Urological Society of India: Indian Guidelines on Management of BPH/ BPO

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Introduction

a) Aims, Objectives and scope

Evidence based medicine has been defined as “the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients”. In the era of Evidence based medicine “high-quality healthcare implies a practice that is consistent with best available evidence”. However, obtaining and critically appraising the current evidence, as well as considering that evidence in the context of an individual’s circumstances, is beyond the time, skills, and resources of most clinicians. To overcome those limitations, clinical practice guidelines have been developed with the aim of providing “an evidence-based framework on which clinicians base their practice, with the purpose of reducing unwanted variations by setting agreed standards based on the best available evidence.

Lower urinary tract symptoms are quite common in ageing male and these do affect the quality of life (QOL). Previously more emphasis was on the pathology of the enlarged prostate i.e. benign prostatic hyperplasia (BPH). But currently the focus is shifted to management of LUTS rather than the pathology itself. The current guidelines try to devise evidence-based management of LUTS in ageing male. Although the letter "B" in BPH denotes a pathological terminology, these guidelines also attempt to address the management of non BPH causes of LUTS. In spite of objections by purists about the terminology, we have included terms BPH and bladder outlet obstruction BOO interchangeably sometimes in these guidelines(1). The proposed guidelines are pertaining more towards the ways and means of evaluating and managing clinical manifestations of men with benign prostatic hyperplasia (BPH) in form of lower urinary tract symptoms (LUTS) than the histopathological diagnosis. But we also would line to presume that other causes of LUTS like neurogenic voiding dysfunction, stricture urethra, osmotic diuresis, cancer of prostate etc. have been ruled out.

Disclaimer

The guidelines are limited to the scientific evidence available to the panel members. Many times, these guidelines take form of expert opinion. There is scarcity of Indian data on this subject of common importance. It is not necessary that following these guidelines will result in the best outcome. The guidelines do not override the decisions made by an expert clinician in given clinical scenario. These guidelines are meant to help a clinician and patient focus their plan of action in given circumstances. These guidelines should not be viewed as legal standards of care.

Methods

We performed a non-systematic review of the literature available on the subject. Majority of the search was done on Medline and Google scholar. No particular time frame was applied to the available literature. Literature published before 2000 was studied to see if it is relevant to the current practice and expert opinion regarding that issue was formed. These guidelines are a collection of various guidelines published on the subject. In addition, individual literature searches were made for different clinical scenario. Many of the studies, meta-analyses were combined in a simple narrative fashion. Best practice guidelines for these cases were decided by the panel members looking at the available literature and expert opinion and experience of the panel members.

Systematic cost analysis of different treatment modalities was not performed. There is a vast difference between cost of treatment in developed world, where majority of literature comes from, and India. In

India, we do not have uniform healthcare infrastructure. Moreover, in India the cost of medicines as well as surgical procedures do vary. So, relevance and applicability of these guidelines would also vary amongst many Indian practitioners and patients. These guidelines should not be viewed as legal standards of care.

Defining the disease and the patient:

Benign Prostatic Hyperplasia (BPH):

A histological diagnosis that refers to the hyper-proliferation of smooth muscles and glandular epithelial cells in transition zone of prostate gland caused by complex cellular alterations.

Bladder Outlet Obstruction (BOO):

It is the generic term indicating obstruction during voiding characterized by increased detrusor pressure and decreased urine flow rates, clinically presenting as lower urinary tract symptoms.

Lower Urinary Tract Symptoms (LUTS):

A variety of symptoms of storage failure, voiding failure and post-micturition symptoms that result from variety of complex and dynamic interactions between bladder, prostate and urethra as well as a result of several systemic diseases and neurological conditions.

Definition of the guidelines:

Clinical practice guidelines are defined as systematically developed statements designed to assist clinicians in taking appropriate and evidence based decisions to provide optimum healthcare for specific clinical conditions in given circumstances.

