Does Metabolic Syndrome Increase Erectile Dysfunction and Lower Urinary Tract Symptoms?

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Purpose: To evaluate the impact of metabolic syndrome (MS) on erectile dysfunction (ED) and lower urinary tract symptoms (LUTS).

Materials and Methods: We included patients who had presented at the urology outpatients with LUTS or ED complaints and at the endocrinology outpatients for diabetes between May 2012 and April 2013. MS was present in 50 of the 107 patients (42.7%). The blood pressure, fasting blood sugar, serum lipid profile, triglyceride, total cholesterol, body mass index (BMI) and total prostate specific antigen (PSA) values were recorded. The international prostate symptom score (IPSS), quality of life score and international erectile function index (IIEF-5) values were determined for the patients. All patients also underwent uroflowmetry together with prostate volume and residual urine volume measurement.

Results: There was a significant negative correlation between the IPSS and IIEF scores of the patients ($P < .001$, $r = -0.42$). There was no significant difference regarding IPSS scores between patients with and without MS ($P = .6$), while the IIEF-5 scores were significantly lower in the MS group ($P = .03$).

Conclusion: We found that metabolic syndrome did not significantly affect LUTS but could significantly contribute to ED. We therefore feel patients presenting with ED complaints should also be carefully evaluated for MS.

Keywords: erectile dysfunction; physiopathology; metabolic syndrome; risk factors; urination disorders; lower urinary tract symptoms.

INTRODUCTION

The lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) rates increase with advancing age and they are important health problems decreasing the quality of life. Bladder outflow obstruction due to benign prostate hyperplasia (BPH) is thought to be one of the major causes of LUTS.[1,2] It is postulated that vascular problems such as pelvic atherosclerosis and endothelial dysfunction in the elderly male can cause bladder dysfunction and play a role in LUTS pathogenesis.[3] ED is another pathology that increases with advancing age. ED etiology is multifactorial and has been shown to be associated with many risk factors such as hypertension, cardiac disease, aging, obesity, dyslipidemia, diabetes mellitus, smoking and vascular pathologies.[4] Studies have shown a BPH prevalence of 56% and ED prevalence of 40% in males over the age of 40 years.[5]

The metabolic syndrome (MS) is an endocrinopathy that starts with insulin resistance and continues with the addition of abdominal obesity, glucose intolerance or diabetes mellitus (DM), dyslipidemia, hypertension and coronary artery disease. It has been shown to be associated with many disorders including cardiovascular disease.[6] A study by the Metabolic Syndrome Association in Turkey in 2010 revealed an MS rate of 41.4% in males, increasing to 57% with age.[7] The aim of our study was to evaluate impact of MS on ED and LUTS.

MATERIALS AND METHODS

Study Subjects

We included a total of 107 patients who had presented at the urology outpatients with LUTS or ED complaints and at the endocrinology outpatients for DM between May 2012 and April 2013. The consent of the Uludag University School of Medicine Ethics Committee was obtained for the study. Study inclusion criteria were defined as sexually active patients aged 44 years and over who were mentally able to provide consent for the study. We excluded patients using α-blockers or 5 α-reductase inhibitors or medical treatment for ED, and those with a history of chronic obstructive pulmonary disease, urogenital system tumor, urogenital system surgery, neurogenic bladder, hypogonadism, liver or kidney failure, urethral stenosis, bladder stone, hyperactive bladder or chronic pancreatitis. Depressed patients and those using medication that affected libido and erection negatively were also excluded from the study.

The blood pressure, fasting blood sugar, serum lipid profile, triglyceride, total cholesterol, body mass index (BMI) and total prostate specific antigen (PSA) values were recorded.

Measurements

Fasting blood glucose, total cholesterol, triglycerides and HDL were studied by standard biochemical methods. Serum total testosterone and total PSA levels were measured by radioimmunoassay methods on the Advia Centaur® (Siemens Diagnostics, NJ, USA) auto analyzer. The Advia Centaur testosterone assay is a competitive immunoassay using direct chemiluminescent technology and the age-related reference intervals are 241-827 ng/dL for males aged 20-39 years and 141-703 ng/dL for males aged 40-89 years. The Advia Centaur PSA assay is a sandwich immunoassay utilizing two antibodies that bind to different sites on the PSA molecule and the suggested cut off level is 4 ng/mL.

