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·*Review*·

# Common approach to managing lower urinary tract symptoms and erectile dysfunction

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**Abstract**

The present paper serves as a review of the associations between lower urinary tract symptoms (LUTS) and erectile dysfunction (ED), with a focus on common and combined pathways for treatment. LUTS and ED are common conditions seen in general urologic practice. Research has started to establish epidemiologic and pathophysiologic links between the two conditions and a strong association confirmed across multiple studies. Men seeking care for one condition should always be interviewed for complaints of the other condition. Proposed common pathways include α-1 adrenergic receptor imbalance, Rho-kinase overactivity, endothelial cell dysfunction and atherosclerosis-induced ischemia. Medical therapy has replaced surgery as the first-line treatment for LUTS in most patients, with the incorporation of α-adrenergic receptor antagonists (α-ARAs) and 5-α-reductase inhibitors (5-ARIs) into everyday practice. Treatment with α-ARAs contributes to some improvement in ED, whereas use of 5-ARIs results in worsened sexual function in some patients. Phosphodiesterase-5 (PDE-5) inhibitors have revolutionized the treatment of ED with a simple oral regimen, and new insights demonstrate a benefit of combined use of PDE-5 inhibitors and α-ARAs. The mechanisms of action of these medications support these observed benefits, and they are being studied in the basic science and clinical settings. In addition, novel mechanisms for therapy have been proposed based on clinical and research observations. The minimally invasive and surgical treatments for LUTS are known to have adverse effects on ejaculatory function, while their effects on erectile function are still debated. Much remains to be investigated, but it is clear that the associations between LUTS and ED lay the foundation for future therapies and possible preventative strategies. *(Asian J Androl 2008 Jan; 10: 45–53)*

**Keywords:** erectile dysfunction; lower urinary tract symptoms; benign prostatic hyperplasia; medical therapy

## 1 Introduction

In the practice of urology, lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) are conditions encountered on a daily basis. Both LUTS and ED demonstrate increasing prevalence with advancing age, and a great deal of epidemiologic and clinical research has been done to study the two processes. The two conditions are strongly linked, and investigation continues into the etiology of each condition, with particular attention being paid to common pathways. There are several avenues of treatment for each condition, and research is ongoing into the overlap and interactions of these therapies.

## 2 Epidemiology

The symptom spectrum of LUTS in men is the manifestation of benign prostatic hyperplasia (BPH) and bladder outlet dysfunction as obstructive and irritative voiding symptoms, which can include frequency, urgency, nocturia, decreased force of stream, intermittent stream and incomplete bladder emptying. BPH is a histological diagnosis indicating cellular proliferation of the stromal

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and epithelial elements of the prostate gland. This histological diagnosis is made at autopsy in 8% of men aged 31–40 years, 50% of men aged 51–60 years, 70% of those aged 61–70 years, and 90% in those aged 81–90 years [1]. These data compiled from 10 studies of more than 1 000 prostates clearly illustrate the increasing prevalence of BPH with age. BPH can lead to complaints of LUTS; however, the incidence of pathologic BPH is much higher than the incidence of symptoms attributable to BPH. Clinically, the International Prostate Symptom Score (IPSS) is a widely-used, validated instrument for evaluating symptoms of LUTS and tracking response to treatments. The prevalence of symptomatic BPH (IPSS score > 8) is estimated to be between 18% in men 40–49 years old to 56% in men 70–79 years old, based on IPSS responses from over 4 000 men in Asia [2]. Similarly reported prevalence in other regions of the world ranges from 8% to 36% in men 50–59 years old and from 27% to 37% in men 70–79 years old [3]. Clearly, not all patients with BPH develop LUTS, and not all patients presenting with LUTS have objective evidence of BPH. The symptoms of LUTS can also be attributed to the smooth muscle tone of the prostatic capsule and bladder neck. This etiology has been confirmed through the efficacy of α-adrenergic receptor antagonists (α-ARAs) in the treatment of LUTS; by their mechanism of smooth muscle relaxation, they facilitate bladder emptying.

