The Relationship between Pulmonary Function and Serum Uric Acid Level in the Korean Population

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Background: Forced vital capacity (FVC), forced expiratory volume in the first second (FEV₁), and the ratio of FEV₁ to FVC (FEV₁/FVC) are considered as the major spirometry parameters. Serum uric acid is associated with increased risk of gout and cardiovascular disease. We analyzed the relationship between pulmonary function and serum uric acid level in the Korean men and women.

Methods: This study was based on the data collected during the 2016 Korea National Health and Nutrition Examination Survey (KNHANES VII-1). A total of 3,411 adults were retrieved from KNHANES VII-1. Among 3,411 adults, 1,500 were men and 1,911 were women.

Results: In this study, a significant negative correlation was observed between serum uric acid level and pulmonary function values only in females. Also, in the male non-smoker group, pulmonary function values were negatively associated with serum uric acid level (FVC %predicted, β=-0.014; FEV₁ %predicted, β=-0.015).

Conclusions: In this study, hyperuricemia was associated with the low lung function in males and females. In order to obtain an accurate assessment of the association between hyperuricemia and pulmonary function values, further prospective cohort study in the future is necessary.

Keywords: Uric acid, Lung diseases, Hyperuricemia, Vital capacity, Forced expiratory volume
uric acid have been reported to differ depending on the gender.6

Chronic obstructive pulmonary disease (COPD) is affected by various environmental characteristics such as aging, infectious diseases, smoking, etc.7 Hyperuricemia is the result of interactions of factors such as the genetic and environmental factors.8 It has been reported that smoking exhibit a significant association with hyperuricemia in Koreans.9 Smoking and FEV1 values are identified as inflammatory markers.10 Smoking leads to a decrease in lung function values.11 A recent study reported that uric acid levels were inversely associated with lung function.5,12 In another Japanese study, the subjects with airflow limitation had higher uric acid levels compared to never-smoking subjects without airflow limitation.13 However, relevant literature on the relationship between pulmonary function and serum uric acid considering smoking status is sparse in Korea. Thus, the aim of this study was to evaluate the association between pulmonary function and uric acid level with respect to smoking status.

METHODS

1. Study design and participants

This study was based on data collected from the 2016 Korea National Health and Nutrition Examination Survey (KNHANES VII-1). The KNHANES has been conducted since 1998, which is a collection of nationally representative, cross-sectional, population-based health and nutritional surveys. The original data was published on the KCDC website, and the research design and data collection method were approved by the KCDC's Ethics Committee. The participants were interviewed to gather information about sex, year of birth, past history, smoking and drinking, and physical activity. The staff measured the height, weight, waist circumference, and blood pressure of the individuals using standard protocols.14 One cycle consists of 3 years of rolling samples, and in this study, the recently published survey cycle was analyzed. Pulmonary function tests (PFTs) were performed for the subject ≥40 years of age. Among 8,150 participants, participants <40 years and those who did not undergo spirometry were excluded. Also, participants who lacked data on smoking status were excluded. Thus, data from a total of 3,411 adults were retrieved from KNHANES VII-1. Among 3,411 adults, 1,500 were men and 1,911 were women. All participants voluntarily provided written informed consent.

2. Measurement of variables

The PFTs were performed for subjects aged ≥40 years according to guidelines of the American Thoracic Society/European Respiratory Society using a spirometry system (Vytntus Spiro [CareFusion, San Diego, CA, USA] or Dry rolling seal spirometers Model 2130 [SensorMedics, Yorba Linda, CA, USA]).15 Spirometry was repeated at least three times to ensure reproducibility and validity and the results were calculated based on the predictive equation for the Korean population.16 Pulmonary function was assessed based on FEV1, FVC, and percentage predicted values for FEV1 and FVC. The weight (kg), height (m), waist circumference (cm), and blood pressure (mmHg) of the participants were measured in the mobile examination center used for KNHANES. Body mass index (BMI) was calculated as kg/m². Blood pressure was measured thrice by the examiners and the average of the second and third measurement values was used for further analysis. Uric acid levels were measured via colorimetry determination with the uricase-catalase system (Hitachi automatic analyzer 7600-210; Hitachi Corporation, Tokyo, Japan). Hyperuricemia was defined as a serum uric acid concentration of more than 6 mg/dL in females and 7 mg/dL in males. The participants were classified into three smoking status based on the World Health Organization classification (non-smokers, ex-smokers, and current smokers).

