

Review and update of benign prostatic hyperplasia in general practice

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Background

Benign prostatic hyperplasia (BPH) is the most common benign tumour in men. Although men with BPH often need medical or surgical management from a urologist at some point throughout the timeline of their disease, most men are initially assessed and managed by a general practitioner (GP) in the primary healthcare setting.

Objectives

The aim of this article is to highlight the principles of the pathogenesis, presentation, assessment and management of BPH in a primary care setting.

Discussion

Between 2009 and 2011, BPH was managed by GPs at approximately 228,000 general practice visits per annum in Australia. Several changes in pharmaceutical agents and surgical intervention have occurred over the past decade. As a result, it is imperative that GPs remain up to date with assessment and management of BPH, are aware of new therapies and understand when to refer to a urologist.

IT IS COMMON FOR MEN to present to a general practitioner (GP) with symptoms suggestive of bladder outflow obstruction, which is often due to benign prostatic enlargement (BPE). Benign prostatic hyperplasia (BPH) is the histological cause of BPE, which often results in lower urinary tract symptoms (LUTS) related to voiding, storage or post-micturition.¹ Not all LUTS in men are due to BPE, and other causes of voiding dysfunction require exclusion (Table 1).² Management of LUTS due to BPE depends on symptom severity or complicating factors and includes observation (for men with minimal symptoms), medical therapy, minimally invasive surgical procedures, endoscopic prostatectomy and, occasionally, abdominopelvic surgery for very large prostates.

Important history and examination features

International guidelines highlight the importance of determining the severity of LUTS and identifying complicating factors such as urinary retention, macroscopic haematuria, urinary tract infection (UTI) or a personal or family history of prostate cancer. Men may describe (i) voiding (bladder emptying) symptoms such as weak stream, hesitancy and intermittency of flow or (ii) storage (bladder filling) symptoms such as urgency, daytime frequency and nocturia. A predominance of storage symptoms would require exclusion of other conditions such as primary bladder pathology/malignancy, diabetes mellitus, ischaemic heart disease and medications with diuretic properties.³ In cases where the primary complaint is nocturia, efforts should first be made to exclude nocturnal polyuria (then associated factors such as obstructive sleep

apnoea) as the cause of symptoms. The use of a frequency-volume chart or voiding diary, and International Prostate Symptom Score (IPSS) tools, help to assess symptom severity and bother affecting quality of life (QoL; Table 2).⁴

The aim of physical examination is to exclude a palpable bladder as well as phimosis, meatal stenosis or other pathology, including balanitis. A digital rectal examination (DRE) is recommended to evaluate the size of the prostate and exclude a grossly malignant or hard prostate nodule suggestive of prostate cancer, tenderness suggestive of prostatitis, and constipation.⁵

Initial investigations

Initial investigations aim to exclude sinister causes of LUTS or complications of bladder outflow obstruction that require immediate treatment. Such investigations (Table 3) include urinalysis (to exclude haematuria, proteinuria and pyuria), serum creatinine and estimated glomerular filtration rate (eGFR).⁶ Urine cytology should be considered in the presence of haematuria, risk factors for urothelial carcinoma, or significant storage symptoms. In patients with moderate-to-severe symptoms or an abnormal serum creatinine, a renal tract ultrasound will show bladder capacity and post-void urine residual volume, allow for assessment for hydronephrosis and provide an estimation of prostate volume.⁵ Computerised tomography is not routinely recommended unless complicating features are suspected.^{5,6}

Some men are concerned that their urinary symptoms may be due to an underlying prostate cancer. Prostate-specific antigen (PSA) testing remains controversial both in Australia and

internationally. The Royal Australian College of General Practitioners (RACGP) recommends against PSA screening, but acknowledges that the PSA debate remains unclear and open to individual interpretation.⁷ The Prostate Cancer Foundation of Australia and Cancer Council Australia guidelines from 2016 recommend PSA testing every two years for men aged 50–69 years at average risk of prostate cancer.⁸ This recommendation is supported by the Urological Society of Australia and New Zealand (USANZ).

