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ORIGINAL ARTICLE

Relationship between lower urinary tract symptoms and metabolic syndrome in a Chinese male population

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Abstract
Objectives To investigate whether the metabolic syndrome (MetS) is a risk factor for lower urinary tract symptoms (LUTS), as defined by the International Prostate Symptom Score in a Chinese male population with benign prostate hyperplasia (BPH).
Methods We retrospectively analyzed the clinical data obtained from 1,052 Chinese men with BPH. Serum levels of prostate specific antigen, fasting blood glucose (FBG), high-density lipoprotein cholesterol, total cholesterol and triglyceride were determined and recorded. Multiple logistic regression statistical analysis was used to investigate the degree of the association between LUTS and MetS.
Results Of the 1,052 enrolled patients, 648 (61.60 %) had moderate LUTS and 404 (38.40 %) had severe LUTS. A multiple logistic regression analysis showed that age (OR 2.02, 95 % CI 1.04–4.63), FBG (OR 3.65, 95 % CI 1.68–7.98) and presence of MetS (OR 3.64, 95 % CI 1.24–6.14) were significant predictors of severe LUTS.
Conclusions The results of our study suggest that MetS is associated with an increase risk of total volume and annual growth rate of prostate.

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Keywords Metabolic syndrome · Benign prostate hyperplasia · Lower urinary tract symptoms

Introduction

Benign prostate hyperplasia (BPH) is a common disorder among older men and has received more attention as the average human lifespan has increased [1]. BPH is a histological condition affecting more than 50 % of men over 60 years and nearly all men aged over 80 years, frequently resulting in bladder outlet obstruction (BOO) and lower urinary tract symptoms (LUTS) [2]. It is well known that LUTS can, to a large extent, affect the quality of life (QOL) in these aging men and may progress to acute urinary retention. To date, the prevalence of LUTS in community and clinic populations has been extensively evaluated worldwide [3]. In 2008, an estimated 45.2 % of the worldwide population was affected by at least one LUTS, with the regional burden of these conditions estimated to be greatest in Asia [4]. LUTS are also a significant health problem in men in China, a cover with the greatest population worldwide [5].

Over the past two decades, the prevalence of metabolic syndrome (MetS) has sharply increased worldwide and is associated with the global epidemic of obesity and diabetes. MetS is prevalent in countries with western lifestyles, affecting around 34–39 % of the adult population in the USA, with just about equal prevalence in men and women [6]. Increasingly, there is evidence that indicating a relationship between lower urinary tract symptoms and the metabolic syndrome [7]. The key pathophysiology of MetS is hyperinsulinemia, caused by tissue insulin resistance, which induces the autonomic nerve system, particularly sympathetic nerve overactivity, resulting in BOO and

LUTS [8]. Results from the Boston Area Community Health (BACH) survey found that heart disease and diabetes mellitus were significantly associated with moderate and severe LUTS [9]. Therefore, it is considered that MetS may play a role in development of LUTS. However, there has not been any known large population-based survey assessing the effect of MetS on LUTS in China mainland. With this background, we investigated whether the metabolic syndrome is a risk factor for LUTS, as defined by the International Prostate Symptom Score (IPSS) and QOL score.

Materials and methods

The present study was conducted retrospectively in The Second Affiliated Hospital of Guangzhou Medical University from January 2005 to December 2011. All participants enrolled in the study were inpatient diagnosed with BPH who had undergone transurethral resection of prostate (TURP) and further confirmed by histopathological test. All subjects completed the IPSS questionnaire, a digital rectal examination (DRE), prostate ultrasonography and anthropometric measurements such as height, weight, and blood pressure. Body mass index (BMI) was calculated by dividing the weight in kilograms by the square of height in meters. Maximum urine flow rates (Qmax) were measured by uroflowmetry. The volume of the prostate was calculated by elliptical volume measurement ($\pi/6 \times$ transverse $\times$ anteroposterior $\times$ cephalocaudal diameter). The annual prostate growth rate was calculated by the formula: prostate volume−20 mL/age−40. Overnight fasting venous blood specimens were collected and serum levels of PSA, FBG, high-density lipoprotein cholesterol (HDL-C), total cholesterol and TG were determined and recorded.

To minimize potential confounding and bias, the following exclusion criteria were used: (1) history of major pelvic surgery or injury; (2) use of medications that may influence genitourinary system such as diuretic; (3) medication for prostatitis and/or urinary tract infection; (4) diagnosis of neuropsychiatric disease or use of medications that may affect the central nervous system or peripheral nervous system; (5) diagnosis of stroke, coronary heart disease, myocardial infarction, malignancy, liver cirrhosis, known malignant disease such as prostate cancer and chronic renal failure.

