Analysis of the relationship between asthma and benign prostatic hyperplasia

A STROBE-compliant study

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Abstract

The purpose of this study was to evaluate the association between asthma and benign prostatic hyperplasia (BPH) in an adult Korean population and to evaluate this association based on the treatment status of asthmatics.

We utilized the Korean genome and epidemiology study health examinee 2004 to 2016 database. A total of 47,186 participants (826 asthmatics and 46,361 controls) were selected and their BPH histories were analyzed. We categorized the participants according to their asthma treatment status: “well-controlled”; “being treated”; and “not being treated”. The adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for BPH were analyzed using multiple logistic regression. Subgroup analyses were performed according to age (60 years).

The results showed that the prevalence of BPH was higher among asthma patients (17.1%) than among controls (8.7%, P < .001). Asthma patients had a higher risk of having BPH (OR = 1.64, 95% CI = 1.37–2.01, P < .001) than controls, after adjustment for age, income, body mass index (BMI), smoking, alcohol consumption, frequency of physical activity, and the past medical diseases. The ORs for BPH were 1.35 (95% CI = 1.04–1.76) in those aged >60 years and 2.24 (95% CI = 1.70–2.96) in those aged <60 years. The ORs for BPH were 1.82 (95% CI = 1.16–2.87, P = .009) in the “well-controlled” group, 1.05 (95% CI = 0.74–1.49, P = .794) in the “being treated” group, and 2.24 (95% CI = 1.69–2.97, P < .001) in the “not being treated” group.

We found that there is a correlation between asthma and BPH in the adult Korean population. There is a stronger association between asthma and BPH in younger adults and in those who are not receiving treatment for asthma.

Abbreviations: BMI = body mass index, BPH = benign prostatic hyperplasia, CI = confidence interval, CRP = C-reactive protein, IL = interleukin, KoGES = Korean genome and epidemiology study, OR = odds ratio.

Keywords: asthma, chronic disease, population surveillance, prostatic hyperplasia

1. Introduction

Benign prostatic hyperplasia (BPH) is characterized by a benign overgrowth of prostatic tissue around the urethra. It has become one of the most common benign diseases affecting men over age 50. A systematic review of the global prevalence of BPH showed that nearly 1 in 4 (26.2%) men suffer from BPH in their lifetime. In a nationwide survey of Koreans, the nationwide incidence of BPH was reported to be 2105 per 100,000 men (mean age, 59.7 ± 11.4 years). According to data from the Health Insurance Review and Assessment Service in 2019, approximately 760,000 patients were diagnosed with BPH in 2010; this number increased to approximately 1.3 million in 2019.

Although age and genetics play important roles in the etiology of BPH, recent studies have revealed that other modifiable factors such as obesity and smoking play an important role in the development of BPH.

The manuscript was edited for English language, grammar, punctuation, spelling, and overall style by the highly qualified native English-speaking editors at Editage. The authors have no conflicts of interest to disclose.

This work was supported by the National Research Foundation (Choi HG, grant number NRF-2018R1D1A1A02085328) (Wee JH, grant number NRF-2020R1G1A1005390).

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How to cite this article: Wee JH, Bang WJ, Park MV, Byun SH, Choi HG. Analysis of the relationship between asthma and benign prostatic hyperplasia: a STROBE-compliant study. Medicine 2021;100:11(e25214).

Received: 7 July 2020 / Received in final form: 22 January 2021 / Accepted: 23 February 2021
http://dx.doi.org/10.1097/MD.0000000000025214
factors, including obesity, diabetes, metabolic syndrome, diet, exercise, and inflammation, may be involved in the development of BPH. Histological inflammation has been found in BPH specimens, providing evidence that inflammation may play an important role in the development and progression of BPH. In addition, expression of lymphocyte-derived inflammatory cytokines is increased in BPH tissue. Furthermore, a previous study has shown that systemic inflammation increases the risk of BPH. After controlling for age and race, a high C-reactive protein (CRP) concentration was found to be associated with increased risk of BPH (for quartile 4 vs quartile 1, odds ratio [OR] = 1.40, 95% confidence interval (CI) = 1.04–1.88, P = .03); a high interleukin (IL)-6 concentration was also found to be associated with increased risk of BPH (for quartile 4 vs quartile 1, OR = 1.79, 95% CI = 1.32–2.42, P < .001).

