Diabetes and Benign Prostatic Hyperplasia: Emerging Clinical Connections

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Benign prostatic hyperplasia (BPH) and associated lower urinary tract symptoms (LUTS) are highly prevalent in older men and represent a substantial challenge to public health. Increasing epidemiologic evidence suggests that diabetes significantly increases the risks of BPH and LUTS. Plausible pathophysiologic mechanisms to potentially explain these associations include increased sympathetic tone, stimulation of prostate growth by insulin and related trophic factors, alterations in sex steroid hormone expression, and induction of systemic inflammation and oxidative stress. This article presents a comprehensive overview of the current understanding of clinical and epidemiologic research on diabetes and BPH/LUTS, describes hypothesized pathophysiologic mechanisms linking these conditions, and recommends future directions for research and clinical care.

Introduction

Benign prostatic hyperplasia (BPH), the most common benign neoplasm in American men, most often manifests clinically as the progressive development of lower urinary tract symptoms (LUTS). Prevalence estimates based on autopsy and clinical studies range from 25% in men ages 40 to 49 to more than 80% among men ages 70 to 79. In the United States in 2000, 4.5 million visits to physicians' offices for a primary diagnosis of BPH occurred, 87,400 BPH surgeries were performed on inpatients in nonfederal hospitals, and the direct costs of BPH treatment (excluding medications) totaled 1.3 billion dollars. Furthermore, it has been estimated that approximately 6.5 million men would be expected to meet the Agency for Health Care Policy and Research Diagnostic and Treatment Guidelines criteria for discussing treatment for BPH [1].

Despite its significant public health impact, much of the etiology and natural history of BPH remains to be elucidated. Previous causal models have focused primarily on sex steroid hormones (essential to normal prostate growth and development) and genetic susceptibility. Indeed, suppression of androgen-dependent prostate growth pathways (with orchiectomy, luteinizing hormone–releasing hormone agonists, or 5-α-reductase inhibitors) remains the only intervention proven to attenuate or arrest BPH progression.

However, accumulating evidence also indicates that diabetes mellitus, a chronic disorder of carbohydrate, fat, and protein metabolism, may increase the risk of BPH. Associations of BPH with diabetes—a modifiable risk factor of disease—suggest that BPH can be prevented or treated through modifications of metabolic pathways. Moreover, with the incidence of diabetes reaching epidemic proportions in the United States, a potential causal relationship of diabetes with BPH would have substantial implications for the health of the aging male population and underscores the need to further elucidate these processes. Herein, we review epidemiologic associations and clinical studies of diabetes with BPH and suggest a conceptual framework for planning future research and clinical care (Table 1).

Definitions of Benign Prostatic Hyperplasia and Lower Urinary Tract Symptoms in Clinical Research

Although several pathologies may potentially contribute to BPH and the generation of BPH-associated LUTS, there are two general mechanisms by which BPH may induce bladder outlet obstruction: static and dynamic. The static mechanism involves hyperplastic stromal and epithelial prostate growth, which, over time, compresses the prostatic urethra. The dynamic mechanism entails increased tone of prostate smooth muscle, which is mediated by the α-1-adrenergic receptor: stimulation of the α-1 receptors induces a contraction and corresponding reduction in urethral lumen diameter. Obstruction of the bladder outlet induces two pathological changes in the structure of the bladder that

Table 1. Studies on the association between diabetes and benign prostatic hyperplasia/lower urinary tract symptoms

