

Relationship between Lower Urinary Tract Symptoms/Benign Prostatic Hyperplasia and Metabolic Syndrome in Korean Men

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Purpose: To investigate any associations between lower urinary tract symptoms (LUTS)/benign prostate hyperplasia (BPH) and metabolic syndrome (MetS).

Materials and Methods: In all, 1,224 male police officers in their 50s who had participated in health examinations were included. LUTS/BPH was assessed by serum prostate-specific antigen, International Prostate Symptom Score (IPSS), transrectal ultrasonography, maximum urinary flow rate (Q max), and postvoid residual urine volume (PVR). In addition, testosterone was also examined. The MetS was defined using NCEP-ATP III guidelines. We used the multiple linear regression test and logistic regression analyses to examine the relationships.

Results: MetS was diagnosed in 29.0% of participants. There was no significant difference in the percentage of cases of BPH (IPSS > 7, Q max < 15 ml/sec, and prostate gland volume \geq 20 ml) (14.2% in the non-MetS group vs. 17.2 in the MetS group; p value = 0.178). The total IPSS score and the Q max were not significantly different. The prostate volume and PVR were significantly greater in the subjects with MetS. After adjusting for age and testosterone, the presence of MetS was not associated with BPH (multivariate odds ratio, 1.122; 95% confidence interval, 0.593 ~ 2.120). Additionally, MetS was not related to IPSS (Beta, -0.189; p value = 0.819), prostate volume (Beta, 0.815; p value = 0.285), Q max (Beta, -0.827; p value = 0.393), or PVR (Beta, 0.506; p value = 0.837).

Conclusions: According to our results, the MetS was not clearly correlated with LUTS/BPH in Korean men in their 50s.

Key Words: Benign prostatic hyperplasia, Metabolic syndrome, Lower urinary tract symptoms

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a highly prevalent disease of older men caused by nonmalignant, unregulated growth of the prostate gland,¹ and it is a major cause of lower urinary tract symptoms (LUTS).

Despite an extensive research effort, the underlying aetiology of BPH/LUTS has still not been established. Recently, metabolic syndrome (MetS) has been thought to play an important role in the aetiologies of LUTS/BPH. In contrast with results from the United States and from European countries, no results from Asian populations have shown

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a positive association between MetS and LUTS/BPH.² However, studies from Asia have had the following limitations: First, a limited number of men aged 50 years old and older, usually the clinically important age for developing LUTS/BPH, have been enrolled. Gao et al³ collected data from 3,103 men, but the median age for their study population was in the 30s. Additionally, other studies from South Korea and Japan have enrolled fewer than 600 men (>50 years old).⁴⁻⁶ Second, most of these studies have used only self-reporting of the International Prostate Symptom Score (IPSS) questionnaire in evaluating LUTS/BPH.³⁻⁵ This practise introduces a potential for response bias, as the respondents might inaccurately report their urinary symptoms. Additionally, some patients might not fully understand the meanings of the questions posed. Third, serum testosterone levels were not evaluated in any of the data from Asian populations.³⁻⁶ This omission might be a limitation, considering that many studies have established the potential relationship between testosterone levels and MetS, and recent studies have indicated inverse associations between testosterone and LUTS.⁷

To control for these factors in the present study, we administered the IPSS questionnaire, transrectal ultrasonography, and uroflowmetry, and we tested for residual urine volume and serum testosterone, coupled with a full metabolic work-up, in a large middle-aged population (1,224 men in their 50s). Using the data collected, we then investigated the relationship between MetS and LUTS/BPH.

MATERIALS AND METHODS

1. Study subjects

The institutional review board of the National Police Hospital approved this study in May 2011. From August 2011 to December 2011, 1,224 male police officers in their 50s who had participated in health examinations for their prostates at the National Police Hospital were included. This study excluded patients who had been diagnosed with urologic disease, including BPH, urologic malignancies, and neurogenic bladder, or who had been administered a related drug, including alpha blockers, anticholinergics, 5-alpha reductase inhibitors, and phosphodiesterase-5 inhibitors. All of the patients provided written informed consent.