Sexual dysfunction includes ED, ejaculatory dysfunction and hypoactive sexual desire. ED is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance [4]. The prevalence of ED in men ages 40–70 years with comorbidities is estimated at 9.7% overall, with rates of 39% in men with heart disease, 29% in men with diabetes, and 15% in those with hypertension [5]. When stratified by age, prevalence of ED increased from 40% with mild ED and 5% with severe ED at age 40 years, to 70% and 15%, respectively, at age 70 years [6]. In clinical evaluation, the International Index of Erectile Function (IIEF) and Danish Prostate Symptom Score sex questionnaire (DAN-PSSsex) have been validated as tools for assessing erectile ejaculatory function.

Numerous studies have established a link between LUTS and ED. Epidemiologic data cannot establish causality between the two conditions, but they can and do demonstrate reproducible associations between the two conditions. Sexual dysfunction is more prevalent in men with LUTS. The UrEpik study [7] reported questionnaire responses of 4 800 men in four countries and found that men with self-reported LUTS are more likely to report ED after adjustment for age. Other comorbidities are also associated with ED, including diabetes, hypertension and tobacco use. The Cologne Male Study [8] surveyed almost 5 000 men aged 30–80 years, with an overall prevalence of ED of 19%. This prevalence, when stratified for LUTS, was 72% in men with LUTS and 37% in men without LUTS; this statistically significant difference persisted independent of age. Further analysis of this dataset demonstrated LUTS to be an independent risk factor for ED [8]. The Multinational Study of Aging Male (MSAM)-7 study [9], which evaluated questionnaire responses of 12 815 men, confirmed the link by demonstrating that ED is associated with the severity of LUTS; the analysis found that LUTS and age are stronger risk factors for ED than other comorbid conditions such as diabetes, hypertension or hyperlipidemia.

It is important to be aware of the possible positive and negative effects of medication for one condition on the symptoms of the other condition. There is evidence for increased and decreased ED with medical and surgical therapies for LUTS. In addition to common risk factors, it is thought that the psychological impact of LUTS on quality of life might alter a patient's erectile function [10]. The pathophysiologic effects of LUTS on ED might also be an important factor, and research is ongoing to examine and clarify this complex relationship. Given the evidence and ongoing research, a clinician, when seeing a patient for one of the two conditions, should always include questions regarding the other condition.

## 3 Common pathophysiology

Research has identified several possible pathways through which LUTS and ED develop. The predominant theories for association involve changes in α-adrenergic receptor regulation, increased Rho-kinase activity, endothelial dysfunction and atherosclerotic changes.

The various subtypes of α-1 adrenergic receptors have been studied and identified in the bladder, prostate and penile tissue. Table 1 details the subtypes and their locations.

In the corpus cavernosum, adrenergic receptors mediate smooth muscle and vascular tone; decreased adrenergic input mediates smooth muscle relaxation and decreases vascular tone to allow erection while adrenergic receptor activation induces smooth muscle contraction and increases vascular tone to cause detumescence [11]. This knowledge raises the possibility of aberrant smooth muscle contraction as a common etiology of both LUTS and ED. With age, glandular proliferation occurs and the density of α-adrenoceptors increases.

Alpha-1A receptors concentrated in prostate and bladder neck are involved in voiding problems and α-1D receptors found in hypertrophied detrusor muscle are involved in storage problems [3]. α-1A and α-1D receptors

Table 1. α-Adrenergic receptor subtypes and their locations.

| Receptor subtype | Location [12–17] |
|---|---|
| α-1A | Prostatic stromal cells, vascular smooth muscle, urethra, vas deferens, bladder |
| α-1B | Prostatic epithelial cells, vascular smooth muscle |
| α-1D | Prostatic stromal cells, urethra, vas deferens, bladder, detrusor muscle |
| α-1 and α-2 | Penile vasculature, corpus cavernosum smooth muscle |

have been identified as the predominant α-1-adrenoceptor subtypes in penile corpus cavernosum [16].