Management

Treatment is mostly determined by both of symptoms, effect on QoL or whether any complicating features are identified. A conservative approach, with reassurance and behavioural modification, can be considered in men with mild, non-bothersome LUTS and normal baseline investigations, as their risk of progression is low.^{9,10} Behavioural modifications include reducing diuretics (caffeine, alcohol), bladder irritants (acidic, spicy foods), evening fluid intake and constipation.^{9,10} Bladder training and pelvic floor exercises may improve bladder capacity and reduce storage symptoms. A yearly GP review of symptoms, with urinalysis and creatinine/eGFR, is suggested to monitor for progression.²

Medical therapy

Men with bothersome symptoms in the absence of complicating factors are appropriate candidates for a trial of medical therapy.⁶ Monotherapy is usually initiated with an alpha-adrenoceptor antagonist. Combined therapy with a 5-alpha reductase inhibitor (5-ARI) may further improve symptoms in men with large prostate volumes.

Alpha-adrenoceptor antagonists

Alpha-1 adrenoceptor blockade results in smooth muscle relaxation in the prostate and bladder neck.³ Uroselective agents, such as alfuzosin, silodosin, tamsulosin and terazosin, have been shown to produce comparable improvement in symptom score and maximal urinary flow rate with fewer systemic side effects.^{3,11} Prazosin is cheaper than other agents and is commonly used but has a less favourable side-effect profile and requires multiple daily dosing; thus, it is not recommended by international BPH guidelines.³

Men should be warned of the side effects of alpha-adrenoceptor antagonists, including retrograde ejaculation (higher with uroselective agents), erectile dysfunction, nasal congestion, hypotension, dizziness and tachycardia.¹ Caution is also required

in men considering cataract surgery, given the increased risk of floppy iris syndrome.^{3,12}

5-alpha reductase inhibitors

5-ARIs inhibit the conversion of testosterone to dihydrotestosterone (DHT) to reduce prostate growth and prostate volume.¹³ The most common 5-ARIs prescribed on the Australian Pharmaceutical Benefits Scheme (PBS) are dutasteride and finasteride. Dutasteride inhibits type 1 and type 2 isoenzymes of 5-alpha reductase, as opposed to type 2 inhibition alone with finasteride.¹⁴ 5-ARIs are most effective when prostate volume is >40 mL.⁵

The most common side effects of 5-ARIs are erectile dysfunction, decreased libido, decreased ejaculate and decreased sperm count.¹⁵ In contrast to the rapid onset of action of alpha-adrenoceptor antagonists, 5-ARIs can take several months before maximum improvement in symptoms is obtained.¹ Men should be warned that 5-ARI therapy can decrease PSA levels by approximately 50% after 6–12 months of treatment.^{16,17} As a result, in men on a 5-ARI, an increase in PSA above the nadir should prompt closer evaluation of PSA levels to exclude an upward trend suggestive of prostate cancer, rather than waiting for the PSA to be elevated outside the reference range before considering urological evaluation.

Table 1. Differential diagnoses for lower urinary tract symptoms

Benign and neoplastic conditions of the lower urinary tract	Neurological conditions	Other causes of lower urinary tract symptoms
<ul style="list-style-type: none"> • Urinary tract infection • Prostatitis • Bladder calculi • Interstitial cystitis • Urethral stricture • Phimosis • Overactive bladder syndrome • Prostate cancer • Urothelial carcinoma of the bladder including carcinoma in situ • Urethral cancer 	<ul style="list-style-type: none"> • Parkinson's disease • Stroke/cerebrovascular accident • Multiple sclerosis • Cerebral atrophy • Head injury • Spinal cord injury/surgery or degenerative disc disease • Prior pelvic surgery 	<ul style="list-style-type: none"> • Polyuria from renal or cardiac dysfunction • Nocturnal polyuria and sleep apnoea • Iatrogenic from medications

Combination therapy

Since 2016, tamsulosin plus dutasteride has been available to GPs to prescribe as a combined formulation without specialist approval.¹⁸ This fixed-dose combination is subsidised by the PBS and therefore available at a lower cost than both agents separately.²

Two randomised controlled trials of more than 3000 men compared combination therapy with monotherapy. Overall, combination therapy was superior to either alpha-adrenoceptor antagonist or 5-ARI therapy alone in improving LUTS and reducing progression.¹² For men with a prostate volume of >40 mL and a PSA of >1.5,