All patients underwent uroflowmetry (maximum urinary flow rate [Qmax], mean urinary flow rate [Qmean], voiding volume and residual urine volume), prostate volume and residual urine volume measurement by the suprapubic method and determination of international prostate symptom score (IPSS), quality of life score, and international erectile function index (IIEF-5) values. Patients were grouped by IPSS scores as 0-7 mild, 8-19 moderate, 20-35 severe symptomatic and by IIEF-5 scores as 5-7 severe, 8-11 moderate, 12-16 mild to moderate and, 17-21 mild ED and 22-25 no ED. The MS diagnosis of the patients was made using the International Diabetes Federation (IDF) 2005 criteria as validated for the Turkish population (**Table 1**).[8]

Statistical Analysis

The Statistical Package for the Social Science (SPSS Inc, Chicago, Illinois, USA) version 15.0 was used for statistical analyses. Visual (histogram and probability graphs) and analytical (the Kolmogorov-Smirnov test) were used to determine conformance of the variables to normal distribution. Descriptive analysis results for normally distributed variables were presented as mean ± standard deviations. The relatiship between IPSS and IIEF-5 and various parameters was determined by the Spearman/Pearson correlation tests, Pearson chi-square test, student *t*-test and the Mann-Whitney *U* test as necessary. The independent effects of various parameters on the IPSS and IIEF-5 were evaluated using a multivariate linear regression model. Statistical significance was set at $P < .05$.

RESULTS

The mean age of the study patients was 57.11 ± 6.16 (range, 44-73) years. MS was present in 46.7% of the patients. There was a nonsignificant difference for age between patients with and without MS and the mean age was 57.94 ± 6.23 and 56.39 ± 6.05 years, respectively ($P = .19$). Taking all patients into account, 36 patients (33.6%) had hypertension, 59 (55.1%) had DM or disturbed fasting glucose, 46 (43%) had dyslipidemia and 37 (34.5%) had central obesity. These figures were 27 (54%) for hypertension, 37 (74%) for DM or disturbed fasting glucose, 28 (56%) for dyslipidemia and 23 (46%) for central obesity 23 in the MS group. The IPSS scores of the 107 patients (mean 7.33 ± 6.19) were distributed as 67 mild (62.6%), 36 (33.6%) moderate and 4 (3.8%) severe LUTS cases. As regards IIEF5 scores (mean 16.9 ± 7.05) there were 21 severe (19.6%), 13 moderate (12.1%), 13 mild to moderate (12.1%) 26 mild (24.4%) ED patients and 34 (31.8%) patients without ED (**Table 2**).

There was a significant negative correlation between the IPSS scores and IIEF-5 scores of the patients when the total patient group was

Table 1. The Metabolic Syndrome Diagnostic Criteria 2005 as suggested by The Society of Endocrinology and Metabolism of Turkey, Metabolic Syndrome Workgroup (Adapted from the International Diabetes Federation 2005 guide).

At least one of the following:
Diabetes mellitus or impaired glucose tolerance or insulin resistance
and
At least two of the following:
Hypertension (systolic blood pressure > 130 mmHg, diastolic blood pressure > 85 mmHg or use of antihypertensive drugs)
Dyslipidemia (triglyceride levels > 150 mg/dL or high density lipoprotein level male < 40 mg/dL, female < 50 mg/dL)
Abdominal obesity (body mass index > 30 kg/m^2 or waist circumference: male > 94 cm, female 80 cm)*

* There is no local data on International Diabetes Federation 2005 guidelines which are based on the recommended values for Europeans.

taken into account (P < .001, r = -0.42). There was no significant difference between the IPSS score of BPH patients with and without MS (P > .05) while the IIEF-5 scores were significantly lower in the MS group (P = .03). The IIEF-5 scores were also significantly lower in the DM group when compared with the non-diabetic group (P = .005). There was also no significant difference between the prostate volume, Qmax, voiding volume, quality of life score and serum testosterone levels (P > .05) (**Table 3**). We also found no correlation between the waist circumference measurements of the patients and the prostate volume, total PSA, IPSS, Qmax and IIEF-5 scores (P > .05). The mean age was significantly higher in the 21 patients in the severe ED group compared to those in the other 4 ED groups (P < .001). Multiple linear regression analysis revealed that only age and IIEF-5 scores had an effect on IPSS among factors such as age, MS, prostate volume, total testosterone, BMI and waist circumference. The IPSS increased 0.25 for each 1-year increase in age and the IPSS decreased 0.38 for each 1 unit increase of IIEF-5 (P < .001).