Level of recommendations:

Strong Recommendations: (Strong)

They are directive statements that an action should or should not be undertaken because net benefit or net harm is substantial.

Moderate Recommendations: (Optional)

They are directive statements that an action may or may not be undertaken because net benefit or net harm is equivocal.

Weak / Conditional Recommendations: (Selective)

They are nondirective statements used when net benefit or net harm of taking an action is justified only in selective circumstances.

Diagnostic workup

Medical History

Focused medical history regarding urinary tract should be taken. General medical issues which cause bladder dysfunction or impair response to medical or surgical treatment (bowel habits, neurologic conditions, psychiatric conditions, diabetes, cardiac diseases or impaired mobility) should be evaluated. Drug intake (diuretics, antidepressants, anti-histaminic, bronchodilators, anticholinergics, cough suppressants, sympathomimetics and antihypertensives), social or psychological which might have impact on LUTS should be evaluated. In addition, relevant medical history regarding dementia, anxiety and depression should be taken(2).

Recommendation	Recommendation Level
Take a complete medical history from men with LUTS.	Strong

Recommendation taken from EAU guidelines(3)

Symptom assessment

Symptom assessment by a validated symptom score system should be taken. The various symptom score systems used are

American urological association symptom index (AUA-SI):

This index includes seven questions covering incomplete emptying, frequency, intermittence, urgency, weak urinary stream, straining and nocturia. First time published in 1992 (4). This index is clinically sensible, reliable, valid and responsive. This is the most commonly used symptom score in India and is recommended for routine use.

The International Prostate Symptom Score (IPSS):

This is an 8-question index. The first seven questions are as AUA-SI and the last question is a QOL question. This 8th question was added later. World Health Organization International Consultation on BPH adopted it and labeled it the IPSS(5)(6). This is graded as asymptomatic 0/35, mild symptoms 1-7/35, moderate symptoms 8-19/35, severe 20-35/35.

The International Consultation on Incontinence Questionnaire (ICIQ-MLUTS)

This symptom scale contains thirteen items covering hesitancy, straining to continue urination, strength of stream, intermittency, incomplete emptying, urgency, urge urinary incontinence, stress urinary incontinence, unexplained urinary incontinence, nocturnal enuresis, post micturition dribble, nocturia and frequency. This questionnaire is derived from ICSMaleSF questionnaire (7). Its validity, reliability and responsiveness has been established (8). This symptom scale is not commonly used in India.

Danish Prostate Symptom Score (DAN-PSS)

This is mainly used in Denmark and Finland(9). Not used in India. Hence not discussed here.

Visual Prostate Symptom Score (VPSS)

IPSS is a patient administered questionnaire. Grade 6 reading level by American educational standards is necessary to understand the IPSS. Many men require assistance in filling up the IPSS forms. IPSS has been translated to many languages. These translations require separate validation. As an alternative to IPSS, van der Walt et. al. (10) developed a visual prostate symptom score. In VPSS frequency, nocturia, weak stream, and quality of life (QoL) are included in form of pictograms. This can be filled by illiterate people also and correlates well with IPSS and uroflowmetry parameters of average and maximum flow(10). Roy et. al. (11) validated the VPSS in Indian rural population and found it to correlate with IPSS. The VPSS is especially useful for symptom assessment in illiterate people or people with limited education. This symptom scale may be used in literate patients.