3. Statistical analysis

Statistical analyses were performed using the Statistical software (IBM SPSS 25.0; IBM SPSS Statistics; IBM Corp., New York, NY, USA). The characteristics of the participants were described using mean±standard deviation (SD) for continuous variables, and percentages and SD for categorical variables. To compare pulmonary function in the presence of hyperuricemia, the mean values of FVC, FVC %predicted, FEV1, and FEV1 %predicted were compared between the groups. Adjustment variables were age, BMI, smoking status, systolic blood pressure (SBP), diastolic blood pressure (DBP), and fasting blood sugar (FBS). We performed simple and multiple linear regression analysis by first adjusting for age and BMI (model 1), then for age, BMI, smoking (model 2), and
lastly for age, BMI, smoking, FBS, SBP, and DBP (model 3). Associations between variables were examined using Pearson’s correlation coefficient (r). The Pearson’s correlation analysis between FVC, FVC %predicted, FEV₁, FEV₁ %predicted and uric acid in females was performed. The associations were estimated using odds ratios and 95% confidence intervals. All test P values were two-tailed and P<0.05 was considered significant.

Table 1. Characteristics of the study subjects

| Variable                  | Males (n=1,500) | Females (n=1,911) |
|---------------------------|-----------------|-------------------|
| Age, y                    | 58.3±11.5       | 58.1±11.1         |
| Body mass index, kg/m²    | 24.6±3.0        | 24.2±3.4          |
| Fasting blood sugar, mg/dL| 108.3±27.6      | 101.9±25.8        |
| Systolic blood pressure, mmHg | 123.3±15.6   | 121.0±17.0        |
| Diastolic blood pressure, mmHg | 78.1±10.7    | 74.9±9.1          |
| Uric acid, mg/dL          | 5.7±1.3         | 4.4±1.0           |
| FVC, L                    | 4.1±0.7         | 2.9±0.6           |
| FEV₁, L                   | 3.0±0.7         | 2.3±0.5           |
| FVC %predicted            | 88.8±12.3       | 91.8±12.5         |
| FEV₁ %predicted           | 88.3±13.7       | 92.6±13.3         |
| Smoking status            | Non-smoker      | 271 (18.1)        |
|                           | Ex-smoker       | 756 (50.4)        |
|                           | Current smoker  | 473 (31.5)        |

Values are presented as mean±standard deviation or number (%). Abbreviations: FEV₁ %predicted, percent predicted forced expiratory volume in the first second; FEV₁, forced expiratory volume in the first second; FVC %predicted, percent predicted forced vital capacity; FVC, forced vital capacity.

Table 2. Association between lung function and serum uric acids based on a simple linear regression model

| Characteristic            | Males (n=1,500) | Females (n=1,911) |
|---------------------------|-----------------|-------------------|
| Age, y                    | -0.008          | 0.008             |
| Body mass index, kg/m²    | 0.072           | <0.001            |
| Systolic blood pressure, mmHg | 0.002        | 0.396             |
| Diastolic blood pressure, mmHg | 0.008        | 0.021             |
| Fasting blood sugar, mg/dL| -0.005          | <0.001            |
| FVC, L                    | 0.063           | 0.190             |
| FEV₁, L                   | 0.075           | 0.152             |
| FVC %predicted            | -0.005          | 0.099             |
| FEV₁ %predicted           | -0.003          | 0.248             |

Abbreviations: FEV₁ %predicted, percent predicted forced expiratory volume in the first second; FEV₁, forced expiratory volume in the first second; FVC %predicted, percent predicted forced vital capacity; FVC, forced vital capacity.