DISCUSSION

The MS is an endocrinopathy that starts with insulin resistance and continues with the addition of abdominal obesity, glucose intolerance or DM, dyslipidemia, hypertension and coronary artery disease.[6] Several studies have demonstrated a relationship between MS and voiding symptoms.[9,10] Ozden and colleagues have demon strated higher prostate growth rates in BPH patients with MS.[10] There are 4 serious hypotheses indicating a common pathogenesis for LUTS and ED. The decreased nitric oxide synthesis with aging, the increased sympathetic activity following hypertension, obesity and hyperinsulinemia in MS, the decreased smooth muscle relaxation following the activation of the alpha adrenergic mediator rho-kinase and the decreased blood flow to the bladder, prostate and penis following pelvic atherosclerosis indicate that the same pathophysiological mechanisms are active in the emergence of LUTS and ED.[11]

This is the reason phosphodiesterase type-5 enzyme inhibitors are added to α-blockers in the current treatment of LUTS due to BPH.

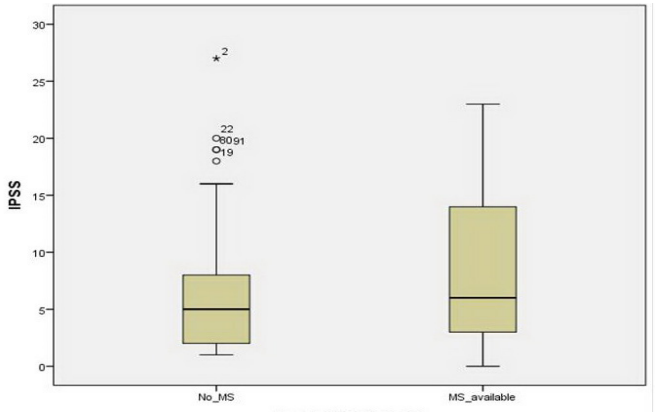

Figure 1. The mean International Prostate Symptom Score (IPSS) of the patients in both groups.

Lee and colleagues found a positive correlation between waist circumference and the prostate volume, PSA and IPSS values and reported that increased waist circumference made urination more difficult.[12] However, there was no difference regarding IPSS and quality of life scores between our groups with and without MS. Aktaş and colleagues also found no effect on LUTS in the presence of MS while ED increases significantly.[13] There was a significant correlation between IPSS and IIEF-5 scores as well in our study when the total patient group was taken into account. Demir and colleagues studied 190 patients with a mean age of 59.7 years and found that obesity, increased fasting blood sugar and hypertension had an effect on the development of severe (IPSS 20-35) LUTS and that all these factors could play a role in ED pathogenesis.[14]

Another study found a relationship between MS and prostate enlargement rate but no significant difference regarding IPSS scores between patients with and without MS.[10] It is still debated whether obesity is a risk factor for LUTS by itself. Some studies have shown increased LUTS rates due to BPH in obese males.[15,16] However, another study reported no relationship between anthropometric values and BPH.[17]

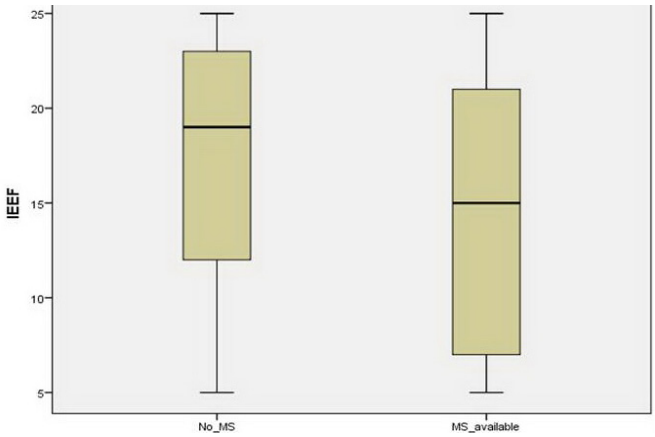

Figure 2. The mean International Index of Erectile Function-5 (IIEF) of the patients in both groups.