Study	Study type	Country	Patients, *n*	BPH definition	Diabetes definition	DM and BPH findings
Van Den Eeden et al. [18]	Cohort	United States	591 (type 1 DM)	LUTS (AUASI)	DM complications, DM duration, HbA1c	No associations between DM complications, duration, HbA1c, and LUTS
Coyne et al. [31]	Cross-sectional	United States, United Kingdom, Sweden	14,141	LUTS defined as voiding + storage + postmicturition symptoms	Self-reported	DM percentage differences: LUTS, 20.5% vs no LUTS, 9.9% ($P < 0.001$)
Kok et al. [32]	Cohort	The Netherlands	1688	LUTS (IPSS)	Diabetes diagnosis	DM HR (age-adjusted), 1.10 (95% CI, 0.58–2.08)
Safarinejad [33]	Cross-sectional	Iran	8466	BPH defined as IPSS > 7 + Qmax < 15 + prostate volume > 30	Self-reported	DM OR (multiple variable-adjusted), 1.82 (95% CI, 1.28–2.21)
Park et al. [34]	Cross-sectional	Korea	348	LUTS (IPSS)	DM defined as fasting glucose (> 110 mg/dL)	DM HR (multiple variable-adjusted) 2.9, (95% CI, 1.76–4.82)
Sarma et al. [22•]	Cross-sectional	United States	2484	LUTS (AUASI), Qmax, prostate volume, PSA	Self-reported	DM OR (age-adjusted): LUTS: 1.42 (95% CI, 1.03–1.95) Prostate volume: 1.40 (95% CI, 0.86–2.28) Qmax: 1.04 (95% CI, 0.72–1.49) PSA: 1.20 (95% CI, 0.67–2.14)
Temml et al. [35]	Cross-sectional	Austria	2371	LUTS (IPSS)	DM defined as fasting glucose (> 100 mg/dL) or DM diagnosis	No association between DM and LUTS
Burke et al. [12••]	Cohort	United States	2115	LUTS (AUASI), Qmax, prostate volume, PSA	Self-reported	Median percentage change by DM: AUASI ($P = 0.04$) Qmax ($P = 0.06$) No difference in prostate volume or PSA by DM

AUASI—American Urological Association Symptom Index; BPH—benign prostatic hyperplasia; DAN-PSS—Danish Prostatic Symptom Score; DM—diabetes mellitus; DRE—digital rectal examination; HbA1c—hemoglobin A1C; HOMA—homeostatic model assessment; HR—hazard ratio; IPSS—International Prostate Symptom Score; LUTS—lower urinary tract symptoms; OR—odds ratio; PSA—prostate-specific antigen; PVR—postvoid residual; Qmax—maximal urinary flow rate; TRUS—transrectal ultrasound.

Table 1. Studies on the association between diabetes and benign prostatic hyperplasia/lower urinary tract symptoms (*Continued*)

Study	Study type	Country	Patients, *n*	BPH definition	Diabetes definition	DM and BPH findings
Parsons et al. [9•]	Cross-sectional	United States	422	Prostate volume	Fasting glucose (> 110 mg/dL); DM defined as elevated fasting glucose or history of insulin treatment	Fasting glucose OR, 2.98 (CI 95%, 1.70–5.23) DM OR, 2.25 (95% CI, 1.23–4.11)
Nandeesha et al. [8]	Case-control	India	50 BPH cases, 30 controls	BPH defined as abnormal DRE or TRUS and BPH surgery	Fasting glucose, fasting insulin, HOMA	Mean differences by BPH: No difference in fasting glucose by BPH Fasting insulin ($P < 0.001$) HOMA ($P < 0.001$)
Berger et al. [36]	Cross-sectional	Austria	28 DM, 24 BPH, 12 controls	LUTS (IPSS), Qmax, prostate volume, PSA, PVR	DM defined as fasting glucose (≥ 7.8 mmol/L)	Mean differences by DM vs control: LUTS ($P < 0.001$) Prostate volume ($P < 0.001$) PSA ($P = 0.005$) Qmax ($P < 0.001$) PVR ($P < 0.001$)
Hong et al. [37]	Cross-sectional	South Korea	641	BPH defined as IPSS > 8 + prostate volume > 25 + Qmax < 15	Self-reported	DM OR (multiple variable-adjusted), 1.42 (95% CI, 0.78–2.58)
Zucchetto et al. [38]	Case-control	Italy	1369 BPH cases, 1451 controls	BPH diagnosis	Self-reported	DM OR, 1.19 (95% CI, 0.90–1.59)
Bozlu et al. [39]	Case-control	Turkey	60 BPH/DM cases, 221 BPH controls	LUTS (IPSS), Qmax, prostate volume, PVR, PSA	Self-reported	Mean differences by DM: Qmax ($P < 0.001$) No difference in LUTS, prostate volume, PVR, or PSA
Yoshimura et al. [40]	Cross-sectional	Japan	4568	Nocturia	Self-reported	DM nocturia OR (multiple variable-adjusted), 1.70 (95% CI, 1.31–2.20)

