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The relationships between metabolic syndrome, erectile dysfunction and lower urinary tract symptoms associated with benign prostatic hyperplasia

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ABSTRACT

Objective: To determine the relationship between erectile dysfunction and metabolic syndrome (MetS) in patients with benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS).

Material and methods: Seventy-eight patients who were admitted to our outpatient clinic because of BPH-related LUTS over 40 years of age were included in the study. Patients with LUTS and erectile dysfunction (ED) were evaluated by International Prostate Symptom Score (IPSS) and International Index of Erectile Function-5 (IIEF-5) forms. The National Cholesterol Education Program Adult Treatment Panel III criteria was used for the diagnosis of MetS. LUTS were classified as mild, moderate, and severe according to IPSS and ED was classified as mild- moderate, moderate, and severe according to the IIEF-5. For the evaluation of data, descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, and maximum) and also for the comparison of the variables with non-normal distribution in 3 or more than 3 groups Student's t test, Mann-Whitney U, ANOVA, chi-square, Fisher Exact tests, and Pearson correlation analysis were used. P<0.05 was accepted as the level of statistical significance.

Results: Mean age of the patients included in the study was 61.83±9.15. In 34.6% of the patients with MetS, 70.5% of the patients with ED and 37.2% of the patients with severe LUTS were determined. There were no significant differences between the mean age of patients with and without metabolic syndrome (p>0.05). There was a positive correlation with age and severity of LUTS but this relationship was not found to be statistically significant (p>0.05). Mean age of the patients with ED was significantly higher than those without (p<0.001). A statistically significant relationship was not observed between the mean IPSS scores and the severity of LUTS with Mets. However, we observed a weakly positive correlation between triglyceride levels and IPSS. Mean IIEF-5 scores of the patients with MetS were significantly lower than those of the patients without MetS. Severity of ED in the patients with MetS was significantly higher than patients without MetS. The percentage of ED in patients with severe LUTS was found to be statistically higher than other patients with mild, and moderate LUTS. In addition, we found a low degree of negative correlation between IPSS and IIEF-5 scores.

Conclusion: In patients with LUTS as a consequence of BPH, when severity of symptoms increases, frequency of MetS increases proportionally and severe ED is observed much more frequently.

Keywords: Erectile dysfunction; lower urinary tract symptoms; metabolic syndrome.

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Introduction

Erectile dysfunction (ED) has been defined as inability of a man to achieve, and/or sustain penile rigidity sufficient for a sexual performance. With aging, as a known fact, prevalences of lower urinary tract symptoms (LUTS), and ED increase in male population which climb to 31.2, and 52.1%, respectively with resultant decrease in quality of life of the patients.^[1-3] Increase in prevalence has been suggested to be related to multifactorial conditions secondary to the aging

process including metabolic syndrome (MetS), diabetes, and hypogonadism. In population-based studies, a common pathophysiological basis for both LUTS, and ED has been reported. Metabolic syndrome (MetS) is an accumulation of metabolic risk factors which accelerates the development of atherosclerotic disease which shares the common genetic, and environmental factors with MetS. Its prevalence increases markedly with aging, and it is seen more frequently over age of 50. LUTS associated with benign prostatic hyperplasia adversely effects

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patient's routine daily life, and hence quality of life. BPH can be seen concurrently with mostly cardiovascular diseases, MetS, and ED which increases in prevalence with age.

The objective of this study, is to determine the correlation between patients with LUTS due to benign prostatic hyperplasia, ED, and MetS.

