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Metabolic Syndrome and Benign Prostatic Hyperplasia/What Component of Metabolic Syndrome Is Related to Benign Prostatic Hyperplasia?

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What's known on the subject? and What does the study add?

One of the most prevalent disorders affecting men in their old age is benign prostatic hyperplasia (BPH). Prostatic enlargement and lower urinary tract symptoms are its defining features. The main risk factors for the development of BPH are recognized to be aging, inflammation, and a hormonal imbalance. The etiology of BPH is not well understood. Additionally, current research indicates that metabolic conditions such hyperinsulinemia, dyslipidemia, and obesity may contribute to the emergence of BPH. Our goal was to assess the relationship between BPH and each metabolic syndrome (MS) feature and identify which feature carries the greatest risk for BPH development. This is the first study in the literature to investigate the risk between BPH and MS with each metabolic syndrome component separately and independently of each other. We discovered at the study's conclusion that there was no difference in BPH prevalence between MS components. We came to the conclusion that while none of the MS components by themselves enhance the likelihood of BPH, when these metabolic problems combine to form a syndrome, BPH becomes more common.

Abstract

Objective: Our objective was to evaluate the association of benign prostatic hyperplasia (BPH) with each component of metabolic syndrome (MS), and determine which component plays the major risk for developing BPH.

Materials and Methods: This cross-sectional observational study was performed on 203 male patients aged over 50, who came to the internal medicine outpatient clinics just for a check-up with/without any known disease. Forty-three of them were healthy control patients and the rest had only 1 criterion of MS. They were searched for the presence of BPH.

Results: BPH prevalence ranged between 45.5-65.6% in the subgroups, there was no statistically significant difference in the presence of BPH between these groups. There was a slight positive correlation between glucose level and prostate volume. Triglyceride levels were positively correlated with Q_{max} and negatively correlated with the grade of hypertrophy. There was also a slight positive correlation between systolic blood pressure and prostate volumes, grade of hypertrophy, and IPSS scores.

Conclusion: BPH prevalence was not different between MS components. We concluded that none of the MS components increase the occurrence of BPH by itself but when those metabolic disorders come together and form a syndrome, the prevalence of BPH increases.

Keywords: Metabolic syndrome, benign prostatic hyperplasia, hyperglycemia, hypertension, dyslipidemia, obesity.

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Introduction

Benign prostatic hyperplasia (BPH) is one of the most common diseases of men in their elderly age. It is characterized by hyperplasic nodules in the prostate gland, prostatic enlargement, and the presence of lower urinary tract symptoms (LUTS). Aging, inflammation, and hormonal imbalance between androgens and estrogen are known as the main risk factors for developing BPH; however, the cause of BPH is not well defined. Recent studies have also shown that metabolic disorders such as hyperinsulinemia, dyslipidemia, and obesity may play a role in the development of BPH (1,2).

Metabolic syndrome (MS) is defined as a combination of hypertension, impaired glucose metabolism, abdominal obesity, hypertriglyceridemia, and low high-density lipoprotein cholesterol (HDL-C) (3). According to the International Diabetes Foundation (IDF)-5 definition, metabolic syndrome is present if abdominal obesity (waist circumference over 94 cm for men or 80 cm for women) + two or more of the following four criteria are met: fasting blood sugar over 100 mg/dL, fasting triglyceride (TG) level greater than 150 mg/dL, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dL (men) or 50 mg/dL (women), and blood pressure over 130/85 mmHg. Similar to BPH, with increasing age, MS is seen more frequently (4). Some studies in the literature give an impulse to an association between MS and prostatic hyperplasia and LUTS (5-8). It is unclear whether MS triggers BPH or whether these two phenomena simply occur together because of aging. In some of these studies, it was shown that this risk is positively associated with the number of MS components. However, there are also some studies conflicting with this relationship (9,10). Furthermore, studies performed on Asian populations have shown a null or even inverse association between MS and BPH and/or its related LUTS (11-15).

In this study, our objective was to evaluate the association of BPH with each component of MS, and determine which component plays the major risk for developing BPH, whether one pathology is responsible for this risk or does the risk occur when 3 or more components get together and named as MS.

Materials and Methods

This is a cross-sectional and observational study that was performed on 203 male patients aged over 50 years, who came to the Internal Medicine outpatient clinics between the years 2015-2018 just for a check-up with/without any known disease. The study was approved by our hospital's non-interventional clinical research ethics committee (University of Health Sciences Turkiye, Kartal Dr. Lütfi Kırdar Training and Research Hospital Ethics Committee - decision no: 89513307/1009/409, dated: 10.02.2015). Informed consent was obtained from all the patients.