Asthma is a common chronic inflammatory disease of the lower airway. A recent study indicated that male asthma patients aged ≥40 years have an increased risk of having BPH (hazard ratio = 1.40 95% CI = 1.30–1.42) compared with males who do not have asthma. Although the authors of that study explained that shared underlying inflammatory response is a possible association between asthma and BPH, further studies are needed to better understand the implication of the inflammation-related interaction between the underlying pathophysiological mechanisms of the 2 diseases.

We searched the PubMed and Embase databases for studies that reported on the association between BPH and asthma using the key words “benign prostatic hyperplasia” AND (asthma) with filters that limited result retrieval to article types other than those conducted on non-human species and articles in the English language. The search results showed that there have been no such studies conducted on a Korean population. Therefore, the aim of this study was to evaluate the association between asthma and BPH in an adult Korean population. Additionally, we assessed the different associations between asthma and BPH based on the status of asthma treatment.

2. Materials and methods

2.1. Study population and data collection

This study was an observational cross-sectional study and was reported according to the STROBE guidelines. This study used data from a prospective cohort study of the Korean Genome and Epidemiology Study (KoGES) accumulated from 2004 through 2016. The ethics committee of Hallym University (2019-02-020) approved the use of these data. The requirement for written informed consent was waived by the Institutional Review Board considering the retrospective study design. A detailed description of the KoGES data is available in a previous report. Out of the data sets provided by the KoGES Consortium, we used the KoGES health examinee data, which consists of the data of urban residence participants aged ≥40 years old. It includes base data from 2004 to 2013 and follow-up data from 2012 to 2016.

2.2. Participant selection

Out of 173,209 participants, we excluded women (n = 113,948) and participants who had no records of height or weight records (n = 232), history of smoking (n = 158), alcohol consumption habit (n = 375), history of medical diseases (hypertension, diabetes mellitus, hyperlipidemia, cerebral stroke, and ischemic heart disease, n = 50), asthma history (n = 2,199), and BPH history (n = 9,061). Several case histories of asthma and BPH were missing because asthma was not surveyed in 2004 and BPH was not investigated from 2006 to 2008. Finally, 825 asthma patients and 46,361 control subjects (with no history of asthma) were selected (Fig. 1). Thereafter, we analyzed the BPH histories of the asthma patients and the control subjects (primary objective). Furthermore, we analyzed their BPH histories based on the statuses of their asthma treatments (secondary objective). Since BPH was not surveyed in 2008, 2,111 participants were excluded from both groups owing to lack of treatment records.

2.3. Survey

Trained interviewers asked the participants questions on histories of asthma, BPH, hypertension, diabetes mellitus, hyperlipidemia, cerebral stroke, and ischemic heart disease (e.g., have you ever been diagnosed with asthma/BPH/hypertension/diabetes mellitus/hyperlipidemia/cerebral stroke/ischemic heart disease by a physician?). Asthma treatment status was categorized into 3 groups: participants who did not need more treatment because they did not have symptoms anymore (well-controlled), participants who were undergoing treatment (being treated), and participants who had been neglected and who never been treated (not being treated). Body mass index (BMI) (kg/m²) was calculated using the health checkup data. Smoking history was categorized as follows: non-smoker (had <100 cigarettes in his lifetime), past smoker (quit more than 1 year ago), and current smoker. Alcohol consumption habit was categorized as follows: non-drinker (less than 12 times a year and not exceeding 1 cup), past drinker (exceeding 1 cup at least 12 times a year but not currently drinking), and current drinker (drinking more than 1 cup at least 12 times a year currently). Physical activity was measured by the frequency of the exercise per a week that was enough to induce sweating. This was surveyed as categories: 0 times/1 to 2 times/3 to 4 times/5 to 6 times/7 times a week.