Material and methods

A total of 78 male patients aged over 40 who consulted to urology polyclinics in Istanbul, Turkey because of LUTS were included in the study. Before enrollment into the study, the patients were informed in detail about the investigation, and their written consent forms were obtained. Patients who received any treatment for LUTS, and ED, those with genital deformities, psychological disorders, major pelvic surgery which could be associated with erectile dysfunction, and those with diseases apart from BPH which led to LUTS were not included in the study. All patients were evaluated with a detailed anamnesis, physical, and rectal examination. Height, waist circumference (cm), weight (kg), arterial blood pressure (ABP) of the patients were measured. Waist circumferences were measured at the level of umbilicus, and over the iliac wing. All patients were subjected to hemaatological tests, complete urinalysis, and analyses of fasting blood sugar, urea, creatinine, lipid profile, and prostate- specific antigen (PSA).

International Prostate Symptom Score (IPPS) forms were completed by study participants so as to evaluate, BPH-realted LUTS. IPSS scores indicate mild (0-7 pts), moderate (8-19 pts), and severely (>19 pts) symptomatic groups. In our study, mild, and moderate groups were combined as a mild-moderate symptomatic group. Thus we had two groups as mild-moderate, and severely symptomatic groups. International Erectile Dysfunction Index-5 (IIEF-5) form was used to evaluate erectile function. Cases with IIEF-5 scores between 6-25 was considered as ED (+) while those with IIEF scores between 26-30 were considered as ED (-) group. [4] Diagnosis of metabolic syndrome (MetS) was made based on the diagnostic criteria of The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III). Positivity of any of the following 3 or more than 3 criteria were required to make a diagnosis of MetS;

Waist circumference: Men >102 cm

- Fasting blood triglyceride level ≥150 mg/dL
- HDL- cholesterol: Men <40 mg/dL
- Fasting blood glucose ≥110 mg/dL
- Blood pressure ≥135/85 mmHg

In patients diagnosed as metabolic syndrome, the correlation between LUTS, and ED was investigated. Besides, the correlations between LUTS, and ED were evaluated separately.

Statistical analysis

For statistical evaluation Student's t test, Mann-Whitney U, ANOVA, Chi-square, Fisher Exact tests, and Pearson correlation analysis were used. P<0.05 was accepted as the level of statistical significance.

Results

A total of 78 patients with a mean age of 61.83±9.15 (range, 45 and 84 years) years were included in the study. Physical characteristics, and laboratory data of the patients are shown in Table 1. When patients' LUTS were classified according to IPSS, mild-moderate, and severe LUTS were detected in 62.8, and 37.2% of the patients, respectively. A statistically insignificant increase in the severity of LUTS in parallel with aging was detected (p>0.05). In 70.5% the patients ED was detected. The percentages of the patients with ED were revealed as; mild (21.8%), mild moderate (24.4%), moderate (9.0%) and severe degree (15.4%), respectively. Mean age of the patients with ED was significantly higher in patients with ED (p<0.001). Increase in the severity of ED was detected with age (Table 2, 3).

MetS was found in 27 (34.6%) patients. A difference was not disclosed between mean ages of the patients with and without metabolic syndrome. (p>0.05). A significant difference was not found between MetS, and mean IPSS values, (p>0.05), while mean IIEF scores were lower than those without MetS (p<0.05).

According to presence of LUTS, MetS was detected in 28.6% of mild-moderate, in 48.3% of severe, in 17.3% of ED (-), and 43.8% of ED (+) patients respectively. As the number of MetS positive criteria increased, severity of LUTS, and ED enhanced (Table 4).

Diagnostic criteria of metabolic syndrome were evaluated between themselves and according to the severity of each lower urinary tract symptom. Apart from triglyceride levels, none of the criteria was significantly correlated with IPSS values. A weakly positive correlation was found between triglyceride levels, and IPSS values (r=0.298, p<0.01).