Another autonomic mediated pathway is that of Rho and Rho-associated kinase. Increased Rho-kinase activity leads to increased smooth muscle contraction, which in turn contributes to impaired erectile function and changes in bladder outlet tone [18]. Jin *et al*. [19] demonstrated in a rat model that increased RhoA/Rho-kinase signaling coincides with the development of ED with aging. Inhibition of Rho-kinase in the rat model has been shown to decrease prostatic smooth muscle cell proliferation and to decrease adrenergic contractions [20]. Administration of an oral Rho-kinase inhibitor, fasudil, prevented atherosclerosis, endothelial injury and associated ED in rats; the control set of rats was found to have elevated cavernosal Rho-kinase activity and decreased eNOS expression with ED [21].

Endothelial dysfunction is central to the development of both conditions. Nitric oxide (NO) induces vasodilation, and it is the basis for using phosphodiesterase-5 (PDE-5) inhibitors in the treatment of ED. NO has also been identified in prostate and bladder tissue, and some nitrenergic receptors are found in human hyperplastic prostate tissue [22]. NO synthase gene expression is reduced with aging in rat prostate tissue and might be a factor for increased smooth muscle tone associated with LUTS [23]. PDE receptors have been characterized in prostatic tissue, but more research is needed regarding their impact on prostatic smooth muscle tone [23].

Atherosclerosis causes chronic ischemia to organs, including the bladder, prostate and penis, and many factors, such as diabetes, hypertension, hyperlipidemia and smoking, are known to contribute to or accelerate its development. The metabolic syndrome, which includes cardiovascular and diabetic risk factors, can cause autonomic hyperactivity, and the sequelae of chronic ischemia might involve many of the above pathways. ED is considered a risk marker for the metabolic syndrome and its associated comorbidities [24].

## 4 Impact of medications used to treat LUTS on ED

### *4.1 α-adrenergic receptor antagonists (α-ARAs)*

Considered first-line therapy for symptoms secondary to BPH, α-ARAs have changed the management of LUTS. The four currently available formulations are alfuzosin, tamsulosin, doxazosin and terazosin. The American Urological Association (AUA) Guideline Committee performed a meta-analysis of over 5 900 men treated for 3 to 9 months and over 6 500 men treated for 10 to 16 months [25]. The analysis demonstrated a mean IPSS improvement of 2–2.5 points and minimal differences in symptom improvement between the four agents studied.

Table 2. Vascular-related effects of α-adrenergic receptor antagonists (α-ARAs) [25].

| Agent | Dizziness (%) | Symptomatic postural hypotension (%) | Asthenia (%) |
|---|---|---|---|
| Placebo | 5 | 1 | 4 |
| Tamsulosin | 11 | 3 | 7 |
| Doxazosin | 13 | 4 | 15 |
| Terazosin | 15 | 6 | 12 |
| Alfuzosin | 5 | 1 | 4 |

However, differences were found in side effect profiles, as noted in Tables 2 and 3. Overall, tamsulosin and alfuzosin were associated with fewer vascular-related adverse effects. They are considered uroselective in nature: alfuzosin is preferentially distributed in prostatic tissues [26], and tamsulosin has shown greater affinity for receptor subtypes 1A and 1D [27, 28].

None of the four agents demonstrated a deleterious effect on erectile function when compared to placebo. In contrast, several basic science and clinical studies have demonstrated a beneficial effect on sexual function while on therapy with α-ARAs for LUTS.

Research involving rabbit cavernosal smooth muscle has demonstrated relaxation of the smooth muscle by alfuzosin, very similar to the effects of phentolamine and sildenafil [29]. This relaxation was instigated by an α-adrenergic blockade, and suggests a beneficial influence of alfuzosin on erectile function.

Nearly 5 000 men in the community setting in multiple countries were followed for 6 months on alfuzosin [30], and symptoms and side effects were assessed using self-administered validated questionnaires. The average changes in self-reported symptoms reflected improvement in both LUTS and ED. IPSS scores improved an

Table 3. Effects of α-adrenergic receptor antagonists (α-ARAs) on sexual function [25].

| Agent | Erectile dysfunction (%) | Ejaculatory dysfunction (%) | Change in libido (%) |
|---|---|---|---|
| Placebo | 4 | 1 | 3 |
| Tamsulosin | 4 | 9 | |
| Doxazosin | 4 | 0.4 | 3 |
| Terazosin | 5 | 1 | 3 |
| Alfuzosin | 3 | | 1 |

average of 6 points, while significant improvement from 2.5 to 2.0 in mean score (both, $P < 0.001$) was seen on the erection rigidity domain of the DAN-PSSsex. Approximately 5% of patients withdrew secondary to postural dizziness, and less than 1% withdrew from the study as a result of diminishing erectile function.