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Table 1. Studies on the association between diabetes and benign prostatic hyperplasia/lower urinary tract symptoms (*Continued*)

Study	Study type	Country	Patients, *n*	BPH definition	Diabetes definition	DM and BPH findings
Joseph et al. [41]	Cross-sectional	United States	708	LUTS (AUASI)	Self-reported	DM LUTS OR, 2.01 (1.37–2.93) Obstructive LUTS OR, 1.54 (95% CI, 1.0–2.35) Irritable LUTS OR, 2.10 (95% CI, 1.44–3.07)
Dahle et al. [42]	Case-control	China	200 BPH cases, 302 controls	BPH surgery	Fasting insulin	BPH OR by quartiles of insulin (multiple variable-adjusted): 2 vs 1: 1.60 (95% CI, 0.87–2.94) 3 vs 1: 1.23 (95% CI, 0.67–2.25) 4 vs 1: 2.19 (95% CI, 1.18–4.05)
Hammarsten and Hogstedt [43]	Cross-sectional	Sweden	307	Prostate volume, estimated BPH growth	DM diagnosis, fasting insulin	Median differences in BPH growth rate: DM diagnosis ($P < 0.001$) Median differences by insulin: Prostate volume ($P = 0.012$) BPH growth rate ($P = 0.019$)
Koskimaki et al. [44]	Cross-sectional	Finland	1963	LUTS (DAN-PSS)	Self-reported	DM OR (age-adjusted), 1.5 (95% CI, 1.1–2.2)
Meigs et al. [17]	Cross-sectional	United States	1019	BPH defined as BPH diagnosis or LUTS and BPH surgery	Self-reported	DM OR (age-adjusted), 1.5 (95% CI, 0.8–2.7)
Prezioso et al. [45]	Cross-sectional	Italy	1033	LUTS (IPSS)	Self-reported	No association between DM and LUTS
Boon et al. [10]	Case-control	The Netherlands	32 LUTS/DM cases, 565 LUTS controls	LUTS (IPSS), Qmax, PVR, prostate volume	DM diagnosis	Mean differences by DM: Volume ($P = 0.046$) No difference in Qmax or PVR
Michel et al. [23]	Cross-sectional	Germany	9856	LUTS (IPSS), Qmax, PVR	Self-reported	DM IPSS OR (age-adjusted), 1.05 (95% CI, 1.03–1.06) DM Qmax OR (age-adjusted), 0.98 (95% CI, 0.93–1.00) No association between DM and PVR

AUASI—American Urological Association Symptom Index; BPH—benign prostatic hyperplasia; DAN-PSS—Danish Prostatic Symptom Score; DM—diabetes mellitus; DRE—digital rectal examination; HbA1c—hemoglobin A1C; HOMA—homeostatic model assessment; HR—hazard ratio; IPSS—International Prostate Symptom Score; LUTS—lower urinary tract symptoms; OR—odds ratio; PSA—prostate-specific antigen; PVR—postvoid residual; Qmax—maximal urinary flow rate; TRUS—transrectal ultrasound.