A weakly negative correlation was found between age, and IIEF scores (r=-0.377, p<0.001). IIEF scores decreased with aging. A correlation was not found between diagnostic criteria of MetS, and IIEF scores. A weak correlation was detected between IIEF, and IPSS scores (r=-0.419, p<0.001). IPSS scores increased as IIEF scores decreased. The incidence rates of ED among mild, moderate, and severe LUTS groups were 40, 61.5, and 93.1%, respectively. Incidence of ED increased significantly in parallel with the severity of LUTS (p<0.005). Rates of ED in mild-moderate, and severe cases with LUTS were 57.1, and 93.1%, respectively (Table 5). In all cases, overall incidence of ED was

Table 1. Physical characteristics and some laboratory parametres of the patients		
	Mean±SD (range)	
Age (year)	61.83±9.15 (45-84)	
Height (cm)	171.08±6.19 (156-186)	
Weight (kg)	78.64±10.60 (50-105)	
WC (cm)	98.88±8.94 (79-126)	
Diastolic BP (mmHg)	84.17±12.49 (60-120)	
Systolic BP (mmHg)	127.11±18.19 (100-180)	
Cholesterol	198.95±26.57 (163-308)	
LDL (mg/dL)	131.37±24.96 (68-216)	
Triglyceride (mg/dL)	129.73±72.32 (23-590)	
HDL (mg/dL)	41.39±9.38 (24.3-78)	
FBG (mg/dL)	106.86±12.3 (73-248)	
SD: standard deviation; WC: waist circumference; ABP: arterial blood pressure; FBG: fasting blood glucose; LDL: low-density lipoprotein; HDL: high-density lipoprotein		

Table 2. Distribution of various degrees of ED among age groups			
	n=78 (%)	Mean age±SD	p
ED (-)	23 (29.5)	56.74±7.90	.001
ED (+)	55 (70.5)	63.96 ± 8.85	
Mild	17 (21.8)	63.35 ± 7.52	
Mild-moderate	19 (24.4)	62.26± 9.55	.012
Moderate	7 (9.0)	64.57±9.02	
Severe	12 (15.4)	67.17±9.59	
ED: erectile dysfunction; SD: standard deviation			

70.5%, while in cases with MetS it was 85.2%. ED was seen significantly more frequently in patients with MetS when compared with those without (p<0.05) (Table 6).

Discussion

Erectile dysfunction, and LUTS are frequently seen complaints in advanced age, and limited information which will explain the relationship between these two conditions exists. [2,5,6] Advanced age is an important factor in the concomitancy between LUTS, and ED, however some studies have demonstrated an association between BPH-related LUTS, and ED independent from advanced age. [7,8]

A multifactorial etiology was proposed for these complaints, and innervation of lower urinary system, and alterations in neuroregulatory factors such as nitric oxide, and RhoA kinase have been blamed. Besides apart from aging, comorbidities ef-

Table 3. Distribution of various degrees of severity of ED, and LUTS among age groups				
				Mild-
	ED (+)	ED (-)	Severe LUTS	Moderate LUTS
40-49	1 (20)	4 (80)	0 (0)	5 (100)
50-59	15 (55.6)	12 (44.4)	10 (37)	17(63)
60-69	24 (82.8)	5 (17.2)	11 (37.8)	18 (62.2)
70+	15 (88.2)	2 (11.8)	8 (47)	9 (53)
FD: erect	FD: erectile dysfunction: LUTS: lower urinary tract symptoms			

Table 4. Mean IPSS, and IIEF-5 scores in cases with and without MetS			
	MetS (+)	MetS (-)	
	Mean±SD	Mean±SD	p
IPSS	17.37±7.04	14.39±7.08	.081
IIEF-5	13.44±6.62	18.20±6.26	.003
MetS: metabolic syndrome; IPSS: International Prostate Symptom Score;			
IIEF: International Erectile Dysfunction Index-5; SD: standard deviation			

fective on these neuroregulatory systems such as hypogonadism, diabetes, and MetS can be also held responsible for the emergence of these complaints. Favourable effects of prevalently used pharmacological agents on the above-mentioned neuronal pathways, reflect the significance of this neuronal pathway.^[8]

Metabolic syndrome is a multifactorial disease related to insulin resistance whose mechanism is not fully known.^[9] Its incidence in patients older than 70 years of age, and 20-29 years are 42, and 6.7%, respectively.^[10]