RESULTS

A total of 1,500 males (44.0%) and 1,911 females (56.0%) were enrolled in our study. Table 1 shows the general characteristics of male and female participants. No big difference was observed in the mean age and BMI of males and females. FBS, SBP, and DBP were high in males. Male participants had higher FVC and FEV₁, but female participants had higher FVC %predicted and FEV₁ %predicted. Mean uric acid value was higher in males than in females (5.7 mg/dL in men and 4.4 mg/dL in women). Also, more male participants were smokers.

In univariable analysis, the uric acid level was strongly associated with a variety of parameters (Table 2). In females, FVC, FEV₁, FVC %predicted, and FEV₁ %predicted were significantly associated with serum uric acid levels. But, in males, FVC, FEV₁, FVC %predicted, and FEV₁ %predicted were not associated with serum uric acid levels (Table 2). In multiple linear regression analysis, FVC, FEV₁, FVC %predicted, and FEV₁ %predicted values were strongly associated with uric acid only in females (Table 3). Among male non-smoker groups in multivariable analysis, uric acid was associated with the pulmonary function and the results are shown in Table 4.

DISCUSSION

Our study revealed the existence of significant negative correlations between pulmonary function and uric acid levels only in females, which supports findings of previous...
A study reported statistically significant uric acid levels in female COPD patients. A Japanese study also reported a negative correlation between female lung function values and serum uric acid values. However, a recent Korean study reported positive correlation between pulmonary function and uric acid levels. The mean age of the study subjects was 40 years old. In our study, mean age in the subjects was 58 years old.

The present study also showed the negative association between pulmonary function values and uric acid level in

### Table 3. Association between lung function and serum uric acids based on a multiple linear regression model

| Characteristic | Males (n=1,500) | Females (n=1,911) |
|---------------|----------------|------------------|
|               | β   | P   | β   | P   |
| Model 1       |     |     |     |     |
| FVC, L        | 0.004 | 0.943 | -0.131 | 0.015 |
| FEV₁, L       | -0.042 | 0.552 | -0.174 | 0.010 |
| FVC %predicted| -0.004 | 0.199 | -0.007 | 0.001 |
| FEV₁ %predicted| -0.004 | 0.131 | -0.006 | 0.001 |
| Model 2       |     |     |     |     |
| FVC, L        | 0.003 | 0.959 | -0.142 | 0.009 |
| FEV₁, L       | -0.041 | 0.572 | -0.177 | 0.008 |
| FVC %predicted| -0.004 | 0.192 | -0.007 | <0.001 |
| FEV₁ %predicted| -0.004 | 0.139 | -0.006 | 0.001 |
| Model 3       |     |     |     |     |
| FVC, L        | -0.012 | 0.842 | -0.154 | 0.005 |
| FEV₁, L       | -0.051 | 0.481 | -0.188 | 0.005 |
| FVC %predicted| -0.005 | 0.107 | -0.007 | <0.001 |
| FEV₁ %predicted| -0.004 | 0.098 | -0.006 | 0.001 |

Model 1 was adjusted for age and BMI. Model 2 was adjusted for age, BMI, and smoking. Model 3 was adjusted like model 2 plus SBP, DBP, and FBS levels.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FBS, fasting blood sugar; FEV₁ %predicted, percent predicted forced expiratory volume in the first second; FEV₁, forced expiratory volume in the first second; FVC %predicted, percent predicted forced vital capacity; FVC, forced vital capacity; SBP, systolic blood pressure.