Rosen *et al.* [31] performed a placebo-controlled study on the effect of alfuzosin on sexual function in 372 men with LUTS on alfuzosin. After 1 month of treatment, responses on the erection rigidity question of the DAN-PSSsex revealed an improvement in erectile function in men receiving alfuzosin versus a decline in function in men receiving a placebo ($P = 0.02$), with dizziness being the main side effect reported in 5% of men on alfuzosin.

A pooled analysis of three randomized, placebo-controlled studies involving alfuzosin evaluated data on 473 men who took alfuzosin and 483 men who used a placebo for 12 weeks [32]; mean improvement in IPSS was 6.0 points with alfuzosin versus 4.2 points with a placebo ($P < 0.005$).

A multicenter study by De Rose *et al.* [33] followed patients with BPH on doxazosin for 3 months. The authors found a statistically significant improvement in IIEF score in 35% of the men with ED at baseline; within this group of men, 66.5% of those with moderate to severe ED at baseline (IIEF score 6–16) reported a significant increase in IIEF score, reflecting a more profound improvement in men with worse erectile function at baseline. Another multicenter, randomized study comparing doxazosin in standard versus extended-release dosing followed 680 men for 13 weeks and noted improvements in sexual function based on IIEF responses in those patients with sexual dysfunction at baseline [34].

Tamsulosin has been found to have the highest incidence of ejaculatory dysfunction, which is thought to be related to its receptor selectivity. Phase III testing of tamsulosin demonstrates a dose-dependent rate of ejaculatory dysfunction, with 8% incidence in men using 0.4 mg and 18% of men taking 0.8 mg versus 0.2% in the placebo arms [35]. Another randomized placebo-controlled, crossover study showed that 0.8 mg of tamsulosin decreased mean ejaculate volume in almost 90% of men with 35% having no antegrade ejaculation, while no change in ejaculatory volume was observed in the men taking alfuzosin [36].

A retrospective study reviewed questionnaire responses of 7 974 men using tamsulosin compared with men taking other medications for BPH symptoms and men on no medication [37]. Linear regression of SHIM (abridged IIEF) scores on AUA symptom scores revealed that erectile function was best preserved in men taking tamsulosin, with the most benefit observed in men with more severe LUTS.

A new α-1A receptor-selective antagonist for treatment of LUTS, silodosin, is currently under investigation. A phase III placebo-controlled comparison of silodosin and tamsulosin (0.2 mg daily) demonstrated comparable reductions in IPSS [38]. It was noted to have a higher incidence of ejaculatory dysfunction, and further investigations for this indication are continuing with this agent.

### *4.2 5-α-reductase inhibitors (5-ARIs)*

There are two 5-ARIs currently on the market: finasteride (Merck & Co., Whitehouse Station, NJ, USA) and dutasteride (GlaxoSmithKline, Beinheim, France). These two agents work through inhibition of 5-alpha reductase, which converts testosterone to 5-dihydroxytestosterone (DHT). DHT is the primary androgen responsible for hyperplastic growth of the prostate, and 5-ARIs are used in men with very enlarged glands. The type 2 enzyme is specific to prostate tissues, whereas the type 1 enzyme is expressed in most tissues. Finasteride is a selective inhibitor of the type 2 enzyme, while dutasteride inhibits both type 1 and type 2 enzymes. Both have been shown to have equivalent efficacy in treating LUTS.