The metabolic syndrome was diagnosed using the 2005 National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) criteria for Asian Americans [10]. The NCEP-ATP III has defined the metabolic syndrome as the presence of three or more of the five characteristics of (1) BMI >30 kg/m^2; (2) triglycerides $\geq$1.7 mmol/L, (3) HDL-C <1.03 mmol/L, (4) blood pressure $\geq$130/85 mmHg or current use of antihypertensive medications, and (5) FBG $\geq$5.6 mmol/L or previous diagnosis of type 2 diabetes mellitus or use of oral antidiabetic agents or insulin.

All participants were assessed based on the Chinese version of the IPSS and IPSS–Quality of life (IPSS-QoL) for LUTS. Each of the first seven categorical items of IPSS can be scored from 0 to 5, with a total score of 0–35. Based on total score, the severity of symptoms was sorted into two groups: moderate symptoms (IPSS 8–19) and severe symptoms (IPSS 20–35). Symptoms were further evaluated and categorized as storage, voiding, and postmicturition using questions 2, 4 and 7, questions 3, 5 and 6, and question 1, respectively [11].

We divided the study population into two groups: MetS group and non-MetS group. Descriptive data are presented as mean and SD for continuous data. We compared the IPSS, voiding symptom subscore, storage symptom subscore, QoL, and prostate-related parameters between the two groups. The Chi Square, Student *t*, and Mann–Whitney *U* tests were used to compare differences in the variables between the subjects with and without MetS. Demographic characteristics and various parameters were compared among different strata of LUTS severity using Wilcoxon rank-sum (Mann–Whitney) test and Fisher exact test between moderate symptoms and severe symptoms group. Multiple logistic regression methods were used to investigate the extent of the association between LUTS and MetS. In all comparisons of values, a P value of <0.05 was considered to be statistically significant.

Results

A total of 1,052 men aged 51–84 years were eligible for analysis. Mean age at baseline in the entire cohort was 70.13 ± 7.83 years old. 139, 369 and 544 men were in their 50 s (13.21 %), 60 s (35.08 %) and 70 s (51.71 %), respectively. The median IPSS, voiding symptom (Q3, Q5 and Q6), storage symptom (Q2, Q4 and Q7), postmicturition symptom (Q1), QoL, Qmax, total prostate volume and annual prostate growth rate were 21.05 ± 4.52, 8.79 ± 2.18 (Q3, 3.28 ± 1.02; Q5, 2.86 ± 0.80; Q6, 3.08 ± 0.84), 9.22 ± 2.40 (Q2, 2.72 ± 0.86; Q4, 2.79 ± 1.01; Q7, 3.29 ± 1.21), 3.04 ± 0.90, 3.96 ± 1.27, 6.63 ± 3.05, 61.93 ± 10.50 and 1.50 ± 0.63. The descriptive data including the residual urine volume, PSA and all anthropometric parameters in the patients are listed in Table 1.

The overall prevalence of MetS was 39.73 % (418/1,052) identified by NCEP-ATP III criteria for Asian Americans. Men with MetS were significantly older as compared with men without MetS ($P < 0.001$). There were

Table 1 Characteristics of participants

Variables	Min	Max	Mean ± SD
Age (years)	51	84	70.13 ± 7.83
Height (cm)	1.64	1.78	1.71 ± 0.34
Weight (kg)	62	93	75.50 ± 7.87
Fasting blood glucose (FBG, mmol/L)	4.00	9.20	5.90 ± 1.58
High-density lipoprotein cholesterol (HDL-C, mmol/L)	0.52	2.18	1.20 ± 0.41
Total cholesterol (mmol/L)	2.01	6.67	4.66 ± 1.06
Triglyceride (TG, mmol/L)	1.02	3.09	1.97 ± 0.44
Body mass index (BMI, kg/m^2)	21.55	31.93	25.75 ± 2.58
Systolic blood pressure (mmHg)	110	155	131.73 ± 10.78
Diastolic blood pressure (mmHg)	75	98	84.25 ± 7.33
International Prostate Syndrome Score (IPSS)			
Q1	1	5	3.04 ± 0.90
Q2	1	4	2.72 ± 0.86
Q3	1	5	3.28 ± 1.02
Q4	1	5	2.79 ± 1.01
Q5	1	4	2.86 ± 0.80
Q6	1	4	3.08 ± 0.84
Q7	1	5	3.29 ± 1.21
Total	13	31	21.05 ± 4.52
Voiding symptom	7	18	11.83 ± 2.79
Storage symptom	4	13	9.22 ± 2.40
Quality of life	2	6	3.96 ± 1.27
Residual urine volume (mL)	34	480	143.20 ± 116.05
Qmax (mL/s)	2.40	11.20	6.63 ± 3.05
Prostate specific antigen (PSA, ng/mL)	0.20	6.30	2.75 ± 1.51
Total prostate volume (mL)	44.20	84.91	61.93 ± 10.5
Annual prostate growth rate (mL/year)	0.58	4.55	1.50 ± 0.63