2. LUTS/BPH assessment

Medical histories were collected using a standardised structural questionnaire. The Korean version of the IPSS was administered to the respondents to evaluate urinary symptoms. The prostate volume was calculated using transrectal ultrasonography (UltraView 800; BK Medical, Herlev, Denmark), and the glands were examined by digital rectal examination. The maximum flow rate (URODYN[®]; Medtronic Inc., Minneapolis, MN, USA) and postvoid residual urine volume (UltraView 800) were also assessed. Serum prostate-specific antigen (PSA) levels and serum total testosterone were measured in the morning (between 7:00 and 9:00 AM) after an overnight fast, and these levels were determined using radioimmunoassay.

3. MetS assessment

Two blood pressure (mmHg) measurements were obtained 5 minutes apart with a mercury sphygmomanometer under the right arm, and the measurements were averaged. Waist circumference (cm) was measured midway between the lowest rib and the ilium to the nearest 0.1 cm. Body weight (kg) and body height (cm) were also measured. Blood samples were obtained with the subject in the fasting state at the same time as PSA and testosterone. The biochemical analyses included serum glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol (HDL-C). The other laboratory tests performed included a complete blood cell count, routine clinical chemistry (i.e., liver function tests, electrolyte battery, blood urea nitrogen, creatinine), and urinalysis. The diagnostic criteria for MetS had to satisfy three or more of the NCEP-ATP III criteria,⁸ as follows: 1) blood pressure $\geq 130/85$ mmHg and/or antihypertensive medication; 2) fasting blood sugar ≥ 110 mg/dl and/or antidiabetic medication; 3) waist circumference ≥ 90 cm; 4) HDL-C < 40 mg/dl and/or antihypercholesterolaemic medication; and 5) triglycerides ≥ 150 mg/dl and/or antihypercholesterolaemic medication.

4. Statistical analysis

The 1,224 men were classified into two groups according to the presence of MetS. We compared the two groups'

IPSS total score, IPSS quality of life (QoL) score, maximum flow rate, postvoid residual urine volume, prostate volume, and serum PSA. The proportions of severity of LUTS according to IPSS total score (moderate: IPSS >7; severe: IPSS >19), maximal flow rate <15 ml/s, prostate size ≥ 20 ml, and an obstructed flow pattern diagnosed by Siroky nomogram,⁹ were also examined in the two groups. Finally, the association of MetS with BPH^{10,11} (IPSS >7, maximal flow rate <15 ml/s, prostate gland volume ≥ 20 ml), prostate gland volume, IPSS, maximal flow rate, or postvoid residual urine volume was evaluated after adjusting for age and serum testosterone level.

Because of the markedly skewed distribution of IPSS scores and demographic characteristics, medians and interquartile ranges were adopted. Statistical analyses were performed with the Mann-Whitney test, χ^2 tests, multiple linear regression test, and logistic regression analyses, using the SPSS program, version 11.0 (SPSS Inc., Chicago, IL, USA). $p < 0.05$ was considered statistically significant.

RESULTS

1. Patient characteristics

The characteristics of this study population are shown in Table 1. Of a total of 1,224 men, 355 (29.0%) had MetS. There were no differences in age or height. However, body weight, body mass index, waist circumference, sys-

tolic blood pressure, diastolic blood pressure, triglycerides, and fasting blood sugar were significantly higher in the subjects with MetS. Additionally, HDL-C was significantly lower in the MetS group, and there was a significant difference in median serum testosterone (5.3 ng/ml in the non-MetS group vs. 4.7 ng/ml in the MetS group; p value <0.001).

2. Comparison of LUTS/BPH between the MetS and non-MetS groups

As shown in Table 2, there was no significant difference in the percentage of cases of BPH (14.2% in the non-MetS group vs. 17.2 in the MetS group; p value=0.178). In terms of LUTS, the total IPSS score and QoL score were not significantly different between the two groups. Additionally, the percentages of subjects with moderate to severe LUTS and severe LUTS did not show any differences. There was no significant difference in the percentage of cases of maximal flow rate less than 15 ml/s and obstructive patterns on Siroky nomography. Prostate volume and postvoid residual urine volume were significantly greater in the subjects with MetS. However, the prostate gland volume (>20 ml) did not show significant differences. The PSA levels were not significantly different between the two groups.

