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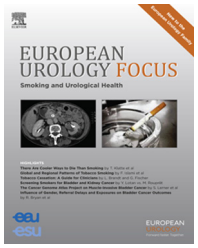

Review – Benign Prostatic Hyperplasia

Erectile Dysfunction and Lower Urinary Tract Symptoms

Cosimo De Nunzio [a,*], *Claus G. Roehrborn* [b], *Karl-Erik Andersson* [c], *Kevin T. McVary* [d]

[a] *Department of Urology, Sant'Andrea Hospital, "La Sapienza" University, Roma, Italy;* [b] *Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX, USA;* [c] *Institute of Clinical Medicine, Aarhus University, Aarhus, Denmark;* [d] *Southern Illinois University School of Medicine, Springfield, IL, USA*

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Abstract

Context: Lower urinary tract symptoms (LUTSs) and erectile dysfunction (ED) are substantial health concerns with a significant impact on the overall male quality of life.
Objective: To evaluate the available evidence of the association between LUTSs and ED in patients with benign prostatic hyperplasia (BPH), and discuss possible clinical implications for the management of LUTS/BPH.
Evidence acquisition: A systematic review of the existing literature published between 1997 and June 2017 and available in the Medline, Scopus, and Web of Science databases was conducted using both the Medical Subject Heading (MeSH) and free-text protocols. The MeSH search was conducted by combining the following terms: "lower urinary tract symptoms," "LUTS," "benign prostatic hyperplasia," "BPH," "erectile dysfunction," "sexual dysfunction," "BPE," and "benign prostatic enlargement." The Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines were followed.
Evidence synthesis: Several community-based studies in different geographical areas have provided strong evidence of an age-independent association between LUTSs and ED. Several biological mechanisms have been proposed to explain this association, but further research is required to better understand the molecular pathways involved. It is necessary to evaluate the possible impact of the metabolic syndrome treatment on LUTS/ED management. Considering the possible relationship between LUTSs and ED, their impact on the quality of life, and the possible adverse effects associated with LUTS medical treatment, clinicians should always evaluate ED in patients with LUTSs and take the opportunity to evaluate patients reporting ED for LUTSs.
Conclusions: Data from the peer-reviewed literature suggest the existence of an association between LUTS/BPH and ED, although their casual relationship has not been established yet. Emerging data also suggest that pathophysiological mechanisms involved in the metabolic syndrome are key factors in both disorders. Considering the association, it is also recommended that men presenting with LUTSs or ED should be evaluated for both disorders. A better understanding of the molecular pathways behind this association may also help identify new possible targets and develop novel therapeutic approaches to manage LUTSs and ED.
Patient summary: In this manuscript, we report on all the available evidence linking erectile dysfunction and lower urinary tract symptoms. Our findings suggest the existence of a strong relationship between these two conditions. On the basis of these findings, we recommend that clinicians always explore both conditions in male patients presenting with either of symptoms.

* Corresponding author. Department of Urology, Sant'Andrea Hospital, "La Sapienza" University, Via di Grottarossa 1035-00189, Rome, Italy. Tel.: +390633777716; Fax: +390633775059.
E-mail address: cosimodenunzio@virgilio.it (C. De Nunzio).

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1. Introduction

Lower urinary tract symptoms (LUTSs) and erectile dysfunction (ED) are significant health concerns that will become even more serious in the next few years because of the increase in population aging. Moreover, both conditions have—a significant impact on male quality of life [1]. LUTSs, including voiding, storage, and postmicturition symptoms, are common in aging individuals and benign prostatic hyperplasia (BPH) is considered the primary cause in men over 50 yr [2]. Autopsy prevalence of histological BPH is approximately 8% in men in their 40s, 50% in those in their 50s, 70% in those in their 60s, and about 90% in the octogenarians [3].