statistically significant differences between the two groups regarding median weight, FBG, HDL-C, total cholesterol, TG, BMI, systolic blood pressure and diastolic blood pressure. Men with MetS had significantly higher level of the above-mentioned parameters compared with men without MetS (P both <0.001, Table 2).

Table 2 also indicates comparison of the IPSS and IPSS-QoL for LUTS between the MetS group and non-MetS group. In patients with BPH and MetS, the median IPSS (24.80 ± 3.93), voiding symptom (10.32 ± 2.27), storage symptom (10.76 ± 1.91), postmicturition symptom (3.72 ± 0.67), and QoL (4.94 ± 1.06) were significantly higher, and Qmax (3.84 ± 1.51) were significantly lower compared with patients with BPH who did not have metabolic syndrome. There was no statistically significant difference between the two groups regarding median PSA level (2.78 ± 2.00 for MetS versus 2.72 ± 1.08 for non-MetS, $P = 0.58$). Furthermore, the median total prostate volume (69.01 ± 8.77 mL) and median annual prostate growth rate (1.92 ± 0.73 mL/year) were significantly higher in the MetS group compared with Non-MetS group (57.26 ± 8.80 mL and 1.23 ± 0.33 mL/year).

Of 1,052 patients, 648 (61.60 %) had moderate LUTS and 404 (38.40 %) had severe LUTS, with a median age of 71.52 ± 5.32 for moderate group and 67.91 ± 10.32 for severe group, respectively. Weight, FBG, HDL-C, total cholesterol, TG, BMI, systolic and diastolic blood pressure, residual urine volume, total prostate volume, and annual prostate growth rate were significantly different between subjects with moderate LUTS and severe LUTS. In BPH patients with severe LUTS, the median IPSS (24.80 ± 3.93), voiding symptom (10.32 ± 2.27), storage symptom (10.76 ± 1.91), postmicturition symptom (3.72 ± 0.67), and QoL (4.94 ± 1.06) were significantly higher compared with those with moderate LUTS. However, the median of height and PSA were not significantly between the two groups. Subjects with severe LUTS presented higher prevalence of MetS (76.98 %) than men with moderate LUTS (16.51 %) and statistical significance was found between them (Table 3).

The presence of MetS and each metabolic risk factor were cross-tabulated with LUTS severity (Table 4). According to those ratios, there is significant association between severe LUTS and presence of MetS and its

Table 2 Comparison of the metabolic components and symptom score between the metabolic syndrome group and non-metabolic syndrome

	MetS group ($n = 418$)	Non-MetS group ($n = 634$)	P value
Age (years)	68.44 ± 9.82	71.24 ± 5.93	<0.001
Height (cm)	1.72 ± 0.26	1.71 ± 0.04	<0.001
Weight (kg)	82.63 ± 6.78	70.80 ± 4.11	0.605
Fasting blood glucose (FBG, mmol/L)	7.47 ± 1.39	4.86 ± 0.41	<0.001
High-density lipoprotein cholesterol (HDL-C, mmol/L)	0.83 ± 0.10	1.44 ± 0.34	<0.001
Total cholesterol (mmol/L)	5.54 ± 0.62	4.08 ± 0.88	<0.001
Triglyceride (TG, mmol/L)	2.34 ± 0.30	1.72 ± 0.34	<0.001
Body mass index (BMI, kg/m^2)	28.20 ± 2.16	24.14 ± 1.20	<0.001
Systolic blood pressure (mmHg)	141.50 ± 5.14	125.29 ± 8.42	<0.001
Diastolic blood pressure (mmHg)	90.39 ± 5.16	80.20 ± 5.51	<0.001
International Prostate Syndrome Score (IPSS)	24.80 ± 3.93	18.58 ± 2.87	<0.001
Voiding symptom	10.32 ± 2.27	7.78 ± 1.40	<0.001
Storage symptom	10.76 ± 1.91	8.21 ± 2.13	<0.001
Postmicturition symptom	3.72 ± 0.67	2.59 ± 0.73	<0.001
Quality of life	4.94 ± 1.06	3.31 ± 0.95	<0.001
Residual urine volume (mL)	258.00 ± 102.39	67.52 ± 31.87	<0.001
Qmax (mL/s)	3.84 ± 1.51	8.47 ± 2.32	<0.001
Prostate specific antigen (PSA, ng/mL)	2.78 ± 2.00	2.72 ± 1.08	0.58
Total prostate volume (mL)	69.01 ± 8.77	57.26 ± 8.80	<0.001
Annual prostate growth rate (mL/year)	1.92 ± 0.73	1.23 ± 0.33	<0.001
Acute urine retention rate (%)	0.82	0.17	<0.001