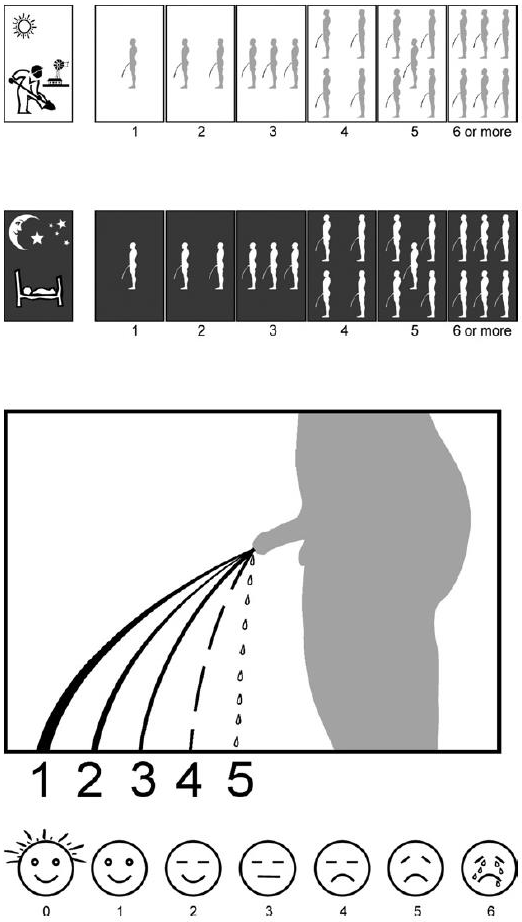


Figure 1. Visual Prostate Symptom Score (VPSS) pictograms in which the patient indicates his urinary frequency during the day (question 1) and night (question 2), his assessment of the force of his urinary stream (question 3), and his feelings about his bladder symptoms (quality of life question). Reprinted with permission, Stellenbosch University © 2011. All Rights Reserved.

taken from van der Walt et. al. (10).

Concerns regarding use of Symptom score:

There are many symptom scores to choose from. The symptom score evaluation is a subjective one which can be influenced by educational status of a patient. An objective variant of symptom score evaluation has possibility of a biased result.

Recommendation	Recommendation Level
Use a validated symptom score questionnaire in initial evaluation and follow up of men with LUTS.	Strong

Visual Prostate Symptom score may be used in illiterate patients	Conditional

Frequency volume charts and bladder diary

Frequency volume chart (FVC): “this records the voided volumes as well as the time of each micturition, day and night, for at least 24 hours.” Preferably for 3 days (12)

Bladder diary: “this records the times of micturition and voided volumes, incontinence episodes, pad usage and other information such as fluid intake, the degree of urgency and the degree of incontinence.”(12) Bladder diary is essential in evaluation of men with storage symptoms. Nocturnal polyuria can be diagnosed by bladder diary only. The recommended duration of FVC is three or more days(13). The compliance of a patient is a strong inhibitory factor. Limiting the duration of bladder diary to 3 days helps in negating the compliance issue.

Recommendation	Recommendation Level
Use bladder diary (for three or more days) in men with storage predominant symptoms	Strong

Physical examination

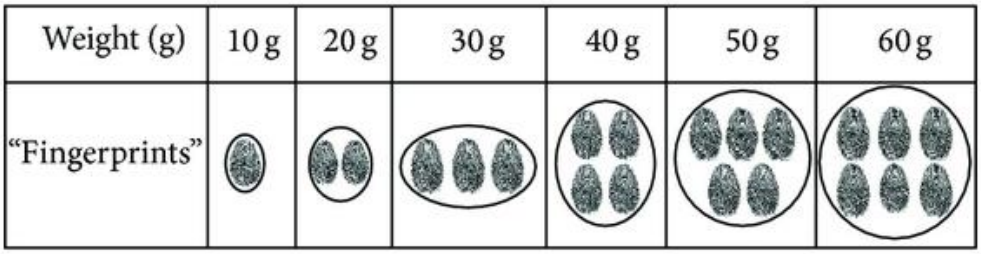
“Physical examination particularly focusing on the suprapubic area, the external genitalia, the perineum and pedal edema should be performed. Urethral discharge, meatal stenosis, phimosis and penile cancer must be excluded.”(3).