Table 1. Studies on the association between diabetes and benign prostatic hyperplasia/lower urinary tract symptoms (*Continued*)

Study	Study type	Country	Patients, *n*	BPH definition	Diabetes definition	DM and BPH findings
Hammarsten and Hogstedt [5]	Cross-sectional	Sweden	250	Prostate volume, estimated BPH growth	DM diagnosis, fasting insulin	Differences in BPH growth rate: DM diagnosis ($P < 0.023$) Fasting insulin ($P = 0.018$)
Klein et al. [15]	Cross-sectional	United States	1612	LUTS (AUASI), BPH diagnosis	DM defined as DM diagnosis with treatment or elevated HbA1c	DM LUTS OR (with BPH), 1.25 (95% CI, 0.78–2.01) DM OR (without BPH), 1.27 (95% CI, 0.99–1.62)
Hammarsten et al. [6]	Cross-sectional	Sweden	158	Prostate volume, estimated BPH growth	DM diagnosis, fasting insulin	Differences by DM: Prostate volume ($P = 0.002$) BPH growth rate ($P = 0.002$) Differences by fasting insulin: Prostate volume ($P = 0.001$) BPH growth rate ($P = 0.006$)
Michel et al. [46]	Cross-sectional	Germany	19,365	LUTS (IPSS), Qmax, PVR	Self-reported	DM OR for global tolerability of tamsulosin: 4-week follow-up: 0.86 (95% CI, 0.75–0.99) 12-week follow-up: 0.84 (95% CI, 0.73–0.95)
Sidney et al. [16]	Cohort	United States	16,219	BPH surgery	Oral glucose test	BPH OR by quartiles of glucose (age-adjusted): 2 vs 1: 1.12 (95% CI, 0.94–1.34) 3 vs 1: 0.95 (95% CI, 0.80–1.13) 4 vs 1: 0.82 (95% CI, 0.68–0.98)
Glynn et al. [11]	Cohort	United States	2036	BPH defined as clinical diagnosis or BPH surgery	2-hour fasting glucose	No association between DM and incidence of clinical diagnosis of BPH or BPH surgery

AUASI—American Urological Association Symptom Index; BPH—benign prostatic hyperplasia; DAN-PSS—Danish Prostatic Symptom Score; DM—diabetes mellitus; DRE—digital rectal examination; HbA1c—hemoglobin A1C; HOMA—homeostatic model assessment; HR—hazard ratio; IPSS—International Prostate Symptom Score; LUTS—lower urinary tract symptoms; OR—odds ratio; PSA—prostate-specific antigen; PVR—postvoid residual; Qmax—maximal urinary flow rate; TRUS—transrectal ultrasound.

may produce LUTS. First, decreased bladder compliance causes urinary frequency and urgency. Second, decreased bladder muscle contractility—resulting from chronic tonicity as the bladder labors to overcome increased urethral pressures—may precipitate urinary hesitancy, decreased force of stream, and high residual volumes [2,3].

Still, these relatively straightforward explanations belie the complexity of diagnosing and researching a disease that most often presents with highly subjective symptoms, has few robust objective markers, and overlaps considerably with other conditions that produce urinary symptoms. In fact, a persistent conundrum in both diagnosing and studying BPH is case definition. Case definitions of BPH in epidemiologic studies vary considerably, and measurement and detection biases are acknowledged limitations of BPH research. As a result, clinical and epidemiologic studies have used a number of objective and subjective measures to define BPH. Objective measures include histological analysis of prostate tissue, radiographically determined prostate enlargement, decreased urinary flow rate, prostate-specific antigen (PSA) concentrations, and pressure–flow studies consistent with bladder outlet obstruction. Subjective measures include history of noncancer surgery on the prostate, physician-diagnosed BPH, and LUTS assessment using the American Urological Association Symptom Index (AUASI) or the International Prostate Symptom Score (IPSS). Importantly, no one definition has been shown to be any more appropriate or robust than the others.