Table 2. The International Prostate Symptom Score⁴

Urinary symptoms over the past month (symptom score criteria)	Not at all	Less than one time in five	Less than half the time	About half the time	More than half the time	Almost always	
1. Incomplete emptying How often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5	
2. Frequency How often have you had to urinate less than two hours after you finished urinating?	0	1	2	3	4	5	
3. Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to push or strain to begin urination?	0	1	2	3	4	5	
	None	One time	Two times	Three times	Four times	Five or more times	
7. Nocturia How many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5	
Quality of life due to urinary problems							
	Delighted	Pleased	Mostly Satisfied	Mixed – about equally satisfied and unsatisfied	Mostly dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	0	1	2	3	4	5	6
The final score is the sum of questions 1–7							

combination therapy resulted in greater reductions in the risk of urinary retention or the need for surgery than monotherapy.¹⁹ However, urological opinion varies regarding balancing the benefit of combination therapy over monotherapy against the risk of increased sexual dysfunction.^{12,20}

Phosphodiesterase 5 inhibitors

BPE and erectile dysfunction can occur concomitantly, and phosphodiesterase 5 (PDE5) inhibitors (eg sildenafil) have been associated with some improvement in voiding symptoms.³ Though not traditionally recognised as a first-line

treatment option, several randomised controlled trials have shown that PDE5 inhibitors improve IPSS, symptoms and QoL, compared with placebo.³ Furthermore, the combination of an alpha-adrenoceptor antagonist and PDE5 inhibitor is superior to PDE5 inhibitor monotherapy.²¹

Table 3. Initial investigations in the general practice setting

Investigation	Reason for investigation	Comments
Urinalysis	Exclude leucocytosis, haematuria, proteinuria, pyuria and glycosuria	Follow up with urine culture if abnormality on urinalysis
Serum creatinine/estimated glomerular filtration rate (eGFR)	Exclude renal injury from primary renal dysfunction or high-pressure bladder outflow obstruction	Follow up with imaging if abnormal eGFR. Can be useful as a follow-up test if renal impairment is suspected
Urinary tract ultrasound	Assessment of prostate volume, bladder wall and residual urine; used to exclude hydronephrosis	Bladder scanners are available for general practitioner use to calculate residual volume, but a formal ultrasound requires a radiology unit
Prostate-specific antigen (PSA)	Exclude prostate cancer	Controversial; most guidelines recommend the use of serum PSA if prostate cancer diagnosis will influence management or if the test will assist in decision making

Triggers for urological referral

There are numerous clinical indications for urological referral including urinary retention, evidence of hydronephrosis on ultrasound, symptoms refractory to medical management, recurrent UTIs, gross haematuria, bladder stones, renal insufficiency or large bladder diverticula.^{1,2}

Surgical management

Endoscopic prostatectomy

Transurethral resection of the prostate (TURP) is the gold standard surgical treatment for symptomatic BPH. Risks are well established and include retrograde ejaculation, impotence, incontinence, urethral stricture, bladder neck contracture, bleeding or perforation of prostate capsule resulting in 'TURP syndrome'.¹ Laser vapourisation and enucleation treatments are also used because of shorter hospitalisation duration, shorter catheter time, lower transfusion rates and less clot retention, compared with a TURP; however, no difference in symptom improvement or QoL has been shown.²²⁻²⁴

Minimally invasive surgical therapy

Transurethral incision of the prostate involves an incision of the bladder neck without removal of prostatic tissue. It is used for men with small prostates and has outcomes comparable with TURP.¹ More recently, aquablation has served to reduce

the morbidity of traditional approaches, especially retrograde ejaculation and bleeding; however, longitudinal outcome data are limited.²⁵ The prostatic urethral lift procedure, which deploys adjustable implants to retract obstructing lateral prostatic lobes, was approved by the Therapeutic Goods Administration in August 2012 and has become a commonly performed day procedure.^{26,27} Patients are often catheter-free on discharge, and there have been no reported de novo cases of sexual dysfunction.²⁸ The prostatic urethral lift is usually unsuitable for men with urinary retention, obstructing median lobes or prostates >80 mL.²⁹

Conclusions

LUTS are a common reason for men to present for GP review. Uncomplicated LUTS and minimal bother warrant an initial conservative approach. Men with more bothersome symptoms can be initially managed with an alpha-adrenoceptor antagonist, while an additional 5-ARI can be considered for men with larger prostates. Surgery is recommended for men who are bothered by symptoms and fail to respond to medical management or have complications such as hydronephrosis, recurrent UTIs, progressive deterioration of residual volume, macroscopic haematuria or very poor maximum velocity on uroflow studies.

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