Digital Rectal Examination

Digital rectal examination (DRE) is an inexpensive and essential examination in the initial evaluation of BPH. DRE is used as a clinical tool to estimate prostate size and consistency as well as the neurological function of the lower urinary tract. However, DRE correlates poorly with prostate size. When compared with radical prostatectomy specimens, the accuracy of DRE was found inferior to trans-rectal ultrasound (TRUS). This discrepancy was larger in smaller prostates(14). Volume of the examined prostate and observer’s index finger also have an important impact on the accuracy of DRE(15). In the study by Loeb (14) et. al. DRE was performed by multiple examiners and the procedure of DRE was not standardized.

Reis et. al. (16) reported their study on standardized DRE by medical students and found that standardized DRE can be used as a clinical tool to classify the patients and guide therapeutic option of needing 5 alpha reductase inhibitor treatment even in inexperienced hands. They inferred that although DRE assesses only the posterior surface area of the prostate, it correlates well with overall prostate volume. Each fingertip area of the posterior surface of prostate was considered equivalent to 10 cubic centimeters (cc) of the prostate. (See figure below)

Proportion: weight (g) × DRE surface (area)



DRE = digitalrectalexamination

Recommendation	Recommendation Level
Perform physical examination and DRE in evaluation of males with LUTS	Strong

Urinalysis

Urine analysis is included as an important test in evaluation of male LUTS in all guidelines. The role of urinalysis in evaluation of men with LUTS without acute frequency and dysuria has been questioned in a prospective blinded observational cohort study by Khasriya et al(17). The authors also recommended routine urinalysis be abandoned. In a recently published work, Lowe et al(18) analyzed three studies carried out to evaluate feasibility of offering over the counter (OTC) tamsulosin. Dipstick urinalysis was conducted as a safety measure not to miss medically important conditions. Dipstick urinalysis identified relatively few undiagnosed non BPH medically important conditions. Authors concluded that urinalysis may not be an effective screening method for men with LUTS (bothersome LUTS included) (18). However, causes of male LUTS other than BPH may need different types of treatment and sometimes

can be troublesome. Urinalysis helps to identify issues like urinary tract infection, diabetes mellitus, and hematuria. It is cheap and easily available. The panel recommends routine use of urinalysis in men with LUTS.

Recommendation	Recommendation Level
Do urinalysis in evaluation of males with LUTS	Strong

Prostate Specific Antigen (PSA)

Serum PSA increases with age and with increasing prostate volume. Both PSA and prostate volume have a log linear relationship with age. Older patients have a steeper rise in prostate volume and PSA than younger men. In men with BPH without prostate cancer, serum PSA has a strong correlation with prostate volume. PSA values of >1.6ng/mL, >2.0ng/mL and >2.3ng/mL correlate with prostate volume of >40mL in men in 50s, 60s, and 70s respectively with specificity of 70% and sensitivity between 65 to 70% (19). Similar results were obtained from a large study of 34857 men in Korea (20). The correlation between free PSA and prostate volume is stronger than the correlation between total PSA and prostate volume (21)(22). PSA value is also a predictor of acute urinary retention (AUR) and BPH related surgery(23).

Different international guidelines have varying recommendations on advising PSA in men with LUTS due to BPH(2). But most of the guidelines recommend a PSA test

- If PSA is going to change the management plan
- If the predicted life expectancy is more than 10 years
- If knowledge of presence of prostate cancer may change the management plan

Recommendation	Recommendation Level
Serum PSA test is optional in evaluation of males with LUTS suspected to be due to BPH	Strong
Serum PSA should be done: if it is going to change the management plan, if life expectancy is more than 10 years and if diagnosis of prostate cancer would alter the management plan	Strong

Renal Function assessment

Renal function is usually assessed by doing serum creatinine estimation (and estimated glomerular filtration rate, eGFR). The risk factors for impaired renal function in these patients are: decreased maximum flow rates, diabetes and hypertension (3). NICE guidelines recommend serum creatinine test only if renal impairment is suspected on clinical grounds like palpable bladder, nocturnal enuresis, recurrent urinary tract infections or history of urinary calculi (24). Routine performance of renal function tests in all the patients presenting with LUTS may be an unnecessary over-investigation in 89-90 % patients.