Diabetes and Benign Prostatic Hyperplasia

A preponderance of the epidemiologic literature supports the concept that diabetes is associated with objective measures of BPH, most notably prostate gland size. A series of early cross-sectional studies from Sweden demonstrated that physician-diagnosed diabetes was significantly associated with increased prostate size consistent with BPH [4–7]. The authors observed that in patients with LUTS, men with diabetes had a larger prostate gland than men without diabetes (78 mL vs 45 mL, respectively; P = 0.006) [6]. Furthermore, they observed that men with fast-growing prostate glands had a higher prevalence of noninsulin-dependent diabetes mellitus (P = 0.02) [5]. More specifically, these and other studies also observed significant associations between increased insulin concentrations and prostate volume. Nandeesha et al. [8] conducted a case-control study of men with and without BPH diagnosed via digital rectal examination and transrectal ultrasound. The authors observed that cases had significantly higher fasting serum insulin and homeostatic model assessment levels than controls. In the Baltimore Longitudinal Study of Aging, men with elevated fasting glucose were threefold more likely and men with diabetes were twofold more likely to have an enlarged prostate (≥ 40 mL), as measured by MRI [9•]. These findings suggest that BPH may be an insulin-resistant condition, with secondary hyperinsulinemia as a possible etiological factor for prostate enlargement.

Boon et al. [10] examined individuals with LUTS only and found little difference in prostate volume, peak urinary flow rate, and postvoid residual volume. This study, however, relied on a control group from a referral population that did not meet the specified exclusion criteria for BPH, and thus it is possible that the effect of diabetes on these measures was underestimated. Furthermore, in contrast to their finding for BPH surgery, the Normative Aging Study found a nonsignificant inverse association between diabetes and clinical BPH [11]. Finally, in the only recent prospective cohort study examining the influence of diabetes on the progression of BPH markers, Burke et al. [12••] observed that men with diabetes reported a larger increase in the AUASI score than those without diabetes. However, they found no differences in change of prostate volume or PSA, suggesting that the presence of diabetes may be less directly associated with prostate growth and more closely associated with the dynamic components of lower urinary tract function.

Studies using surgery for BPH or history of BPH diagnosis as the outcomes have reported mixed results. Although higher serum concentrations of insulin-like growth factor (IGF)-1 and IGF-binding protein (IGFBP)-3 have been associated with increased risk of clinical BPH and BPH surgery [13,14], some studies have reported that men with diabetes were at higher risk [11,15], whereas others have reported high blood glucose levels to be associated with a lower risk [16]. In the Massachusetts Male Aging Study, men with diabetes mellitus were 1.5 (95% CI = 0.8, 2.7) times more likely to be diagnosed with clinical BPH (defined as BPH surgery or LUTS) [17], whereas a decreased risk of BPH and an increased risk of LUTS were observed among those with diabetes in the California Men's Health Study [18]. Because there is clinical overlap between the presence of BPH and LUTS, with LUTS being the primary manifestation of BPH, they can be manifestations of different pathophysiologic pathways mediated through hormonal, environmental, genetic, neuropathic, and (micro-) vascular influences, particularly in the diabetic patient [19••].

Although a substantial proportion of the existing body of literature supports an association between diabetes and LUTS, the failure to differentiate LUTS from BPH has contributed to some of the confusing evidence observed in studies, including more specific measurements of BPH. This could be due, in part, to the largely cross-sectional analyses, the use of selected or different study populations, low response rates and small sample sizes, and inadequate control of potential confounders. Future prospective studies that include large unselected populations to examine the influence of diabetes and the onset and progression of BPH/LUTS are warranted.