A significant correlation has been demonstrated between metabolic syndrome components, annual increase in prostate volume, and LUTS.[11] In an experimental animal study, it was demonstrated that prolonged exposure of neuronal cells to hyperglycemia results in apoptosis of neuronal cells, and eventually exerts significant effects on parasympathetic system with resultant autonomic hyperactivity which might contribute to the development of LUTS.[12] MetS with these pathological effects on these neuroregulatory pathways described for the lower urinary system, can lead to impairment of urine storage, and also voiding, erectile, and ejaculatory dysfunction.[8] In our study, MetS was detected in 34.6% of our patient population. Rates of MetS in our patients with severe LUTS, and ED were found to be 48.8, and 43.8%, respectively. In our study, MetS' rates of patients with severe LUTS and ED were compatible with literature findings and it supports the hypothesis, which asserts that the above mentioned symptoms may develop via similar pathways.

Table 5. Distribution of cases with ED among LUTS				
groups	S			
		ED (-)	ED (+)	
		23 (%)	55 (%)	$\chi^{2}(\mathbf{p})$
LUTS	Mild	6 (60.0)	4 (40.0)	
	Moderate	15 (38.5)	24 (61.5)	
	Severe	2 (6.9)	27 (93.1)	13.10 (0.001)
LUTS	Mild+ Moderate	21 (42.9)	28 (57.1)	
	Severe	2 (6.9)	27 (93.1)	11.33 (0.001)
ED: Erectile dysfunction; LUTS: Lower urinary tract symptoma				

Table 6. Distribution of LUTS, and severity of ED in patients with and without MetS			
	MetS (-)	MetS (+)	
	n (%)	n (%)	
Mild LUTS	8 (15.7)	2 (7.4)	
Moderate LUTS	28 (54.9)	11 (40.7)	
Severe LUTS	15 (29.4)	14 (51.9)	
$\chi^{2}(p)$		4.04 (0.132)	
ED (-)	19.(37.3)	4 (14.8)	
Mild ED (+)	12 (23.5)	5 (18.5)	
Mild-moderate ED (+)	12 (23.5)	7 (25.9)	
Moderate ED (+)	4 (7.8)	3.(11.1)	
Severe ED (+)	4.(7.8)	8.(29.6)	
$\chi^{2}(p)$	4.27.	0.039	
MetS: metabolic syndrome; LUTS: lower urinary tract symptoms; ED: erectile dysfunction			

Erectile dysfunction Prevalence Group in Turkey revealed overall prevalence of ED in Turkish hypertensive patients as 64.7 percent.^[13] In our study, we also detected similar rate (70.5%) of ED with overall prevalence.

Endothelial dysfunction which occurs in metabolic syndrome related to various etiological factors is another factor in the development of ED. In a study where endothelial dysfunction, and ED were evaluated, as an indicator of impaired endothelial function, proinflammatory cytokines were detected at a higher rate in obese men, relative to non-obese men. Also CRP levels were higher in male patients with ED compared with those without. [14] Bal et al.[15] found frequency of MetS as 39.9%, and ED as 79.8% among 393 patients aged between 40, and 70 years. In their study, a significant correlation was detected between waist circumference, fasting blood glucose, blood pressure, and ED. However in our study a significant correlation was not detected between rates of ED, increased trigyceride levels, and lower

HDL values which are etiological factors for ED. Besides a significant correlation was not observed between waist circumference, and IIEF scores.

Esposito et al. [16] reported increase in the incidence of ED in line with the increase in the components of MetS. Therefore, they feverently recommended a healthy life style so as to decrease the incidence of MetS with resultant improvement in ED. In our study ED was observed more frequently among cases with MetS relative to those without (85.2 vs. 62.7%). In compliance with the above-mentioned study, in parallel with increased number of diagnostic criteria, IIEF scores decreased significantly in our study. In the group without ED, 17.3% of the patients had ≥3 diagnostic criteria of MetS, however 43.8% of the patients with ED had ≥3 diagnostic criteria of MetS. Incidence of ED increases with increased number of diagnostic criteria of MetS. In conclusion, also in our study significantly higher rates of ED were detected among cases with MetS.

