Updated Definition, Prevalence and Association between Metabolic Syndrome, Erectile Dysfunction, LUTS and BPH

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ABSTRACT

Increasing evidence recently has pointed toward a relationship between the presence of metabolic syndrome (MetS), lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) and erectile dysfunction (ED). This relationship has been supported by epidemiological findings, their mechanisms of interaction and possible pathophysiological links between these conditions. This paper provides a discussion of the updated definitions, the prevalence and the association between MetS, ED, LUTS and BPH. *Key words:* metabolic syndrome, lower urinary tract symptoms, benign prostatic hyperplasia, erectile dysfunction

INTRODUCTION

Conditions, such as metabolic syndrome (MetS), lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) and erectile dysfunction (ED), which occur with relatively high frequency in aging men, have received a great deal of attention over the past decade [1-5]. These are common disorders, where the prevalence increases with advancing age, are frequently co-associated in the same aging male group and contribute significantly to reducing their overall quality of life. Thus, at a time when life expectancy is rising steadily in our country, an increasing number of aging men will be affected by one or more of these conditions and a larger patient reservoir will present with these associated symptoms during daily urology practice. As an up-to-date urologist, we can not take care of our ED and BPH patients without understanding the relationship and possibly impact of MetS on these two disease entities.

DEFINITION OF METABOLIC SYNDROME (METS), ERECTILE DYSFUNCTION (ED), LOWER URINARY TRACT SYMPTOMS (LUTS) AND BENIGN PROSTATIC HYPERPLASIA (BPH)

MetS: the simultaneous occurrence of at least three out of five risk factors including abdominal obesity (waist circumference >102 cm), hypertension (blood pressure >130/85 mmHg or taking antihypertensive medication), hyperglycemia (fasting blood glucose ≥10 mg/dL), hypertriglyceridemia (serum triglyceride levels ≥150 mg/dL) and reduced levels of HDL-C (<40 mg/dL) [6].

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ED: a consistent inability to achieve or maintain a penile erection of sufficient quality to perform satisfactory sexual intercourse [7].

LUTS: According to the International Continence Society (ICS), LUTS can be classified into 3 major categories [8]:

Storage symptoms: include increased daytime frequency, nocturia, urgency and various types of urinary incontinence. Frequency is a subjective complaint where the patient believes that he/she voids too often during the day. Nocturia is a complaint that the individual has to get out of bed one or more times at night to void. Urinary incontinence is any involuntary leakage of urine.

Voiding symptoms: include a slow stream, splitting or spraying, an intermittent stream of urine, hesitancy (difficulty in starting) and straining to initiate, maintain or improve the urine stream.

Postmicturition symptoms: are experienced immediately after micturition in men, usually after leaving the toilet and include a feeling of incomplete emptying and terminal dribble, a prolonged final part of micturition.

Benign prostatic hyperplasia (BPH): the term reserved for the typical histological pattern that defines the disease.

Benign prostatic enlargement (BPE): prostatic enlargement because of histological BPH. In the absence of histology, the term prostatic enlargement should be used.

Benign prostatic obstruction (BPO): a form of BOO and it may be diagnosed when the cause of BOO is known to be BPE because of BPH.