2.4. Statistical analyses

The Chi-Square test was used to compare the rates of the different income levels, smoking, alcohol consumption, and history of hypertension, diabetes mellitus, hyperlipidemia, cerebral stroke, and ischemic heart disease. The independent t test was used to compare age and BMI.

To address the primary objective (the association between asthma and BPH), the OR for BPH was calculated using a logistic regression model; crude and adjusted models (age, income group, BMI, smoking, alcohol consumption, frequency of physical activity, and medical histories [hypertension, diabetes mellitus, hyperlipidemia, cerebral stroke, and ischemic heart disease]) were used. In the subgroup analyses, the cut-off point was determined by the age (<60 years old and ≥60 years old). To address the secondary objective (associations between asthma and BPH based on the status of asthma treatment), ORs for BPH in the “well controlled,” “being treated,” and “not being treated” groups compared with the control group were calculated using a logistic regression model.
Two-tailed analyses were conducted, and $P$ values less than .05 were considered to indicate significance. The results were statistically analyzed using SPSS v 24.0 (IBM, Armonk, NY).

### 3. Results

The general characteristics of the participants (age, income, smoking status, and alcohol consumption) in the asthma and control groups were significantly different (Table 1). The prevalence of BPH was higher in the asthma group (17.1%) than in the control group (8.7%) ($P < .001$). The numbers of subjects with hypertension ($P < .001$), diabetes ($P < .001$), hyperlipidemia ($P < .001$), cerebral stroke ($P = .012$), and ischemic heart disease ($P < .001$) were higher in the asthma group than in the control group.

The results of the analysis with the multiple logistic regression model (Table 2) revealed that asthma patients had a higher risk of having BPH (adjusted OR = 1.64, 95% CI = 1.37–2.01, $P < .001$) than controls, after adjustment for age, income, BMI, smoking, alcohol consumption, frequency of physical activity, and past medical diseases. Asthma patients showed a 1.35-fold (95% CI = 1.04–1.76) and a 2.24-fold (95% CI = 1.70–2.96) higher adjusted OR for BPH in the >60 and ≤60 years old age groups, respectively.

Table 3 presents the ORs for BPH according to status of asthma treatment and stratified by age subgroups. The adjusted OR for BPH was 1.82 (95% CI = 1.16–2.87, $P = .009$) in the “well-controlled” asthma group, 1.05 (95% CI = 0.74–1.49, $P = .794$) in the “being treated” asthma group, and 2.24 (95% CI = 1.69–2.97, $P < .001$) in the “not being treated” asthma group. After stratification by age (≤60 years old vs >60 years old), the results of the younger subgroup showed a similar pattern with those of the total participants. Patients in the “not being treated” group had the highest ORs for BPH 3.01 (95% CI = 2.03–4.45, $P < .001$); those in the “well controlled” group had a significant association with BPH 2.03 (95% CI = 1.03–4.00, $P = .041$), whereas those in the “being treated” group had no association with BPH 1.59 (95% CI = 0.96–2.62, $P = .071$). In the older subgroup, only patients in the “not being treated” group had the high ORs for BPH 1.77 (95% CI = 1.20–2.62, $P = .004$), while those in the “well controlled” and “being treated” groups had no association with BPH (1.76, 95% CI = 0.96–3.20, $P = .067$; 0.79, 95% CI = 0.49–1.27, $P = .331$).

![Figure 1](https://example.com/f1.png)

Figure 1. A schematic illustration of the participant selection process that was used in the present study. A total of 47,186 participants were selected.
4. Discussion

In this study, we evaluated the association between asthma and BPH in an adult Korean population; we also assessed this association based on the treatment status of the asthma patients. The results of the present study showed that there is a positive association between asthma and BPH. The age-defined stratification showed that there was a stronger association between asthma and BPH in the younger subgroup (<60 years old) than in the older age group. The adjusted OR was highest in the “not being treated” group but no significant association was noted in the “being treated” group.