The use of both agents is associated with adverse effects on sexual function. The PROscar Safety plus Efficacy Canadian Two year Study (PROSPECT) study evaluated the use of finasteride versus placebo over 2 years and reported a 16% incidence of ED and 8% incidence of ejaculatory dysfunction among the finasteride-treated patients versus 6% and 2%, respectively, in the placebo arm [39]. In a non-placebo-controlled study comparing use of finasteride versus dutasteride in 1 630 men over 48 months, the rates of ED were comparable, at 8% and 7%, respectively [5]. In three placebo-controlled 2 year trials evaluating

dutasteride treatment in a total of over 4 300 men, worsening sexual function, including ED, decreased libido and ejaculatory dysfunction, was observed within 0–6 months of treatment compared to the placebo; however, as treatment continued to a total of 24 months, the rates of these adverse effects were comparable to placebo rates with no statistically significant difference [5]. Similarly, the use of finasteride versus a placebo for 4 years in over 3 000 men was studied in the Proscar Long-Term Efficacy and Safety Study (PLESS); 15% of patients taking finasteride versus 7% of those taking a placebo developed sexual dysfunction during the first year [40]. However, the rate of self-reported sexual adverse events from years 2 to 4 leveled off to 7% in both the finasteride and placebo groups.

Mondaini *et al.* [41] examined the sexual side effects in 107 men taking finasteride, comparing those who were informed and those who were not informed prior to treatment of the possible sexual side effects; interestingly, the researchers found that the men informed of the potential side effects reported a significantly higher rate of sexual dysfunction at 6 and 12 months [41].

Despite differences in enzyme type specificity, with dutasteride demonstrating greater reduction in serum levels of DHT, no significant difference in efficacy has been recorded. A review of trials involving both finasteride and dutasteride found similar effects on reduction in prostate volume, flow rate, symptom improvement, and progression [42].

Notably, 5-ARIs have proven to be effective in reducing the risk of acute urinary retention and progression to surgery, as demonstrated in the PLESS trial, with review of the data at 4 and 6 years [43, 44]. A retrospective review of the use of α-ARAs versus 5-ARIs among 4 500 men demonstrated significantly greater rates of progression, as measured by documentation of urinary retention or BPH-related surgery, with α-ARAs at all intervals from 6 to 24 months following initiation of treatment [45]. Over 24 months, surgery or documentation of retention was recorded for 18.2% of men taking α-ARAs *vs.* 10.7% of men taking 5-ARIs ($P < 0.001$). This is a significant finding unique to 5-ARIs, which warrants additional confirmation in clinical trials.

*4.3 Combination therapy*

Kaplan *et al.* [46] compared the effects of doxazosin alone, finasteride alone, combination therapy, and a placebo in 3 047 men over 4.5 years, and found a benefit in treatment with combination therapy of finasteride and doxazosin, specifically in men with a baseline prostate volume of greater than 25 g [46]. This study did not report the effect of therapy on sexual function.

A retrospective review over 6–8 years in 192 men treated with alpha-blockers alone and 149 men treated with combination therapy of an α-ARA and 5-ARI [47] found statistically significant differences in the outcomes of episodes of acute urinary retention (17.7% with α-ARA alone, 12.1% with combination, $P < 0.05$) and surgical intervention (10.9% with α-ARA alone, 6% with combination, $P < 0.05$). The effects of therapy on sexual function were also not reported.

However, McConnell *et al.* [48] found a cumulative risk of sexual side effects with combination therapy when compared to monotherapy or placebo. The rates of ED in the finasteride-alone (4.53 per 100 person-years) and combination therapy (5.11) groups were significantly higher than the rate in the doxazosin-alone group (3.56), which was not significantly higher than in the placebo group (3.32). The rates of decreased libido and ejaculatory dysfunction were also increased.

Combination therapy might reduce symptoms of LUTS, but clinicians should be aware of the potential additive effect on sexual function.

## 5 Impact of medications used to treat ED on LUTS: PDE-5 inhibitors

This class of medication for the treatment of ED act by potentiation of the action of NO on penile smooth muscle cells. NO activates guanylate cyclase, the enzyme that produces cyclic GMP, which mediates hyperpolarization and subsequent relaxation of smooth muscle cells. PDE-5 inhibitors block the degradative action of phosphodiesterases on cyclic GMP and thereby prolong the relaxation of smooth muscle cells causing an erection.