Active LUTS treatment can exert an impact on ED. Sexual functions of the patients can decrease with administration of 5-alpha reductase inhibitors which are used in the treatment of LUTS. Besides transurethral prostate resection used for the treatment of BPH/LUTS can effect sexual function in various ways.[17] As the most important outcome of The Multi-National Survey of The Aging Male (MSAM-7) survey study performed on 12.815 men aged between 50-80 years living in Europa, and USA, it has been demonstrated that independent from other risk factors, LUTS is a serious risk factor for erectile dysfunction. [18] In a Turkish patient population with LUTS, compared with the mild LUTS, the incidence of ED was reported to be 4.4, and 6.2-fold higher in cases with severe LUTS.[13] According to MSAM-7 study, 83% of the patients with LUTS maintained their sexual functions, while 48.7% of them had a certain degree of ED, and in 10% of them complete loss of erectile dysfunction was detected. ED was found to be correlated with the severity of LUTS. Incidence of ED was reported in mild, moderate, and severe LUTS as 43, 66, and 83%, respectively. In separate analyses of each risk factors, frequency of ED was found to be increased in the presence of mild (1.9-fold), moderate (3.7-fold), and severe (7.6-fold) ED.[18] In a study by Demir et al.[19] a significant degree of concomitancy was detected between LUTS, and ED. They found 2.4-fold higher incidence of ED in patients with LUTS. In our study, ED was seen at a rate of 70.5% in overall study population, while incidence rates of ED were determined as 57.1% in mild-moderate, and 93.1% in severe LUTS. This finding is in compliance with the literature findings which demonstrated the incidence of ED increases in line with the severity of LUTS.

Still a significant correlation was found between IIEF, and IPSS scores. IPSS scores increase in parallel with decreases in IIEF scores.

In our study rates of severe LUTS differed between various age groups (49-50, 37%; 60-69, 37.8%; and >70, 48%). Though severity of LUTS increases with age, because of limited number of our cases, a significant correlation was not detected between age of the patients, and IPSS scores.

On the contrary, Demir et al.^[19] could not find a significant association between LUTS, hypertension, diabetes mellitus, and abdominal obesity. In their study significantly higher frequency of lower urinary tract symptoms were found in cases with hypertriglyceridemia (28.8% vs. 53.8%).

Temml et al.^[20] investigated the role of MetS in 2.371 men, and detected MetS in 33.8% of the cases. However in their study IPSS score of >7 was not correlated significantly with MetS. In our study a significant difference was not found between cases with and without MetS as for the presence of LUTS. Cases with severe LUTS constituted 37.2% of our study population. In cases without MetS severe LUTS was seen at a relatively lower rate (29.4%) when compared with cases with MetS (51.9%), without any statistically significant intergroup difference.

As the number of positive criteria of metabolic syndrome increases, incidence of LUTS, and ED also increases. In our study 28.6% of the patients with mild-moderate LUTS, and 48.3% of those with severe LUTS had ≥3 diagnostic criteria for MetS.

In conclusion, MetS is seen in increasing frequency in patients with severe LUTS, when compared with mild-moderate LUTS both associated with BPH. ED is more frequently seen in patients with severe ED. Despite our limited number of cases, we think that our findings can be evaluated in favour of a presence of a correlation between MetS, and LUTS. Large scale prospective studies should be performed on this issue.

Ethics Committee Approval: Our study was made in the urology department of our hospital between March 2009 and October 2009. Ethics committees did not work effectively and actively in many parts of Turkey as well as in our hospital at that time. Furthermore, this study was accepted as a urology specialist thesis by the Ministry of Health.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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