The underlying pathophysiologic mechanisms of this association between asthma and BPH are not yet established. However, the possible mechanism for this association could be estimated from the findings of previous studies. First, it is known that both diseases are related to chronic inflammation; the causative role of inflammation in the pathogenesis of BPH was first proposed in 1937.[14] However, several studies have shown that BPH may be an immune-mediated inflammatory disease,[15,16] factors involved in the inflammation of the prostate have been identified as well. Activated T cells contribute to the production and growth of prostatic growth factors by releasing several cytokines such as

### Table 1
General characteristics of participants.

| Characteristics              | Total participants | Asthma (n = 825) | Control (n = 46,361) | P value |
|------------------------------|--------------------|------------------|----------------------|--------|
| Age (mean, SD, y)           | 57.4 (8.8)         | 54.1 (8.7)       | **<.001**            |
| BMI (mean, SD, kg/m²)       | 24.6 (3.0)         | 24.4 (2.7)       | **.060**             |
| Income (n, %)               | Missing, no response 118 (14.3)  | 4,667 (10.1)       |     |
| Lowest                      | 247 (29.9)         | 11,319 (24.4)    |     |
| Middle                      | 270 (32.7)         | 18,553 (40.0)    |     |
| Highest                     | 190 (23.0)         | 11,622 (25.5)    |     |
| Smoking status (n, %)       | Nonsmoker 240 (29.1) | 12,906 (27.8)     |     |
| Past smoker                 | 399 (48.4)         | 18,978 (40.9)    |     |
| Current smoker              | 186 (22.5)         | 14,477 (31.2)    |     |
| Alcohol consumption (n, %)  | Non drinker 209 (25.3) | 9,263 (20.0)     |     |
| Past drinker                | 96 (11.6)          | 3,462 (7.5)      |     |
| Current drinker             | 520 (63.0)         | 33,636 (72.5)    |     |
| Physical activity (n, %)    | 0 times a week 371 (45.0) | 20,512 (44.2)    | **<.001**            |
| 1–2 times a week            | 116 (14.1)         | 8,231 (17.8)     |     |
| 3–4 times a week            | 154 (18.7)         | 8,572 (18.5)     |     |
| 5–6 times a week            | 83 (10.1)          | 4,112 (8.9)      |     |
| 7 times a week              | 101 (12.2)         | 4,934 (10.6)     |     |
| Hypertension                | 277 (33.6)         | 12,611 (27.2)    | **<.001**            |
| Diabetes mellitus           | 135 (16.4)         | 5,249 (11.3)     | **<.001**            |
| Hyperlipidemia              | 154 (18.7)         | 6,334 (13.7)     | **<.001**            |
| Cerebral stroke             | 28 (3.4)           | 982 (2.1)        |     |
| Ischemic heart disease      | 71 (8.6)           | 2,139 (4.6)      | **<.001**            |
| Benign prostate hyperplasia | 141 (17.1)         | 4,019 (8.7)      | **<.001**            |

*Independent t test or Chi-Square test. Significance at P < .05.

### Table 2
Crude and adjusted odds ratios (95% confidence interval) for benign prostate hyperplasia in asthma and control groups.

| Characteristics                  | Crude          | Adjusted† | P value |
|----------------------------------|----------------|-----------|--------|
| Total participants (n = 47,186)  |                |           |        |
| Asthma                           | 2.17 (1.81–2.61) | 1.64 (1.37–2.01) | **<.001** |
| Control                          | 1.00           | 1.00      |        |
| Age ≤60 years old (n = 34,391)   |                |           |        |
| Asthma                           | 3.63 (2.47–5.34) | 2.24 (1.70–2.96) | **<.001** |
| Control                          | 1.00           | 1.00      |        |
| Age >60 years old (n = 12,795)   |                |           |        |
| Asthma                           | 1.59 (1.29–1.96) | 1.35 (1.04–1.76) | .025    |
| Control                          | 1.00           | 1.00      |        |

†Logistic regression model. Significance at P < .05.