3. Correlation between MetS and LUTS/BPH

After adjusting for age and testosterone, there was no

Table 1. Patient characteristics

Variable	All men	Non-MetS	MetS	p value*
Men	1,224 (100.0)	869 (71.0)	355 (29.0)	-
Age (yr)	54.0 (52.0~56.0)	54.0 (52.0~56.0)	54.0 (52.0~56.0)	0.230
Height (cm)	172.0 (170.0~175.0)	172.0 (169.0~175.0)	172.0 (170.0~175.0)	0.138
Body weight (kg)	73.0 (69.0~79.0)	72.0 (67.0~76.0)	78.0 (74.0~83.0)	<0.001
BMI (kg/m ²)	24.7 (23.2~26.4)	24.2 (22.9~25.6)	26.4 (24.2~27.7)	<0.001
Waist Cir. (cm)	86.0 (84.0~90.0)	85.0 (82.0~88.5)	91.0 (86.0~91.0)	<0.001
SBP (mmHg)	131.0 (123.0~140.0)	130.0 (120.0~140.0)	137.0 (130.0~144.0)	<0.001
DBP (mmHg)	83.0 (77.0~90.0)	82.0 (76.0~88.0)	86.0 (80.0~91.0)	<0.001
TG (mg/dl)	121.0 (85.0~176.0)	104.0 (77.0~140.0)	186.5 (152.0~262.0)	<0.001
HDL-C (mg/dl)	48.0 (41.0~55.0)	50.0 (45.0~57.0)	40.0 (37.0~48.0)	<0.001
FBS (mg/dl)	102.0 (96.0~111.0)	100.0 (94.0~107.0)	110.0 (100.0~122.0)	<0.001
Testosterone (ng/ml)	5.1 (4.1~6.2)	5.3 (4.3~6.4)	4.7 (3.9~5.7)	<0.001

Values are presented as number (%) or median (interquartile range).

MetS: metabolic syndrome group, BMI: body mass index, Waist Cir.: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, TG: triglycerides, HDL-C: high-density lipoprotein cholesterol, FBS: fasting blood sugar.

*Mann-Whitney test.

Table 2. Comparison of lower urinary tract symptoms/benign prostate hyperplasia between metabolic syndrome and non-metabolic syndrome groups

Variable	Non-MetS	MetS	p value
BPH	14.2	17.2	0.178 [†]
IPSS			
Total score	10.0 (5.0~15.0)	10.0 (5.0~15.0)	0.896*
QoL score	2.5 (1.0~4.0)	2.5 (1.0~4.0)	0.384*
Moderate to severe LUTS	63.3	63.1	0.949 [†]
Severe LUTS	14.3	12.7	0.754 [†]
Uroflowmetry			
Voiding volume (ml)	369.0 (243.0~526.0)	351.0 (232.0~486.0)	0.164*
Maximal flow rate (ml/s)	20.0 (15.0~27.0)	21.0 (15.2~27.0)	0.525*
Maximal flow rate <15 ml/s	23.4	23.7	0.910 [†]
Obstructive pattern on Siroky nomogram	13.7	13.2	0.833 [†]
Postvoid residual urine			
Volume (ml)	28.0 (17.0~43.0)	34.0 (23.0~54.0)	<0.001*
TRUS			
Prostate gland volume (ml)	25.0 (21.0~29.0)	26.0 (23.0~31.0)	0.002*
Prostate gland volume ≥20 ml	83.2	87.3	0.071 [†]
PSA (ng/ml)	0.8 (0.5~1.1)	0.8 (0.5~1.2)	0.765*

Values are presented as percentage or median (interquartile range).

MetS: metabolic syndrome group, BPH: benign prostatic hyperplasia (IPSS >7, maximal flow rate <15 ml/s, and prostate gland volume ≥20 ml), IPSS: International Prostate Symptom Score, QoL: quality of life, LUTS: lower urinary tract symptoms (Moderate to severe LUTS: IPSS >7, Severe LUTS: IPSS >19), TRUS: transrectal ultrasound, PSA: prostate-specific antigen.