ED, defined as persistent inability to achieve and maintain an erection sufficient for satisfactory sexual performance, is generally considered the result of para-aging factors [1,4]. In 1994, the Massachusetts Male Aging Study (MMAS) was the first population-based study to evaluate ED prevalence in aging men [5]. Its results showed an overall ED prevalence of 52%, with about 35% revealing moderate/severe ED [5]. Moreover, ED prevalence was age dependent, increasing from 5% for men in their 40s to 15% for those aged 70 yr. As well, several age-independent comorbidities such as diabetes, depression, hypertension, and heart disease were found to be significantly associated with ED prevalence. Based on these data, it was estimated that in 2025 ED will affect more than 200 million men worldwide [1,6].

Although the MMAS study did not evaluate LUTSs as a possible predictor variable for ED [5], since then several large-scale epidemiological studies in different populations have demonstrated a relationship between these two conditions in aging men, which is, however, independent of the effects of age or other comorbidities [1,6,7]. Although the molecular and pathological pathways potentially linking LUTSs and ED have not been clearly defined, the possible association has resulted in new possible approaches to the evaluation of both disorders and in the identification of new possible targets for their prevention and treatment [8,9]. Medical treatment of LUTS/BPH may also have a significant impact on erectile function [10–12]. In addition, specific drug interactions and the possibility that LUTS/BPH medical therapy may affect erectile function are also causes of concern in today's clinical practice [10–12].

The aim of our review is to provide an update on the association between LUTS/BPH and ED, with an analysis of the possible pathophysiological mechanisms that may be involved in this association. We will also discuss the potential implications of this evidence for LUTS/ED diagnosis and treatment, and suggest directions for future research.

2. Evidence acquisition

A systematic review of the literature published between 1997 and June 2017 was performed using both the Medical Subject Heading (MeSH) and free-text protocols as entries in Medline, Scopus, and Web of Science databases. The MeSH search was conducted by combining the following terms: "lower urinary tract symptoms," "LUTS," "benign prostatic hyperplasia," "BPH," "erectile dysfunction," "sexual dysfunction," "BPE," and "benign prostatic enlargement." The searches on Embase and Web of Science were conducted using only the free-text protocol, with the same key words. In addition; the references contained in the reference sections of the selected/retrieved publications were also added to the list. The use of the English language was not a specific parameter; however; only English-language publications were considered. Evidence was not limited to human data; data from animal studies were also included in this review. The title and abstract of each article were reviewed for their appropriateness and relevance with regard to the relationship between ED and LUTSs. In particular; we have selected articles focusing on the possible relationship between ED and LUTSs and addressing potential implications for treatment. In case of availability of more than one article sharing the same information; the most recently published one was used for this review. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines have been followed.

A flow chart showing the selection process is shown in Figure 1. The initial list of the selected papers was further enriched with titles suggested by a pool of international experts in the topic, who also acted as coauthors of the present review.

3. Evidence synthesis

3.1. *LUTSs and ED: epidemiological evidence*

Although the casual relationship between LUTSs and ED has not been established yet, several community-based studies conducted in different geographical areas (including Europe, Asia, and America) and with different tools for assessing ED and LUTSs have provided strong evidence of an age-independent association between these two disorders (Table 1).

The landmark study of their association was the Multi-National Survey of the Ageing Male-7 (MSAM-7), which was conducted in the USA and six European countries (France, Germany, Italy, the Netherlands, Spain, and the UK) on 12 815 men, representative of the population aged 50–80 yr in each country [7]. Patients were evaluated using the International Prostatic Symptom Score (IPSS), International Index of Erectile Function (IIEF), and Danish Prostate Symptom Score. The survey reported that most men aged >50 yr were sexually active but with a decrease in the number of sexual intercourse with LUTS severity (ranging from with 7.5 per month in men in their 60s to 3.2 per month in men in their 80s). ED was reported by almost 49% of the overall sample, and the IIEF score was strongly related to LUTS severity: in the cohort aged 50–59 yr, the mean IIEF was 22.3 in patients with no LUTS and 14.9 in patients with severe LUTS; in the cohort aged 60–69 yr, it was 19.2 and 12.4, respectively; and in the cohort aged 70–79 yr, it was 15.3 and 7.5, respectively. LUTS severity resulted in the

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