Recommendation	Recommendation Level
Assessment of renal function should be done **1. If renal function impairment is suspected on history and clinical examination** **2. In presence of hydronephrosis** **3. When surgery is contemplated for BPH** **4. If patient has diabetes or hypertension**	Strong

Uroflowmetry

Uroflowmetry is a commonly used noninvasive office urodynamic test. Maximum flow rate (Qmax) of less than 10 mL/s has specificity of 70%, a PPV of 70%, and a sensitivity of 47% for diagnosis of BOO(25). Qmax more than 15 mL/s is usually considered “normal”, but does not entirely rule out BOO. In addition to BOO, low Qmax can be due to detrusor underactivity or inadequately filled bladder. As a diagnostic test uroflowmetry has limited value (3). High quality evidence regarding the role of uroflowmetry in BPH is lacking (26).

Recommendation	Recommendation Level
Perform uroflowmetry in the initial evaluation of Male LUTS	Conditional/ selective

Ultrasound: Abdominal and Transrectal (including post void residual urine measurement)

Post void residual urine (PVR) measurement by bladder scan and catheterization is not routinely practiced in India. Rather abdominal ultrasound is widely available, hence the panel decided not to discuss PVR by bladder scan but concentrate on PVR by abdominal ultrasound.

Men with LUTS are not at increased risk of upper tract malignancies or abnormalities. Upper tract evaluation is warranted in the setting of large PVR. A longitudinal study (27) of 529 men followed over 12 year period revealed progressive bladder dysfunction in community dwelling men. Persons with AUA score of >7 were more likely to have increase in PVR. Correlation of raised PVR and UTI and severity of LUTS is not clear. There is little correlation between PVR and bladder outlet obstruction. A recent study by Peterson et. al. (28) did not find significant differences in PVR among patients with LUTS and asymptomatic participants. However, almost half of the participants in the study group were female.

In day-to-day practice, prostate imaging is routinely performed by transabdominal (TAUS) or transrectal ultrasound (TRUS). It is commonly stated that TRUS is more accurate than TAUS in predicting the adenoma volume enucleated during the open surgery (29). In this study, TRUS slightly underestimated the prostate weight by 4.4%. Whereas TAUS overestimated it by 55.7%. In this study the TAUS imaged the prostate as whole including the adenoma and capsule. TRUS imaged the transitional zone of the prostate, so such a disparity was expected. However, when the whole prostate gland is imaged by either TAUS or TRUS route and correlated with radical prostatectomy specimen, prostate weight estimated by TAUS and TRUS are not significantly different (30)(31)(32). With this evidence, we must consider both TAUS and TRUS as equivalent so far as the weight of whole prostate gland is considered. TRUS has a better role than DRE for estimation of prostate weight.

Prostate ultrasonography is also helpful in estimating intravesical prostate protrusion (IPP). IPP is graded as mild (<5mm), moderate (5-10mm) and severe (>10mm). IPP correlates with the degree of bladder outlet obstruction (33)(34)(35). Korean(36) and Singapore(37) BPH guidelines recommend measurement of IPP on ultrasound. IPP correlates with the degree of prostatic obstruction, likelihood of successful voiding after trial of voiding without catheter (TWOC) and progression of BPH. IPP can be measured by TAUS as well as TRUS. In addition, prostate ultrasound also measures other parameters like Presumed circle area ratio (PCAR), Prostate Urethral angle (PUA), BWT (Bladder wall thickness), ultrasound estimated bladder weight.

Recommendation	Recommendation Level
Measure PVR in men with LUTS	Conditional/ selective
Perform Ultrasound for upper tracts in men with LUTS	Conditional / Selective
Perform prostate ultrasound for prostate size if it will change the medical management	Optional
Perform prostate ultrasound before deciding the surgical management in BPH	Strong

Computed Tomography and Magnetic resonance Imaging

CT and MRI are not routinely performed in evaluation of male LUTS.