*Models adjusted for age, income group, BMI, smoking, alcohol consumption, frequency of physical activity, and the past medical histories (hypertension, diabetes mellitus, hyperlipidemia, cerebral stroke, and ischemic heart disease).
IL-17, IFN-γ, IL-2, IL-4, IL-13, and FGF-2, and indirectly increasing the production of IL-6, IL-8, and IL-13.[17,18] Asthma is also known as a chronic inflammatory disease mediated by several cytokines that regulate airway inflammation, bronchial smooth muscle hyper-reactivity, and bronchoconstriction. In vitro study showed that activated T-lymphocytes in BHP specimen expressed significant amounts of IL-2, IL-4, and IL-17, leading to proliferation of BPH stromal cells.[7] A previous study have shown that IL-2 levels are increased in the bronchoalveolar lavage fluid of symptomatic asthma patients.[19] IL-4 is a key cytokine in the development of allergic inflammation, and it mediates important pro-inflammatory functions in asthma including induction of the IgE isotype switch, expression of vascular cell adhesion molecule-1, promotion of eosinophil transmigration across the endothelium, mucus secretion, and differentiation of T helper type 2 lymphocytes.[20] In a case control study, IL-17 was significantly increased in BPH cases compared to controls.[17] There is evidence that IL-17 is increased in the sputum, bronchoalveolar lavage fluid, bronchial biopsies, and serum of asthma patients in comparison with those of healthy control subjects.[21]

Second, epidemiological evidences have demonstrated that obesity increases the risks of BPH surgery, urinary symptom progression, and initiation of medical therapy for BPH.[22,23] A meta-analysis demonstrated the existence of a dose-response relationship between obesity and asthma. In the meta-analysis, the OR for incident asthma for overweight subjects was 1.38 (95% CI: 1.17–1.62) compared to normal weight; the OR for obese subjects was further elevated (OR = 1.92; 95% CI: 1.43–2.59, P < .0001 for the trend) compared to normal weight.[24] Third, alcohol consumption is also associated with a decreased likelihood of having BPH. In a meta-analysis of 19 studies (120,091 men), an alcohol intake of 36 gm daily or greater was associated with a 35% decreased risk of BPH compared with no alcohol intake (OR = 0.65, 95% CI = 0.58–0.74, P < .001).[25] However, alcoholic drinks appear to be significant triggers for asthma attacks.[26] Since Asians have been reported to have a higher incidence of bronchial contractions after alcohol consumption,[27] physicians advise asthma patients to avoid alcohol. In the present study, the proportions of non-drinkers and past drinkers were higher in the asthma group than in the control group.

The results of the present study showed a stronger association between asthma and BPH in the younger subgroup (< 60 years old). This finding is consistent with that of a recent published study on the association between asthma and BPH.[10] In that study, the increased risk of BPH in asthma patients appeared to decline with age compared with that of those without asthma. Since BPH is an age-dependent disease, the effects of other risk factors may be emphasized in the younger subgroup. In a meta-analysis, only men aged under 60 were selected to investigate the role of metabolic syndrome in BPH.[28] These results may be attributed to an increase in comorbidities with increasing age. Previous studies have reported that BPH is associated with several age-related comorbidities such as diabetes, metabolic syndrome, cardiovascular disease, and hypertension.[29] Therefore, the interaction between several comorbidities reduces the association between asthma and BPH.

In the present study, the association between asthma and BPH was highest (OR = 2.24) in the “not being treated” group. Although we could not exactly explain the mechanism underlying this association, we suggest a possible mechanism for which poor asthma treatment may be associated with BPH. Firstly, patients who have poor asthma treatment have increased systemic inflammatory conditions. Elevated concentration of circulating CRP is known to be an indicator of intraprostatic inflammation in symptomatic BPH.[30] A previous study in India demonstrated that the standard treatment advised by the current guidelines decrease the levels of systemic inflammation markers (serum CRP, total leukocyte count, and erythrocyte sedimentation rate) in asthma patients.[31] In the present study, there was no significant association between asthma and BPH in the “being treated” group of the total participants (P = .794), and in both younger (P = .071) and older (P = .331) subgroups. Secondly, limitation of physical activity is a common symptom of uncontrolled asthma. In the United State Real-world Evaluation