Diabetes and Lower Urinary Tract Symptoms

Although much of the epidemiologic literature also supports the notion that diabetes increases the risk of LUTS,

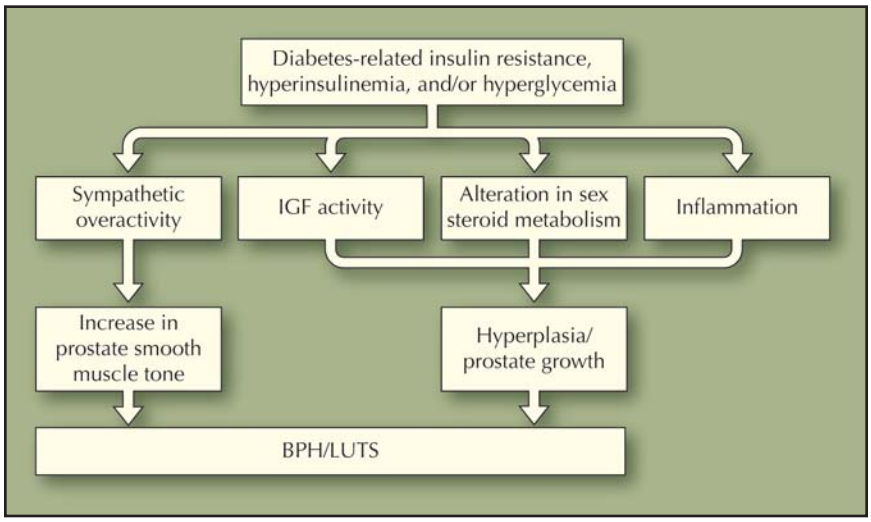

Figure 1. Hypothesized mechanisms of diabetes in the pathogenesis of BPH/LUTS. BPH—benign prostatic hyperplasia; IGF—insulin-like growth factor; LUTS—lower urinary tract symptoms.

associations of diabetes with LUTS are complicated by two issues. First, LUTS is a syndrome with multiple potential etiologies, including primary detrusor instability (ie, overactive bladder) and interstitial cystitis. Second, diabetes may precipitate urinary storage symptoms through neurologic mechanisms that are completely independent of any potential links with BPH. Diabetic cystopathy, a common complication of diabetes characterized by impaired sensation of bladder fullness, increased bladder capacity, and reduced bladder contractility, has been estimated to occur in as many as 45% of patients with diabetes [20]. The prevalence of cystopathy increases with the duration of diabetes (25% for 10 years; > 50% for 45 years) [21]. This dysfunction typically involves autonomic neuropathy, leading to functional parasympathetic and possibly sympathetic denervation of the detrusor.

These caveats not withstanding, several epidemiologic studies that have examined the association between LUTS and self-reported history of diabetes also suggest that LUTS may occur more frequently among men with diabetes, with an estimated 25% to threefold increased risk of LUTS in men with diabetes. In a recent cross-sectional evaluation of two population-based cohorts, Sarma et al. [22•] observed that men with diabetes were 1.42 times more likely to report moderate to severe LUTS compared with their nondiabetic counterparts after adjustment for age (95% CI = 1.03, 1.95). In addition, among 9856 men with clinically diagnosed BPH, the presence of diabetes (13%) was associated with increased LUTS severity, affecting voiding more than storage function [23]. Patients with BPH and diabetes had a significantly higher baseline IPSS and a significantly lower maximal urinary flow rate (Qmax) than those without diabetes ($P < 0.001$). The authors hypothesized that diabetes not only impairs detrusor function but also may affect bladder outlet resistance, which could occur by altering the responsiveness of smooth muscle α-1-adrenoreceptors, which have an important role in the regulation of bladder outlet resistance. In the Baltimore Longitudinal Study of Aging, Parsons et al. [9•] noted that men with elevated fasting glucose were 2.5-fold and men with diabetes were threefold more likely to have LUTS.