Voiding Cystourethrography

VCUG is not routinely performed in evaluation of men with LUTS. VCUG has a role if reflux, diverticulum or urethral stricture is suspected

Urethrocystoscopy

The most accepted indications for urethrocystoscopy in men with LUTS are microscopic or gross hematuria, urethral stricture, or bladder cancer. However, there is no strong association between cystoscopy findings and urodynamic observations. In a large study (38) comprising 492 patients, authors evaluated urethrocystoscopy findings and urodynamic findings in men with LUTS. They reported significant correlation between bladder trabeculations and grade of bladder outlet obstruction. Prostatic occlusion of the outlet and median lobe correlated with grade of obstruction. It is interesting to note that bladder outlet obstruction was found in 15% of the patients with normal cystoscopy findings.

The conclusive test for diagnosing bladder outlet obstruction is urodynamics. In India the urodynamic testing is not widely available. Many urologists still depend on cystoscopy to diagnose bladder outlet obstruction and it does correlate with urodynamics in substantial number of patients. This may not be of value in an individual patient. Finally, the panel feels that cystoscopy does have a role to play in diagnosis of bladder outlet obstruction. It does give additional information about bladder pathologies and plays a role in deciding the mode of surgical therapy for BPH.

Recommendation	Recommendation Level
Perform urethrocystoscopy in men with LUTS if it may change the plan of action	Conditional / Selective
Perform urethrocystoscopy before minimally invasive or surgical therapy for BPH	Conditional / Selective
Perform urethrocystoscopy for diagnosis of bladder outlet obstruction when urodynamics testing is not available or not feasible (if there is diagnostic uncertainty and surgical therapy is contemplated)	Conditional / Selective
Perform urethrocystoscopy in men with LUTS if they have haematuria, suspected stricture or suspected bladder cancer	Strong

Urodynamics (UDS)

Filling cystometry and pressure flow studies (PFS) are the mainstay of UDS in men with LUTS. UDS is considered definitive objective diagnostic test for bladder outlet obstruction. In this study urodynamic Qmax and detrusor pressure (Pdet) at Qmax are measured. Pdet and Qmax are used to calculate bladder outlet obstruction index (BOOI). High pressure low flow micturition pattern when the BOOI is >40 is diagnosed as obstruction (39). A Cochrane meta-analysis (40) evaluated the effect of performing UDS on the number of men with continuing voiding symptoms. This included 339 men. UDS did change the clinical decision making, but the evidence whether this led to reduced voiding symptoms after treatment was lacking.

A systematic review and meta-analysis of 19 articles including 2321 patients was published in 2017 (41). Twelve studies in this meta-analysis were retrospective and 9 were non-randomized prospective. There was no randomized prospective study in this analysis. In UDS proven BOO patients, the outcome of surgical and other therapies was better in form of improvement in IPSS, QoL score, PVR and Qmax as compared to non-BOO patients. Preoperative UDS may predict better understanding of post-operative outcomes.

The main purpose of UDS is to differentiate bladder outlet obstruction (BOO) from Detrusor underactivity (DUA). UDS is an invasive test. It is usually reserved for men in whom conservative treatment has failed. Robust evidence supporting the utility of UDS in evaluation of BOO is lacking. Moreover, UDS is not freely available in India. The panel was unable to recommend any strong indications for performing UDS in men with LUTS. UDS is usually performed in following conditions(3)(42):

Recommendation	Recommendation Level
Perform UDS in men with LUTS in following situations	
Only if there are specific indications for evaluation of underlying pathology	Conditional / Selective
Unsuccessful invasive treatment of BPH	Conditional / Selective
Voided volume <150 ml	Conditional / Selective
Bothersome voiding symptoms with Qmax >10ml/s	Conditional / Selective
Men with bothersome voiding symptoms with PVR >300 ml	Conditional / Selective
Men >80 years with bothersome voiding symptoms when invasive treatment is planned	Conditional / Selective
Men<50 years with bothersome voiding symptoms when invasive treatment is planned	Conditional / Selective