### Table 4. Association between lung function and serum uric acids by male smoking status based on a multiple linear regression model

| Characteristic | Non-smoker (n=271) | Ex-smoker (n=756) | Current smoker (n=473) |
|---------------|-------------------|-----------------|---------------------|
|               | β   | P   | β   | P   | β   | P   |
| Model 1       |     |     |     |     |     |     |
| FVC %predicted| -0.014 | 0.034 | -0.006 | 0.107 | 0.003 | 0.546 |
| FEV₁ %predicted| -0.013 | 0.031 | -0.067 | 0.069 | 0.086 | 0.065 |
| Model 2       |     |     |     |     |     |     |
| FVC %predicted| -0.011 | 0.103 | -0.004 | 0.355 | -0.001 | 0.798 |
| FEV₁ %predicted| -0.013 | 0.038 | -0.044 | 0.251 | -0.020 | 0.691 |
| Model 3       |     |     |     |     |     |     |
| FVC %predicted| -0.014 | 0.047 | -0.005 | 0.258 | -0.002 | 0.708 |
| FEV₁ %predicted| -0.015 | 0.013 | -0.006 | 0.069 | 0.003 | 0.552 |

Model 1 was a simple linear regression analysis. Model 2 was adjusted for age and BMI. Model 3 was adjusted like model 2 plus SBP, DBP, and FBS levels.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FBS, fasting blood sugar; FEV₁ %predicted, percent predicted forced expiratory volume in the first second; FEV₁, forced expiratory volume in the first second; FVC %predicted, percent predicted forced vital capacity; FVC, forced vital capacity; SBP, systolic blood pressure.
the male non-smoker group. The association between lung function and uric acid level was not observed in the male smoking group. In a Japanese study, serum uric acid levels in subjects with airflow limitation were higher than those in the never-smoking subjects with airflow limitation. In our study, we did not analyze the association between lung function and uric acid by female smoking group because of small sample size for current female smokers.

Hyperuricemia can affect the status of diabetes, hypertension, kidney disease, and independently influence mortality. In addition, the prevalence of hyperuricemia is recognized as a public health problem worldwide. Kidney function and serum uric acid level exhibit a significant correlation, hyperuricemia can occur due to an increase in serum uric acid levels under the condition of kidney disorder. The higher uric acid levels have been linked with coronary heart disease (CHD) and there has been an increase in the risk of CHD associated with hyperuricemia. According to the studies conducted in Korea, the prevalence rate of gout has been increasing annually. Kidney function and serum uric acid level exhibit a significant correlation, hyperuricemia can occur due to an increase in serum uric acid levels under the condition of kidney disorder. Also, it has been reported that serum uric acid concentration is positively correlated with high sensitivity C-reactive protein (hs-CRP), an inflammatory factor linked with hypertension. Serum uric acid levels are sensitive to tissue injury and inflammation and exhibit an increase in a nonspecific way. The COPD patients were reported to have higher CRP values than the control group.

In a study, patients with COPD had higher uric acid levels than the control group. In a study, the uric acid level was higher for patients with severe COPD. In some studies, hyperuricemia in COPD patients was identified as the biomarker of early death. Compared to patients with low serum uric acid levels, patients with high serum uric acid levels had more severe airflow disorders and oxygen supply disorders; the uric acid level was higher in people with cardiovascular comorbidities than those without cardiovascular comorbidities.

In the present study, we did not consider the differences between socio-economic status and lifestyle among the participants nor the data of patients diagnosed with the disease. In addition, participants who were taking uric acid-lowering agents were not identified. The frequency of food intake that could affect uric acid levels was not considered. Consequently, further analyses could not be performed. As this was a cross-sectional study, we were unable to verify the causality between pulmonary function values and differences in clinical outcomes of hyperuricemia. In future studies, it is necessary to investigate the association between the pulmonary function values and the inflammatory factor, and the linkage between uric acid and inflammatory factors.

In conclusion, FVC, FEV1, FVC %predicted, and FEV1 %predicted exhibited a significantly negative association with serum uric acid levels only in females. In this study, hyperuricemia was associated with the low lung function in males and females. FVC %predicted and FEV1 %predicted were significantly negatively associated with serum uric acid levels in male non-smokers. This study suggests that uric acid levels can be a biomarker for the lung function. In order to obtain an accurate assessment of the association between hyperuricemia and pulmonary function values, further prospective cohort study in the future is necessary.
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