Hypothesized Mechanisms

There are several mechanisms by which diabetes may potentially influence BPH (Fig. 1). First, while the trophic effect of increased insulin concentrations secondary to diabetes may induce an enlarged prostate, high insulin levels may, in turn, increase sympathetic nerve activity, which probably contributes to an increase of prostate smooth muscle tone [24]. BPH patients with hyperinsulinemia may have increased sympathetic nervous system activity because insulin resistance is associated with sympathetic activation, and higher sympathetic nervous activity would likely contribute to an increase of prostate smooth muscle tone. Additionally, hyperglycemia itself may play a role by increasing cytosolic-free calcium in smooth muscle cells and neural tissue, thus leading to sympathetic nervous system activation. This would coincide with observations by Rohrmann et al. [3] of increased LUTS severity in men with elevated postload glucose concentration and men with a higher percentage of glycosylated hemoglobin compared with men with lower levels. Changes in insulin and glucose metabolism also have been found to be associated with hypertension via stimulation of the sympathetic nervous system activity, which were observed to be associated with prostate size and LUTS [25].

Second, because of its structural similarity to IGF, insulin can bind to the IGF receptor in prostate cells, possibly activating the receptor to induce growth and proliferation. Alternatively, as insulin levels increase, IBFBP-1 declines, thus increasing the bioavailability of IGF [24]. Several studies have observed various components of the IGF axis to be associated with the risk of BPH and LUTS [3,14,26].

Third, insulin may influence BPH risk directly by increasing the transcription of genes involved in sex hormone metabolism, thus influencing androgens and estrogens or indirectly through altered hormone metabolism as a result of obesity [24]. Higher insulin is associated

with lower sex hormone–binding globulin, which may increase the amount of androgen/estrogen entering prostatic cells, thereby increasing the risk of BPH. Sex hormones are involved with androgenic actions within the prostate where androgens bind to the androgen receptor and activate DNA synthesis and cellular proliferation, which may then increase the risk of BPH.

Finally, accumulating data suggest that inflammation may play an important role in the development of BPH and the development and progression of LUTS. Although the mechanisms by which inflammation may lead to prostatic growth have not been elucidated, it has been suggested that inflammatory mediators may directly contribute to prostatic epithelial and stromal cell growth through growth induction via cytokines that stimulate production of prostatic growth factors, and indirectly through decreases in prostate cell death via downregulation of prostate cell apoptosis [27•]. Moreover, glucose insensitivity is a component of the metabolic syndrome. The metabolic syndrome is associated with systemic inflammation and oxidative stress. Histological BPH is usually associated with inflammation, and the extent and severity of the inflammation corresponds to the severity of the BPH [28–30].

Conclusions

Overall, these data suggest that diabetes increases the risks of BPH and LUTS and support the concept that BPH and LUTS are, to some extent, preventable disorders associated with modifiable exposures, challenging us to revisit traditional paradigms of diagnosis and treatment. Previously, BPH and LUTS have been viewed as immutable processes of aging resulting from relatively nonmodifiable stimuli. This paradigm resulted in reactive approaches to clinical management and research that focused on the categorization and management of symptoms rather than on proactive identification of at-risk individuals or the design of population-based prevention programs.

Additionally, these data suggest alternative etiologies for BPH outside of sex steroid hormone growth pathways, including sympathetic nervous system and/or IGF activity and systemic inflammation. The elucidation of alternate etiologies necessitates the development of novel descriptions for BPH and LUTS. Although LUTS are the primary clinical manifestation of BPH, they also represent a syndrome generated by a host of bladder-related etiologies that may or may not coexist with true pathological BPH. Distinguishing BPH-associated LUTS from non-BPH LUTS may reveal patterns by which diabetes influences BPH and LUTS phenotypes, suggest new methods for diagnosis, and allow more precise tailoring of treatments.

Regardless of etiology, the prevention of BPH and LUTS is of substantial importance to public health. Current disease trends in the United States suggest that as the population ages, diabetes, BPH, and LUTS will markedly increase in prevalence and will place substantial strains on finite health care resources. Future research is therefore needed to identify the magnitude of onset and progression of BPH associated with diabetes; to elucidate mechanisms by which diabetes exerts its effects on BPH; and to identify the most effective treatment and prevention strategies for BPH associated with diabetes to reduce the psychosocial, medical, and economic costs of these highly prevalent and chronic disorders affecting men.

Disclosure

No potential conflicts of interest relevant to this article were reported.

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