Conservative Management

Watchful waiting

Many men with non-bothersome mild symptoms can be observed as the disease is slowly progressive. Moreover, the symptoms do fluctuate with time. In men with non-bothersome symptoms, progression to AUR and complications is rare (43)(44). One of the concerns about watchful waiting is that it may delay the effective treatment. Flanigan (45) et. al. reported greater improvements in Qmax and IPSS in patients who underwent immediate TURP vs watchful waiting, in patients with moderate LUTS. Baltimore longitudinal study (46) of ageing identified following risk factors for risk of AUR and need for surgery

- Change in size and force of urine stream
- Sensation of incomplete emptying
- Enlarged prostate on DRE

Recommendation	Recommendation Level
Offer watchful waiting for men with non-bothersome mild to moderate symptoms	Strong

Behavioral, dietary and Lifestyle Modification

Patient should be educated about the disease and reassured that cancer is not the cause of his trouble.

Various lifestyle modifications suggested are(47)

- Obesity: Obesity is associated with large prostate size, progression of BPH and poor response to 5 alpha reductase inhibitors treatment. Weight loss may improve LUTS but robust studies are lacking
- Diet: Diets that increase the risk of LUTS: red meat, fat, cereals, bread, poultry and starch; Diets that decrease the risk of LUTS: total protein, dairy, vegetables, fruits, polyunsaturated fatty acids, linoleic acid, carotenoids, vitamins A, C and D
- Physical activity: Moderate to vigorous physical activity decreases the risk of LUTS, lowers the risk of nocturia
- Fluid intake: Drink most liquids during the day, fluid restriction after dinner, reducing or eliminating caffeine, alcohol restriction (48)
- Management of constipation

Self-management(48) like lifestyle modification, specific behavioral modification like bladder retraining, double voiding and urethral milking reduce the risk of treatment failure.

Recommendation	Recommendation Level
Offer lifestyle advice to all men with LUTS	Strong

Pharmacological Management

Alpha blockers

It is generally presumed that alpha blockers act by decreasing the smooth muscle tension in prostatic stroma, bladder neck and urethra. However, this has been questioned (49). Approximately 4-6-point improvement in IPSS score is expected with alpha blockers. The alpha blockers available for treatment of BPH are prazosin, alfuzosin, doxazosin, terazosin, tamsulosin, silodosin and naftopidil. Alpha blockers are efficacious in improving both storage and voiding LUTS.

Djavan et. al. (50) published a state of the art article on efficacy and tolerability of alpha blockers. They reviewed placebo controlled and some direct comparisons between alfuzosin, terazosin, doxazosin and tamsulosin. There was no study with silodosin in this review. There was around 30-45% improvement in symptom score and 15-30% improvement in Qmax. All these alpha blockers had similar efficacy. Another meta-analysis (51) on this topic reiterated that the clinical efficacy all alpha blockers (terazosin, doxazosin, alfuzosin, tamsulosin) is similar. One more systematic review and meta-analysis of 17 studies of 656 patients (39) found that alpha blockers improve the LUTS mainly by reducing the detrusor pressure at maximum flow rates (Pdet at Qmax). In patients presenting with urodynamic obstruction, this effect is higher. The mean change in the BOOI was -14.19.

Naftopidil is currently available in Asian countries. A Cochrane meta-analysis (52) regarding naftopidil reported similar effects in symptom scores and QOL compared to tamsulosin or silodosin. Singh et. al. (53) reported a prospective randomized non-placebo controlled study to compare tamsulosin and naftopidil in Indian patients. Both the drugs were equally effective and safe. Naftopidil appeared to have earlier onset of action and was better in storage sub-scores. Postural hypotension, headache was more common in in tamsulosin group. But this effect was not statistically significant. Another study by Griwan (54) et al, reported similar efficacy of naftopidil and tamsulosin.