An investigation of PDE-5 receptor expression and PDE-5 inhibitor activity in rat bladder and prostate tissue noted that PDE-5 signaling was involved in bladder smooth muscle tone and prostatic stromal proliferation [49]. PDE-5 inhibitor activity led to reduced contractions in the tissues and decreased proliferation of prostatic stromal cells, and the lessened irritative symptoms in an outlet obstruction model. This study found vardenafil to be more potent than either sildenafil or tadalafil and suggested a possible role for use of PDE-5 inhibitors in the treatment of irritative LUTS. Vardenafil was administered as 10 mg twice a day for 8 weeks in a randomized, double-blind, placebo-controlled study in 215 men with LUTS for at least 6 months [50]. The results presented at the 2007 AUA meeting showed that Vardenafil significantly improved the mean IPSS from 16.8 to 11.0 compared to placedo with a change from 16.8 to 13.2 ($P = 0.0013$).

A pilot study evaluated IPSS and IIEF questionnaire responses among 112 men treated with sildenafil on an as-needed basis over 3 months [51]. The results demonstrated improvement in the IPSS scores with sildenafil treatment and noted that men with lower IPSS

scores at baseline responded better to treatment with sildenafil. Currently, placebo-controlled studies with sildenafil and tadalafil are underway to further study their effects in men with LUTS [52].

One such study, with a double-blind placebo-controlled design, examined the effect of 12 weeks of daily sildenafil on ED and LUTS, finding that the men receiving sildenafil had significant improvements in erectile function (9.17 *vs.* 1.86 point increase on IIEF erectile function domain) and LUTS (6.32 *vs.* 1.93 point decrease in IPSS score) [53]. Daily tadalafil administration was also studied in 281 men in a placebo-controlled setting and found to be beneficial for LUTS, with significant improvements in self-reported IPSS scores [54]; following a 4-week placebo run-in period and 12 weeks of treatment, the mean IPSS decreased by 7.1 points in men taking tadalafil versus 4.5 points in men taking a placebo.

This preliminary evidence opens avenues for further investigation into the benefits of PDE-5 inhibitors on LUTS. A new PDE-5 inhibitor, udenafil, is approved for use in South Korea and the UK. It is currently under further investigation in phase II and phase III trials in the USA [55]; no data have been published as to its effect on LUTS, but will be worth following.

## 6 Effect of combined PDE-5 inhibitors and α-ARAs on ED and LUTS

Researchers are investigating the effects α-ARAs might have in the treatment of ED and the possible influence that PDE-5 inhibitors might have on LUTS [3].

The presence of α-adrenoceptors types 1 and 2 in penile tissue has been established, and it has been noted that norepinephrine acting on these receptors caused contraction of trabecular smooth muscle. α-adrenoceptor antagonists facilitate penile erection and may result in priapism in rare circumstances [56]. Several α-ARAs are available and have been used in the treatment of ED, including phentolamine (α-1, α-2) as an injectable agent, prazosin (α-1) as an oral or intraurethral agent, and yohimbine (α-2) as an oral agent [57].

Researchers have examined the relaxant effects of alfuzosin, phentolamine and sildenafil on corpus cavernosal tissue from rabbits and demonstrated α1-adrenoceptor responsiveness in the tissues, with relaxation seen with alfuzosin and phentolamine [29]; sildenafil's ability to relax the tissues involves NO-mediated pathways.

Kaplan *et al.* [58] demonstrated that oral doxazosin potentiated the erectile effect of alprostadil injected intracavernosally [58]. The Treatment of Mild Hypertension Study (TOMHS) documented that patients receiving doxazosin reported a lower incidence of ED [59]. Another trial, which randomized 28 men with ED who had failed sildenafil monotherapy to treatment with either sildenafil plus doxazosin or sildenafil plus a placebo, found a statistically significant improvement in the IIEF score in 78% of the men receiving combination therapy *vs.* 7% of the men receiving sildenafil alone ($P = 0.0016$) [60]. Similarly, a retrospective study that looked at the effect of adding oral alfuzosin to tadalafil, in men who had previously failed use of tadalafil, found improved erectile function in 71% of those treated [61].