*Mann-Whitney test, [†] χ^2 tests.

Table 3. Correlation of BPH with metabolic syndrome and components of metabolic syndrome

Variable	Age and testosterone adjusted OR	95% CI	p value*
Waist Cir. (≥90 cm)	1.526	0.935~2.491	0.091
HTN	1.450	0.972~2.163	0.068
TG (≥150 mg/dl)	0.757	0.495~1.160	0.201
HDL-C (<40 mg/dl)	1.295	0.828~2.025	0.258
FBS (≥110 mg/dl)	0.878	0.585~1.318	0.530
MetS	1.122	0.593~2.120	0.724

BPH: benign prostatic hyperplasia (IPSS >7, maximal flow rate <15 ml/s, and prostate gland volume ≥20 ml), OR: odds ratio, CI: confidence interval, Waist Cir.: waist circumference, HTN: hypertension, TG: triglycerides, HDL-C: high-density lipoprotein cholesterol, FBS: fasting blood sugar, MetS: metabolic syndrome.

*Logistic regression analysis.

association between MetS and BPH (odds ratio [OR]=1.122, 95% confidence interval [CI]=0.593~2.120; p value=0.724) (Table 3). Also, components of MetS were not significantly related to BPH. Additionally, MetS and its components were not correlated with prostate gland volume, IPSS total score, maximal flow rate, or postvoid residual urine volume after adjusting for age and testosterone using a multiple linear regression test (Table 4).

DISCUSSION

To our knowledge, these are the first data assessing LUTS/BPH using uroflowmetry among studies evaluating the associations between BPH/LUTS and MetS. Most studies have assessed LUTS/BPH using the IPSS only or in combination with transrectal ultrasound. There are no data concerning uroflowmetry or postvoid residual urine volume. Our results indicate that MetS is not clearly asso-

Table 4. Correlation between prostate gland volume, IPSS, maximal flow rate, or postvoid residual urine volume and components of metabolic syndrome, or metabolic syndrome

	Prostate gland volume			IPSS			Maximal flow rate			PVR		
	Beta	SE	p value*	Beta	SE	p value*	Beta	SE	p value*	Beta	SE	p value*
Waist Cir. (≥ 90 cm)	-0.641	0.596	0.282	-0.676	0.647	0.296	0.393	0.757	0.603	-0.655	3.702	0.860
HTN	-0.187	0.455	0.682	0.166	0.494	0.737	-0.550	0.578	0.342	-2.706	2.828	0.339
TG (≥ 150 mg/dl)	-0.366	0.496	0.461	-0.034	0.539	0.950	0.169	0.631	0.789	-1.195	3.082	0.698
HDL-C (< 40 mg/dl)	-0.998	0.551	0.071	0.151	0.599	0.801	1.189	0.701	0.090	-3.071	3.425	0.370
FBS (≥ 110 mg/dl)	-0.003	0.480	0.994	0.782	0.521	0.134	-0.749	0.610	0.220	-5.134	2.980	0.085
MetS	0.815	0.761	0.285	-0.189	0.827	0.819	-0.827	0.968	0.393	-0.975	4.732	0.837

IPSS: International Prostate Symptom Score, PVR: postvoid residual urine volume, SE: standard error, Waist Cir.: waist circumference, HTN: hypertension, TG: triglycerides, HDL-C: high-density lipoprotein cholesterol, FBS: fasting blood sugar, MetS: metabolic syndrome.

*Multiple linear regression test: adjusted for age and testosterone.

ciated with BPH/LUTS in Korean men in their 50s.

We defined BPH as an IPSS > 7 , maximal flow rate < 15 ml/s, and prostate gland volume ≥ 20 ml. This definition is open to dispute. However, this definition has been widely used in investigating the prevalence of BPH.^{10,11} According to this definition, the rate of BPH was 14.2% in subjects without MetS and 17.2% in subject with MetS. There was no significant difference between the two groups. In addition, LUTS severity, depending on the IPSS questionnaire, was no different between the two groups, nor was the IPSS total score or QoL score. Additionally, the IPSS subscore (obstructive symptoms and irritative symptoms) was not significantly different (data not shown). After adjusting for age and testosterone, MetS was not associated with BPH, IPSS total score, prostate gland volume, maximal flow rate or postvoid residual urine volume. The prostate volume and postvoid residual volume were significantly greater in subjects with MetS. Nevertheless, the differences (1 ml in prostate size and 6 ml in postvoid residual urine volume) were too small to accept them as clinically significant differences.