components. A multiple logistic regression analysis was performed with the presence of moderate/severe LUTS as the dependent variable and the following as predictive variables: age, hypertension, BMI (>30 kg/m^2 versus ≤30 kg/m^2), triglycerides s (≥1.7 mmol/L versus <1.7 mmol/L), HDL-C (<1.03 mmol/L versus ≥1.03 mmol/L), FBG (≥5.6 mmol/L versus <5.6 mmol/L) and presence of MetS or not. Analysis showed that age (OR 2.02, 95 % CI 1.04–4.63), FBG (OR 3.65, 95 % CI 1.68–7.98) and presence of MetS (OR 3.64, 95 % CI 1.24–6.14) were significant predictions of sever LUTS.

Discussion

In this survey of 1,052 Chinese men, we examined the cross-sectional association of MetS and its components with BPH. We noted that the presence of MetS was significantly associated with the annual growth rate and total volume of prostate. We also found that MetS was risk factor for the clinical progression of BPH. The overall prevalence of MetS was 39.73 % (634/1,052) identified by NCEP-ATP III criteria for Asian Americans. In our study, total prostate volume and annual prostate growth rate in the MetS group were significantly higher than in the non-MetS group.

A growing number of studies have found relations between the metabolic syndrome and urologic disorders, including BPH and LUTS [12]. Initially, Hammarsten et al. [13] found correlations between the annual prostate growth rates, metabolic syndrome, and fasting plasma insulin levels and concluded that BPH might be an insulin resistance-related disorder. This finding is supported by the study of Kaplan et al. [14] that a high correlation was found among the waist circumference, components of the metabolic syndrome, and the prostate volume. MetS is difficult to properly diagnose, because its presentation varies according to the different components that constitute the syndrome. LUTS have three categories, with postmicturition symptoms added to conventional storage and voiding symptoms. The storage symptoms include increased daytime frequency, nocturia, and urgency. The voiding symptoms include a slow stream, splitting, intermittency, and straining. Finally, the postmicturition symptoms include a feeling of incomplete emptying and postmicturition dribble [15].

Several studies have suggested a relationship between voiding symptoms and the presence of the metabolic syndrome. Men with the metabolic syndrome are more likely to have severe LUTS. Rohrmann et al. [16] in a large population-based survey found that the components of the metabolic syndrome were likely to be associated with

Table 3 Demographic, laboratory and questionnaire data of participants according to LUTS severity

	LUTS severity		
	Moderate	Severe	*P* value
n	648	404	–
Age (years)	71.52 ± 5.32	67.91 ± 10.32	<0.001
Height (cm)	1.71 ± 0.04	1.71 ± 0.28	0.237
Weight (kg)	71.73 ± 4.82	81.56 ± 8.04	<0.001
Fasting blood glucose (FBG, mmol/L)	5.01 ± 0.63	7.32 ± 1.60	<0.001
High-density lipoprotein cholesterol (HDL-C, mmol/L)	1.37 ± 0.36	0.91 ± 0.31	<0.001
Total cholesterol (mmol/L)	4.23 ± 0.99	5.35 ± 0.77	<0.001
Triglyceride (TG, mmol/L)	1.83 ± 0.45	2.20 ± 0.32	<0.001
Body mass index (BMI, kg/m^2)	24.44 ± 1.53	27.86 ± 2.54	<0.001
Systolic blood pressure (mmHg)	126.92 ± 9.64	139.46 ± 7.51	<0.001
Diastolic blood pressure (mmHg)	81.78 ± 6.46	88.21 ± 6.90	<0.001
International Prostate Syndrome Score (IPSS)	15.31 ± 2.24	22.34 ± 1.71	<0.001
Voiding symptom	7.58 ± 1.54	10.72 ± 1.61	<0.001
Storage symptom	7.73 ± 1.69	11.63 ± 1.01	<0.001
Postmicturition symptom	2.71 ± 0.74	3.57 ± 0.87	<0.001
Quality of life	3.18 ± 0.87	5.21 ± 0.67	<0.001
Residual urine volume (mL)	70.59 ± 44.42	259.68 ± 99.39	<0.001
Qmax (mL/s)	8.34 ± 2.35	3.90 ± 1.79	<0.001
Prostate specific antigen (PSA, ng/mL),	2.68 ± 1.05	2.85 ± 2.04	0.076
Total prostate volume (mL)	58.63 ± 8.44	67.22 ± 11.30	<0.001
Annual prostate growth rate (mL/year)	1.26 ± 0.33	1.89 ± 0.78	<0.001
Metabolic syndrome (*n*, %)			
No	541 (84.49)	93 (23.02)	<0.005
Yes	107 (16.51)	311 (76.98)	