### Table 3

| Characteristics | Crude | P value | Adjusted | P value |
|-----------------|-------|---------|----------|---------|
| Total participants (n = 45,075) |       |         |          |         |
| Well controlled | 2.23  | <.001*  | 1.82     | .009*   |
| Being treated  | 1.50  | .019    | 1.05     | .794    |
| Not being treated | 2.70  | <.001*  | 2.24     | <.001*  |
| Control         | 1.00  |         | 1.00     |         |
| Age < 60 years old (n = 32,915) |       |         |          |         |
| Well controlled | 1.80  | .326    | 2.03     | .041*   |
| Being treated  | 3.19  | .002*   | 1.59     | .071    |
| Not being treated | 4.85  | <.001*  | 3.01     | <.001*  |
| Control         | 1.00  |         | 1.00     |         |
| Age ≥ 60 years old (n = 12,160) |       |         |          |         |
| Well controlled | 2.01  | .004*   | 1.76     | .067    |
| Being treated  | 0.98  | .018    | 0.79     | .331    |
| Not being treated | 2.01  | <.001*  | 1.77     | .004*   |
| Control         | 1.00  |         | 1.00     |         |

* Logistic regression model, significance at P < .05.

† Models adjusted for age, income group, BMI, smoking, alcohol consumption, frequency of physical activity, and the past medical histories (hypertension, diabetes mellitus, hyperlipidemia, cerebral stroke, and ischemic heart disease.)

Wee et al. Medicine (2021) 100:11 www.md-journal.com
of Asthma Control and Treatment study, uncontrolled asthma was associated with a greater than 2-fold risk of outdoor activity limitations (OR=2.58, 95% CI=1.90–3.51) or physical (OR=2.62, 95% CI=1.90–3.61), and a 66% increased risk of daily activity limitations (OR=1.66, 95% CI=1.09–2.51) compared to controlled asthma.\[32\] Further studies may be required to clarify the pathophysiology behind this finding.

Although the strength of present study is that the results are representative of the general population after adjusting for several confounders including age, income, BMI, smoking, alcohol intake, physical activity, and several age-related comorbidities, some limitations should be addressed. Firstly, details of BPH parameters including uroflowmetry, prostate volume, prostate specific antigen, and post-void residual volume, are lacking in this study. The participants were asked to report their histories of BPH using a questionnaire. However, a population-based study such as the National Health and Nutrition Examination Survey also used the physician’s diagnosis of BPH via a questionnaire.\[33\] Secondly, the prevalence of asthma was relatively low. However, in a previous Korean population study, the prevalence of asthma ranged from 1.2% to 1.7% in 1998 to 2013 and ranged from 1.7% to 2.1% according to the Korea Community Health Survey 2008 to 2013.\[34\] It was similar to the prevalence of asthma (1.7%) in the present study. Furthermore, the asthma prevalence was consistently higher in women than in men according to the Korean national health survey datasets.\[31\] Since the present study only included Korean adult males, it could explain why the prevalence of asthma was relatively low. Thirdly, as this study had a cross sectional design, we cannot identify causality. A prospective longitudinal study design would better allow a determination of relationship between asthma and BPH. Fourthly, we could not assess the various inflammatory cytokines, although we explained that the association between asthma and BPH may be linked to chronic systemic inflammation, which is mediated by several cytokines.\[30,31\] Finally, the types of medication and severity of asthma could not be evaluated. Other variables such as chronic obstructive pulmonary disease and chronic bronchitis were not included as the variables due to the large number of missing participants. Future studies are needed to further evaluate the pathophysologic mechanisms of this association.

In conclusion, we found that there is a correlation between asthma and BPH in the adult Korean population. There is a stronger positive association between asthma and BPH among younger adults and among those who are not receiving treatment for asthma. However, further studies are needed to clarify the relationship between these 2 diseases.

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