Patients with a history of prostatic malignancy, those taking 5 alfa reductase inhibitor medications that decrease prostate volume, or patients who had surgery related to the urinary bladder or prostate were excluded from the study. For the inclusion criteri, patients must have just one component of MS (not more than 1 component). According to these components, the patients were divided into five groups [Group 1: just having abdominal obesity, Group 2: just having blood pressure over 130/85 mmHg, Group 3: just having fasting triglyceride (TG) level greater than 150 mg/dL, Group 4: just having fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dL, Group 5: just having fasting blood sugar over 100 mg/dL]. Patients that have more than 1 criterion were excluded. In addition, there was a control group composed of healthy volunteers without any diagnosed disease and without having any criteria for MS.

These patients involved in the study were later examined by urologists for the existence of BPH. The following measurements were recorded: waist circumference, height, weight, body mass index, blood pressure, lipid profile, fasting blood glucose, urea, creatinine, prostate-specific antigen (PSA), prostate volume, and urine specimen. The drugs used by these patients were recorded. The prostate gland was evaluated by digital rectal examination, and ultrasound was used to measure the prostate volume. To specifying the severity of LUTS, the International Prostate Symptom Score (IPSS) was used. With the total score changing from 0 to 35 points, patients who had 0-7, 8-19, and 20-35 points were classified as mild, moderate, and severely symptomatic respectively. Uroflowmetry was performed for each patient to detect the Q_{max} value. In men who had a serum PSA concentration of more than 4.0 ng/mL and/or a suspected digital rectal examination, prostate biopsy was performed. PSA levels ≥4 µg/L, prostate volume ≥40 ccs, digital rectal examination result ≥ grade 1, Q_{max} ≤15 mL/sn, or IPSS >7 (at least having one of them) were considered as having BPH.

Statistical Analysis

SPSS version 24 software (SPSS Inc., Chicago, IL, USA) was used to perform the statistical Inc. Mean, SD, median, minimum, maximum, frequency, and percentage values were used as descriptive statistics. The distribution of the variables was evaluated using the Kolmogorov-Smirnov test. In continuous variables, for non-parametric data Mann-Whitney U test, and parametric data Independent Samples t-test were used. The chi-square test was used for categorical variables. Pearson correlation analysis for parametric variables and Spearman correlation analysis for non-parametric variables were applied to examine the relationships between them. A p-value <0.05 was considered statistically significant.

Results

The prevalence of BPH ranged between 45.5-65.6% in the groups, there was no statistically significant difference between these groups. Also, there was not any statistically meaningful difference in prostate volumes, PSA levels, digital examination results, IPSS scores, and Q_{max} values between these groups (Table 1).

According to the correlation coefficient between BPH parameters and MS syndrome parameter, there was a slight positive correlation between glucose levels and prostate volumes. Triglyceride levels were positively correlated with Q max and negatively correlated with the grade found in digital rectal examination. There was also a slight positive correlation between systolic blood pressure and prostate volumes, IPSS scores, and rectal examination grading of the patients.

When these patients were grouped as having BPH (n=117) or not having BPH (n=86), statin usage in BPH (-) patients were 4.7%, whereas in BPH (+) patients it was %0 (p=0.0.13). There was no statistical difference in anti-hypertensive and anti-diabetic drug usage percentages between patients.

A prostate biopsy was wanted from 13 patients. One of them did not accept biopsy. In four patients, prostate adenocarcinoma was detected (Patient 1: 65 years old +high triglyceride, patient 2: 62 years old + low HDL, patient 3: 63 years old + abdominal obesity, patient 4: 71 years old + low HDL).

Among their follow-up, 1 patient was diagnosed with angiomyolipoma (61 years old + high blood pressure), and 1 patient was diagnosed with renal cell ca (65 years old +low HDL).

Discussion

Metabolic syndrome is a combination of cardiovascular and metabolic risk factors. The association between MS and BPH was first observed by Hammarsten et al (7). In their study, prostate volume was significantly higher in patients with BPH with MS compared with those without MS. After this study, several authors have supported a possible link between MS and BPH (5-8,16-18), but some others did not confirm this association (9-15).

The pathogenetic mechanisms of the association between MS and BPH are not well known. Clinical studies corroborate the role of chronic inflammation as a possible factor (19). In addition, the role of the impaired immune response has recently been emphasized in BPH pathogenesis (19).

Studies up to now related to this article have all been performed in patients diagnosed with MS. As it is known, it is a combination of metabolic disorders. There has been no study

Table 1. Clinical features of patients with different components of MS and the control group