In a recent review article,² results from an Asian population did not consistently show a positive association between MetS and LUTS/BPH. The results of the present study correspond with the results of earlier studies. In data from China³ collected from 3,103 men with a median age of 35 years, MetS was not associated with the severity of LUTS according to IPSS (multivariate OR=0.97, 95% CI=0.67~1.39) after adjusting for age, smoking status, and alcohol consumption. Data from 900 men in Japan,

with a mean age of 56.7 years in the non-MetS group and 56.4 years in the MetS group who underwent digital rectal examinations of the prostate and who completed the IPSS, did not show a clear association between LUTS and MetS. Data from 538 men in South Korea with a mean age of 48.8 years did not show differences in scores on the IPSS or on an overactive bladder questionnaire short form.⁴ In another Korean study of 348 men assessing IPSS and transrectal ultrasonography, no significant differences were found in the mean IPSS score (11.1 in MetS vs. 12.3 in non-MetS) or prostate volume (20.7 ml in MetS vs. 19.4 in non-MetS).⁶ However, these studies had clear limitations, as discussed in introduction. We tried to compensate for the weaknesses of the former studies. Our data are from the largest study sample of men in their 50s to date. Furthermore, we evaluated the prevalence of BPH synthetically, depending on uroflowmetry, transrectal ultrasonography, and IPSS, and we also evaluated associations between BPH/LUTS and MetS after adjusting for confounding factors, including testosterone. In addition, we evaluated single occupational clusters, with the result that both subjects in the MetS and non-MetS groups had similar socioeconomic backgrounds. However, there was no clear association between LUTS/BPH and MetS.

We speculate that there were several reasons that a positive association between MetS and LUTS/BPH was not found in the present study or formerly among Asian data, unlike non-Asian data.

The reason for this difference might be population characteristics. We collected data from policemen through

prostate health examinations. In general, policemen exercise more regularly than the general population. A recent meta-analysis showed that moderate to heavy physical activity was associated with a decreased risk of BPH/LUTS. The OR for moderate activity was 0.74 (moderate activity: 95% CI=0.60~0.92, p=0.005) and for heavy activity was 0.74 (95% CI=0.59~0.92, p=0.006).¹² We speculate that the protective effect of physical activity could counterbalance the negative effects of MetS for BPH/LUTS.

A second explanation for our findings is eating habits. In general, Asians eat vegetables frequently compared to people in Western countries. Such eating habits would reduce the effects of MetS on LUTS/BPH. A cross-sectional study including 2,397 men older than 60 years of age showed that men in the top four quintiles for vitamin E, lycopene, and selenium had a non-statistically significant 25% to 50% reduced odds of LUTS, compared with men in the bottom quintile. Similarly, a case-control study including 1,369 cases and 1,451 controls reported that the risk of BPH significantly decreased with increasing intake of carotene (OR=0.80), alpha-carotene (OR=0.83), beta-carotene (OR=0.82), and cis-beta-carotene (OR=0.82).¹³

Several limitations of the present study warrant mentioning. First, the cross-sectional nature of the data set rendered causal inferences problematic. Additionally, because this study was performed at a single institution and was conducted in a single occupational cluster, there might be a potential for selection bias. However, despite these limitations, we believe that the results of this study are highly relevant because it is the first study to use uroflowmetry, transrectal ultrasound, and IPSS simultaneously, and because it is the largest study to date recruiting men in their 50s among studies evaluating BPH/LUTS and MetS.

CONCLUSIONS

In conclusion, the present results have shown that LUTS/BPH is not clearly associated with MetS in Korean men in their 50s. Future investigations should explore the temporal relationship between MetS and LUTS in Asian men. The confirmation of these associations in a prospective, longitudinal data set would be informative.

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