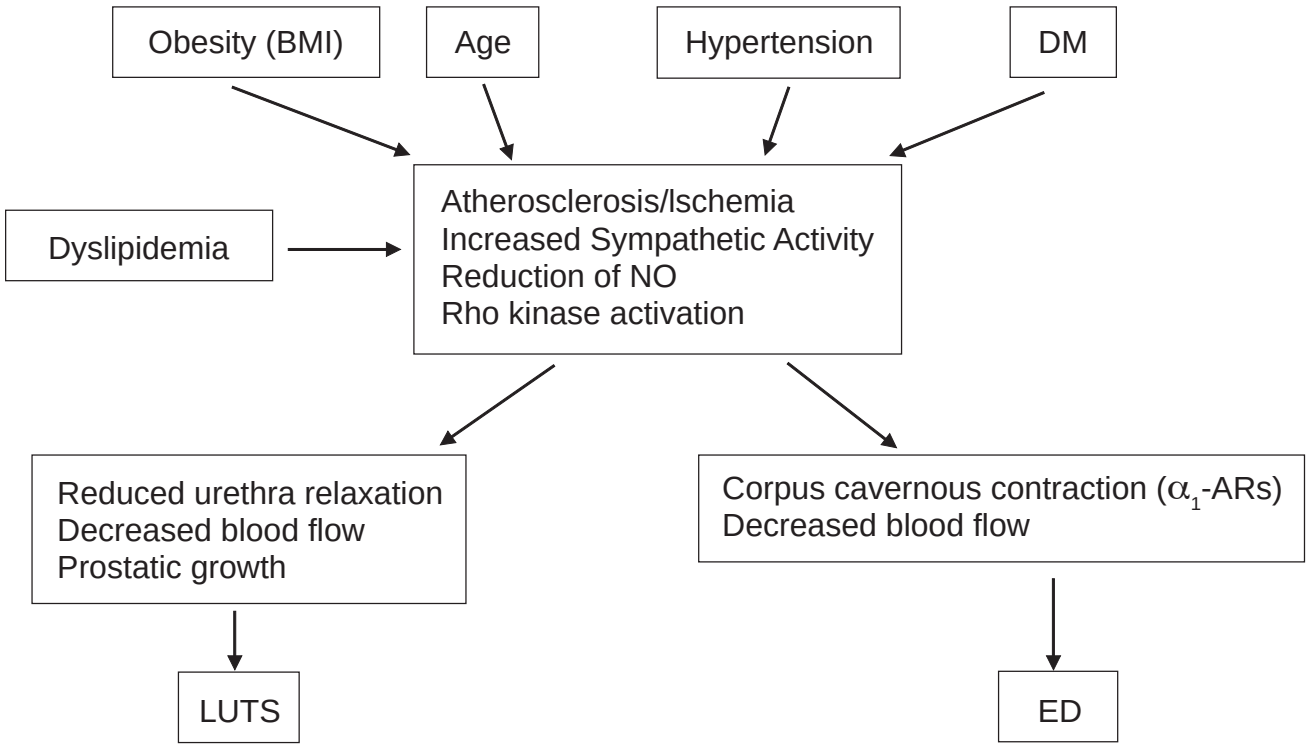
Bladder outlet obstruction (BOO): the generic term for obstruction during voiding, which is characterised by increased detrusor pressure and reduced urine flow rate.

LUTS can be associated with either bladder or prostate conditions in men. It is important for the clinician to carefully evaluate male patients presenting with LUTS to determine the root of the problem.

AGE, THE COMMON FACTOR BETWEEN METS, LUTS/BPH AND ED

The rate of MetS increases with age. In a cross-sectional study of Greek adults (4153 participants older than 18 years), the age-standardized prevalence of the MetS was 24.2% in men and 22.8% in women [2]. The prevalence increased with age in both sexes, with MetS being present in 4.8% of participants aged 19-29 years and 43% of participants aged over 70 years old. There was a 14.7-fold increase in the odds ratio for having MetS in the age group >70 years old compared with 19-29 years old.

BPH is an age-related and progressive disease. As the prevalence of histological hyperplasia of the prostate increases with advancing age, so does the incidence of moderate to severe LUTS. The prevalence of BPH increases progressively from 8% between 40 and 49



years to 82% between 80 and 89 years. A population based study has revealed that 26% of men aged 40-49 years have moderate to severe LUTS and this increases to 46% in men aged 70-79 years [9]. The severity of LUTS increased with time and age. There was a mean increase in the IPSS of 0.18 per year for men in their forties to 0.44 for men in their sixties [9].