A recent study randomized 62 men to alfuzosin 10 mg daily, sildenafil 25 mg daily, or a combination of both agents daily for 12 weeks [62]. Based on IPSS and IIEF responses, the researchers found greatest improvement in LUTS and ED with the combination therapy (24.1% change in IPSS and 58.6% change in IIEF with combination, $P = 0.002$). These pilot studies provide a foundation on which further investigation may be based.

Some degree of caution is advised with using PDE-5 inhibitors in conjunction with α-ARA. Several placebo-controlled studies have examined the hemodynamic effects of simultaneous administration. One trial found that, when compared to those given doxazosin plus placebo, 89% of men given doxazosin plus tadalafil exhibited significantly greater reductions in standing and supine blood pressures [63]. The same article reported on a trial of the simultaneous administration of tamsulosin and tadalafil and found that the changes in blood pressure were similar to those with a placebo. Another study, using tadalafil and alfuzosin versus a placebo demonstrated no significant hemodynamic interaction between tadalafil and alfuzosin [64]. In men who have been on long-term therapy with α-ARAs, the effect of PDE-5 inhibitors on blood pressure might be less significant [65].

## 7 Impact of surgery for BPH on erectile function

Surgical therapy for LUTS is indicated in men for whom medical therapy has failed. The specific technique used depends on the urologist's judgment of the patient's clinical presentation and consideration of his comorbidities. Surgical approaches range from minimally invasive ablation with cautery procedures to open extirpation of the entire gland.

The risk of ED after transurethral resection of the prostate (TURP) is approximately 2%–10%, according to the AUA Guideline's analysis of 15 trials. Notably, the VA Cooperative Study, which randomized 556 men to TURP or watchful waiting and followed them for 3 years, found that the rate of ED among men following TURP was slightly lower than that among men managed with watchful waiting [66]; the rate of worsening ED over the course of the study was 19% in the surgery group and 21% in the watchful waiting group. A randomized comparison of TURP with holmium laser enucleating of the prostate (HoLEP) in 120 patients with a mean age of

approximately 65 years found similar rates of preexisting ED in both groups. Following surgery, the patients' IIEF responses reflected new ejaculatory dysfunction in over 60% of the patients in both groups and marginal improvement in erectile function in both groups [67]. After 24 months, mean IIEF scores improved from 21.4 and 22.3 to 23.8 and 24.1, and the prevalence of ED in the two groups decreased from 53.3% and 51.6% to 51.8% and 48.3 %, respectively. Another randomized comparison of TURP with HoLEP over 1 year in 200 patients with mean age of approximately 68 years found the rates of diminished erectile function to be similar, 10.5% after TURP and 11.2% after HoLEP, and found improved erectile function in 1 TURP patient and 3 HoLEP patients [68].

Alternative transurethral procedures exist, including transurethral needle ablation (TUNA) and transurethral microwave thermotherapy (TUMT). According to the AUA Guideline [25], the risk of ED after TUMT is no worse when compared to a sham procedure and the risk after TUMT or TUNA is less than the risk of ED associated with TURP.

The number of TURPs performed for BPH-related disease in the SA has decreased from 250 000 in the late 1980s to 88 000 in the year 2000 [69]; this change is largely due to the use of effective medical therapies for symptomatic relief. This method still remains a valuable option, particularly with large-volume glands. Among these interventional therapies, open surgery is associated with a high incidence of sexual dysfunction, cited as 10% for ED and 65% for ejaculatory dysfunction [11].

## 8 Conclusion

Many theories on the pathophysiology of these two conditions have been proposed and remain to be investigated. Testing of these theories might lead to novel and integrated treatments. For now, the treatments available are proving to be beneficial in ways not previously known or studied. As research continues, men with LUTS, ED or the coexistence of both will gain greater benefit. This benefit might one day be extended to men who have yet to suffer from LUTS or ED; through better understanding of the mechanisms of how they develop, prevention of both conditions simultaneously might be possible.

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