Table 2. The distribution of IPSS and IIEF-5 scores in both study groups.*

Variables	Groups			
IPSS Severity	With MS (n =50)	Without MS (n=57)	Total	*P* Value
Mild	30 (44.8)	37 (55.2)	67 (100)	.87
Moderate	18 (50)	18 (50)	36 (100)	
Severe	2 (50)	2 (50)	4 (100)	
Total	50	57	107	
ED Severity				
No ED	10 (29.4)	24 (70.6)	34 (100)	.08
Mild	14 (53.8)	12 (46.2)	26 (100)	
Mild to moderate	5 (38.5)	8 (61.5)	13 (100)	
Moderate	8 (61.5)	5 (38.5)	13 (100)	
Severe	13 (61.9)	8 (38.1)	21 (100)	
Total	50	57	107	

Abbreviations: MS, metabolic syndrome, IPSS: international prostate symptom score; IIEF, international index of erectile function; ED, erectile dysfunction.
* Data are presented as no. (%).

It is widely accepted that DM causes bladder dysfunction through the functional parasympathetic route due to autonomic neuropathy. Decreased detrusor function leads to a further decrease in Qmax and the bladder outflow obstruction causes increased post voiding residual urine volume.[18] We also found significantly higher voiding volume and residual urine values with uroflowmetry in our diabetic patients. Abnormal fasting blood sugar is one of the diagnostic criteria of MS. However, it was not correlated with the presence of LUTS in our study. The reason may be that the actual fasting blood sugar does not enable making a diagnosis for diabetes mellitus and it would be low in patients receiving diabetes mellitus treatment. This study was a joint study between the urology and endocrinology clinics. Patients who were on medical treatment or had undergone surgery for lower urinary system symptoms or a diagnosis of ED were excluded from the study, decreasing the mean age of BPH patients.

Some limitations of our study were the relatively low number of patients, the large number of diabetics (55.1%) as this was a joint study with the Endocrine Department, and the resultant slightly high rate of MS patients. However, we did not find a significant difference between the IPSS scores of the diabetic and nondiabetic groups and the groups with and without MS despite these limitations. Christian and colleagues failed to find any correlation between LUTS and MS in a wide-ranging study on 2371 males and 731 females.[19] As regards ED, Jun Ho and colleagues found IPSS and IIEF-5 scores to be 9 and 19 respectively with a significant correlation between the two values in their study on 2564 patients with a mean age of 49 years.[20] We found the IPSS and IIEF-5 scores of our patients to be 7.33 and 16.9, respectively, with a significant correlation between them. There was also a significant decrease in IIEF-5 scores in the MS group. Weinberg and colleagues have shown that poor glycemic control, disturbed insulin sensitivity and MS are found together with ED.[21]

Table 3. Demographic and clinical characteristics of study patients.

Variables	With MS (n = 50)	Without MS (n = 57)	*P* Value
Age (years)	57.94 ± 6.23	56.39 ± 6.05	.19
IPSS	8.10 ± 6.64	6.65 ± 5.74	.37
IIEF	14.52 ± 7.14	17.42 ± 6.75	.03
Fasting blood glucose (mg/dL)	166.90 ± 86.36	132.61 ± 86.79	< .001
Total cholesterol (mg/dL)	201.50 ± 39.89	188.37 ± 51.14	.26
Triglycerides (mg/dL)	179.94 ± 80.88	128.80 ± 71.83	< .001
HDL (mg/dL)	43.88 ± 8.61	44.11 ± 13.59	.70
Total testosterone (ng/mL)	337.22 ± 108.96	346.52 ± 151.08	.49
Total PSA (ng/mL)	1.71 ± 1.08	1.09 ± 0.97	.25
Prostate volume (mL)	41.78 ± 51.35	39.33 ± 23.46	.81
Qmax (mL/s)	14.96 ± 9.38	13.70 ± 10.07	.54
BMI (kg/m^2)	29.98 ± 3.54	27.62 ± 3.44	.001
Waist circumference (cm)	104.76 ± 8.80	96.83 ± 9.45	< .001
Quality of life	2.26 ± 1.72	2.04 ± 1.69	.52

Abbreviations: MS, metabolic syndrome; IPSS, international prostate symptom score; IIEF, international index of erectile function; PSA, prostate specific antigen; Qmax, maximum urinary flow rate; BMI, body mass index; HDL, high density lipoprotein.

CONCLUSION

In conclusion, we found a significant correlation between increasing age and LUTS and ED. However, we found that MS did not significantly affect LUTS due to BPH while contributing significantly to ED. We believe that patients who present with ED complaints should be evaluated for MS.

CONFLICT OF INTEREST

None declared.

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