	Control group (n=43)	Abdominal obesity (n=29)	High glucose level (n=38)	Low HDL cholesterol level (n=28)	Hipertension (n=32)	High triglyceride level (n=33)	p-value
BPH prevalence (n, %)	**25 (58%)**	**18 (62.1%)**	**23 (60.5%)**	**15 (53.3%)**	**21 (65.6%)**	**15 (45.5%)**	**0.646**
Age	60.5±8.0	59.9±0.6	60.4±6.8	57.5±6.5	63.4±7.3	57.9±5.4	0.016
Prostate volume (cc)	33.0±16.0	36.4±20.2	38.3±16.5	30.9±11.3	37.9±17.8	32.4±17.7	0.344
PSA (µg/L)	1±0.6	1.24±0.7	0.95±0.5	0.85±0.65	1.1±0.8	0.8±0.5	0.676
IPSS score	6.5±4.1	6.9±4.8	7.4±5.3	5.9±3.9	7.2±3.9	6.0±4.4	0.658
Q_{max} (mL/sn)	19.9±8.7	18.2±7.8	21.8±11.2	20.6±8.5	21.4±10.2	22.5±9.0	0.521
PVR (post void residual volume) (cc)	33±12	39±20	34±15	48±20	35±5	39±18	0.512
Glukoz (mg/dL)	93.3±7.4	99.0±7.2	142.4±46.8	96.1±8.8	96.4±8.0	97.6±6.2	0.000
HDL cholesterol (mg/dL)	53.7±9.1	51.2±9.6	52.2±11.3	35.9±3.1	53.2±8.9	47.5±6.2	0.000
Triglyceride (mg/dL)	100.6±31.2	92.7±28.5	108.7±34.6	114.8±27.0	104.2±26.8	230.7±61.8	0.000
LDL cholesterol (mg/dL)	149.0±37.7	142.8±43.8	157.9±35.0	123.8±29.3	152.7±30.1	161.4±38.8	0.001
Total cholesterol (mg/dL)	222.6±43.2	212.5±46.3	231.5±39.0	182.8±32.1	226.8±33.6	254.9±40.8	0.000
Systolic blood pressure (mm/Hg)	123.7±4.9	126.6±4.6	124.9±5.6	122.4±6.1	134.7±9.8	123.2±4.6	0.000
Diastolic blood pressure (mm/Hg)	77.6±4.7	79.8±2.5	78.2±4.6	78.9±3.9	80.6±6.7	77.5±4.2	0.035
Waist circumference	85.9±2.5	99.2±3.2	86.8±2.8	86.6±3.5	87.4±2.2	86.0±2.1	0.791

on the relationship between each component of metabolic syndrome separately and the BPH. We do not know whether a component of MS is responsible for this or is it just because of inflammation and aging. It is still unclear which metabolic disorder makes those men more prone to BPH.

In our study, we grouped patients according to their metabolic disorders. Patients having more than one criterion for MS were excluded at the beginning. Therefore, the patients included in the study were not MS patients. They were the patients having only one metabolic disorder, which was a component of MS.

There was not any correlation between these groups and BPH prevalence. In groups with abdominal obesity, high glucose levels, and high blood pressure, BPH prevalence was higher than in the control group, but this was not statistically significant.

In the patients that do not have BPH, statin usage was significantly higher. There are some studies in the literature that statin usage has a protective effect on BPH. This result also supports that BPH prevalence is lower in patients using a statins.

With these results, we thought that none of the MS parameters separately increase the risk of BPH, but when they come together and form the syndrome, with the contribution of increased inflammation, aging, and co-existence of metabolic disorders, including hyperinsulinemia, this makes MS patients more prone to BPH occurrence. The role of inflammation and inflammatory mediators should be overviewed once more for this process. It is impossible to say that BPH prevalence is increased in hypertension, or in hyperglycemia or in dyslipidemia. Also, we can not say that obesity is an independent risk factor for BPH. None of the determinants of MS is solely responsible for the risk of BPH existence. All these risk factors should be evaluated together. We should consider increased BPH prevalence when patients have a diagnosis of MS.

Study Limitations

Low number of patients was a limitation of this study. This is because of the difficulties in forming these separate groups that only have 1 MS component. Although we could not find a statistically significant relationship between MS parameters and BPH, studies having a larger number of patients are needed on this subject.

Conclusion

BPH prevalence was not different between MS components. We concluded that none of the MS components increase the occurrence of BPH by itself. But by looking at the results of previous studies, we concluded that when these metabolic disorders come together and form a syndrome, the prevalence of BPH increases.

Ethics

Ethics Committee Approval: The study was approved by our hospital's non-interventional clinical research ethics committee (University of Health Sciences Turkiye, Kartal Dr. Lütfi Kırdar Training and Research Hospital Ethics Committee - decision no: 89513307/1009/409, dated: 10.02.2015).

Informed Consent: Informed consent was obtained from all the patients.

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Authorship Contributions

Surgical and Medical Practices: B.A.T., E.Ç., Ö.K., M.K., K.F.N., Concept: B.A.T., Y.Ö., K.F.N., Design: B.A.T., E.Ç., Ö.K., M.K., Y.Ö., K.F.N., Data Collection or Processing: B.A.T., E.Ç., Ö.K., M.K., K.F.N., Analysis or Interpretation: B.A.T., Y.Ö., K.F.N., Literature Search: B.A.T., K.F.N., Writing: B.A.T., K.F.N.

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