Table 4 Frequency of patients according to the severity of LUTS and the presence of the metabolic risk factors

	Moderate LUTS	Severe LUTS
Hypertension (≥130/85 mmHg)	170 (26.23)	367 (90.84)
BMI (>30 kg/m^2)	28 (4.32)	153 (37.87)
Triglycerides (≥1.7 mmol/L)	392 (60.49)	383 (94.80)
HDL-C (<1.03 mmol/L)	173 (26.70)	383 (94.80)
FBG (≥5.6 mmol/L)	57 (8.80)	296 (73.27)
Presence of MetS	107 (16.51)	311 (76.98)

* *P* both <0.05

LUTS in older men. Some studies [15] found that men with diabetes or hypertension had a greater risk of developing moderate to severe LUTS. Metabolic syndrome is associated with an enlarged prostate and rapid prostate growth. Ozden et al. [7] showed that the prostate growth rate was greater in patients with BPH and the MetS.

Our results are consistent with these previous reports. In the present study, Weight, FBG, HDL-C, total cholesterol, TG, BMI, systolic and diastolic blood pressure, residual urine volume, total prostate volume, and annual prostate growth rate were significantly different between subjects with moderate LUTS and severe LUTS. In BPH patients with severe LUTS, the median IPSS (24.80 ± 3.93), voiding symptom (10.32 ± 2.27), storage symptom (10.76 ± 1.91), postmicturition symptom (3.72 ± 0.67), and quality of life (4.94 ± 1.06) were significantly higher compared with those having moderate LUTS. However, the median of height and PSA were not significantly between the two groups (Table 3). According to those ratios, there were significant associations between severe LUTS and presence of MetS and its components including hypertension, abnormal BMI, abnormal FBG, abnormal TG and HDL-C. A multiple logistic regression analysis showed that age (OR: 95 % CI), FBG (OR: 95 % CI) and presence of MetS (OR: 95 % CI) were significant predictors of severe LUTS.

Recent studies suggest that hyperinsulinemia secondary to insulin resistance and the components of metabolic syndrome are risk factors for BPH development [17]. Hyperinsulinemia has a stimulant effect on the sympathetic nervous system. It increases the intake of glucose to the ventromedial hypothalamic neurons, which regulate the sympathetic nervous system [18]. The increase in the sympathetic activity induced by hyperinsulinemia could be

related to BPH pathophysiology. In a review by McVary [19], according to the theory of autonomic hyperactivity of LUTS, increased autonomic hyperactivity results from increased BMI, hyperinsulinemia, increased age, and decreased physical activity. This increased sympathetic tone affects BPH growth and LUTS. Our study demonstrated that men with MetS had significant higher scores of IPSS both in voiding and storage subscores.

This study has its own limitations. It was conducted in a single institution and may have been subject to a selection bias. Also, only inpatients with BPH were enrolled which can significantly influence the severity of LUTS. Further large-scale studies in the general population and on both inpatients and outpatients will be necessary to confirm our results. Another possible limitation was the use of self-report questionnaires for assessing IPSS. This introduced a potential for response bias, as respondents may inaccurately report their urinary symptoms and elderly men might not have fully understood the meaning of the questions posed. However, the questionnaires selected for this study have all been previously validated in clinical and nonclinical samples and have been widely used in various other studies. Finally, considering the central pathophysiology of the metabolic syndrome is hyperinsulinemia caused by tissue insulin resistance, we did not investigate the nature of the correlation between hyperinsulinemia and LUTS.

Conclusions

The results of our study suggest that metabolic syndrome is highly prevalent in BPH population and it is associated with an increase risk of total volume and annual growth rate of prostate. Our data also suggest that the MetS and its components are associated with LUTS in patients with BPH. Further studies are needed to explore the correlation between LUTS and MetS and its components.

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Conflict of interest The authors Jian Gang Pan, Mo Liu, and Xing Zhou declare that they have no conflict of interest.

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