                                  |             |            |
| <30 (low)    | 3550        | 1085           | 29.3                             | 1           | 1          |
| 30–70 (middle)| 15865       | 4433           | 26.4                             | 0.95        | 0.90       |
| >70 (high)   | 17999       | 4991           | 26.1                             | 0.93        | 0.90       |

HR = hazard ratio, SD = septal deviation.
(3) The data from the National Health Insurance Corporation covers 1 million individuals and is representative of the 50 million people in Korea, and the reliability of the data is high.\textsuperscript{[13–23]}

The disadvantages of this study are

(1) it was difficult to differentiate the left and right position of the septum in the National Health Insurance Corporation data.
(2) Due to the nature of the data, it was difficult to link this to clinical information such as computed tomography, magnetic resonance image, and so on, so that defining the degree of SD and quantitative analysis of the degree of headache were impossible.

5. Conclusion

This cohort study suggests that SD is associated with headache. Therefore, these findings suggest that septoplasty can be considered as 1 of the treatment option in SD patients with headache.

Author contributions

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