Similarly, the prevalence of ED also increases with advancing age. Compared to men in their 40s, men in their 50s have a 2-fold increase risk of ED. Furthermore, men in their 60s have a 5-fold increase in risk [10]. Therefore, it is no surprise that many patients presenting with LUTS will also have ED and vice versa. This relationship has been built up in multiple studies demonstrating not only that patients with BPH and associated LUTS have ED, but also that the severity of LUTS corresponds with the severity of ED [4,5]. A large cross-sectional assessment of sexual function and LUTS was conducted in 3,230 men in Europe, Russia, the Middle East, Latin America and Asia. Multiple logistic regression confirmed that patients with severe LUTS were approximately twice as likely to experience ED (odds ratio [OR], 2.0), as well as reduced ejaculate (OR, 1.8). In addition, men with severe LUTS were 6 times more likely to complain of pain and discomfort on ejaculation [5]. This association between LUTS and ED persisted when the results were controlled for age and other co-morbidities [10].

THE LINK BETWEEN METS, LUTS/BPH AND ED

Patients with MetS are prone to endothelial dysfunction and autonomic hyperactivity, which is considered the initial inciting process of the metabolic risk factors inducing ED and LUTS due to BPH. The mechanisms whereby MetS is linked to BPH and ED seem to be related to a decrease in NO/NOS levels in the prostate and penile smooth muscle, to Rho-kinase activation, to autonomic hyperactivity and to pelvic atherosclerosis [10]. The physiological role of NO/NOS is related to the relaxation of smooth muscle. It has been reported NO/NOS levels are decreased in the prostate of BPH patients and in the penis of ED patients. NO as a donor induces smooth muscle relaxation in the penis and prostate. In contrast, activation of Rho-kinase induces smooth muscle contraction [10]. Autonomic hyperactivity and pelvic atherosclerosis will decrease blood flow in the pelvic organs and induce structural and functional derangements. Taken together, these factors will lead to ED and LUTS related to BPH.

Bal et al reported that among 393 patients seen at a urology clinic, 157 (39.9%) had MetS and of these 124 with MetS (79%) and 146 without MetS (61.9%) also had ED [1]. The presence of MetS was significantly associated with ED among patients aged 40 to 49 years, but this relationship was not obvious in older age groups. An older age itself is a strong risk factor for ED. Fasting blood glucose levels, hypertension and obesity are the most significant risk factors predicting ED. On the other hand, patients with ED and a BMI less than 25 have been shown to have a 2-fold increase in their risk of MetS. Therefore, ED may be a predictor of MetS [11].

BPH patients with MetS have been demonstrated to show higher annual prostate growth than BPH patients without Met S [12]. Hypertension, one of the components of MetS, has been linked to increased sympathetic tone. Sympathetic dysfunction appears to have a mitogenic effect on the prostate as well as resulting in increased smooth muscle tone in the prostate. Previous studies have revealed that autonomic nervous system overactivity in men with LUTS is secondary to BPH [10]. Therefore, BPH may represent another disease in the compendium of ailments caused by the global sympathetic bias that emerges with aging. Furthermore, high insulin levels have been linked to increased growth of the prostate.

A PHARMACOLOGICAL LINK BETWEEN METS, LUTS/BPH AND ED

Increased sympathetic activity may be causally involved in hypertension, BPH/LUTS and ED. On the basis of pharmacological and clinical evidence, it has been shown that α-adrenergic blockers have therapeutic benefits on ED and LUTS secondary to BPH as well as hypertension. However, some evidence also suggests that there are adverse effects of α-adrenergic blockers on sexual function [13]. Furthermore, phosphodiesterase Type 5 Inhibitors have been suggested to be effective as a treatment for ED/BPH/LUTS. Although placebo-controlled studies are needed to confirm the impact of these drugs on these conditions, physicians are possibly in a position to manage these diseases simultaneously as the prevalence of MetS, BPH and ED increases with age [14].

CONCLUSIONS

MetS, LUTS due to BPH and ED are highly prevalent in the adult male population and have an adverse impact on the quality of life of men with these diseases compared to patients without these conditions. Survey and treatment of these conditions in urological clinics may be able to identify the potential risk patients and help to promote a healthy and happy life.

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