Onset of action

Drug with rapid onset of action may be warranted in situations like impending retention of urine or when TWOC is planned. Tamsulosin has a more rapid onset of action than terazosin (50). It is possible that the time lost in dose titration with terazosin might be partly responsible for this. Silodosin has been demonstrated to be efficacious within 2-4 hours of administration (55).

Which alpha blocker is more efficacious?

None of the officially recognized guidelines make any specific recommendations on the choice of any particular alpha blockers. Direct comparisons among different alpha blockers are scant and are limited to small studies. Meta-analysis by Fusco et. al. (39) reported highest level of BOOI improvement with silodosin. The mean BOOI changes observed in this meta-analysis (in increasing order of improvement) were terazosin -6.69; tamsulosin -14.27; alfuzosin -14.88; naftopidil -16.47; doxazosin -19.41; silodosin -30.45. It is possible that silodosin having high pharmacologic selectivity of alpha 1 a receptor subtype might be responsible for this superiority. How this UDS superiority of silodosin reflects in clinical improvement needs further assessment.

In a short term randomized crossover study (56) comparing efficacy of silodosin and tamsulosin reported significant improvement in patients crossed over to silodosin from tamsulosin group. While crossover from silodosin to tamsulosin group showed either worsening or little improvement. However, the dose of tamsulosin used was 0.2mg once daily and silodosin was used at 4 mg twice daily. In routine practice tamsulosin is prescribed at 0.4mg once daily and silodosin is prescribed at 8mg once daily. So the panel suggests that the findings of this study should be interpreted with caution.

Another comparative study (57) of tamsulosin vs silodosin from a tertiary hospital in Tamil Nadu, India, reported similar efficacy in terms of IPSS improvement. In this study, ejaculatory dysfunction was observed only with silodosin and postural hypotension only with tamsulosin. The study included 57 patients followed over a period of 12 weeks. A randomized, comparative, open-label study (58) of efficacy and tolerability of alfuzosin, tamsulosin and silodosin was reported from a tertiary care hospital in Karnataka, India. This study reported similar efficacy and tolerability of these three molecules. Some patients on tamsulosin had QTc prolongation which has not been reported previously. Another double blind RCT from Karnataka, India, (59) comparing tamsulosin, alfuzosin and silodosin as monotherapy reported rapid onset of action with silodosin, also silodosin was found to be most efficacious. Interestingly dizziness was found to be more common (but statistically insignificant) with silodosin in this study. In a review article Lepor (60) commented that of all the alpha blockers, therapeutic effect on LUTS is greatest with silodosin. Maximum clinical efficacy with minimal adverse effects (except for ejaculatory dysfunction) is a hallmark of silodosin.

Considering that these drugs are used on long term basis, financials aspects should be taken into consideration. Choice of the drug should depend on socioeconomic profile, availability of the drug and clinician's experience. The newer and costly drugs should be chosen if the adverse effect profile of these drugs fits the clinical scenario. Cheaper drugs, if effective in a particular patient, may be a more financially viable alternative (61).

Ejaculatory dysfunction:

In placebo-controlled studies, incidence of abnormal ejaculation with alfuzosin (ER: extended release), doxazosin, and terazosin was around 1%, comparable to, or marginally greater than with placebo. Whereas with tamsulosin it was reported to be between 4%-5% and 6%-11% (50). A meta-analysis (51) reported low but statistically significant risk of abnormal ejaculation with tamsulosin and terazosin but not with alfuzosin. In a randomized double-blind cross over trial of silodosin use in 15 healthy male volunteers, all patients had complete lack of ejaculation with silodosin use. But all of them felt the

orgasm despite anejaculation. Most of them felt mild discomfort during orgasm and were greatly dissatisfied with anejaculation (62). Roehrborn et. al. (63)reported that the men experiencing ejaculatory dysfunction were the men who had greatest symptomatic improvement. A randomized trial comparing silodosin and tamsulosin in Indian patients was reported by Pande et. al. (64). Tamsulosin and silodosin were equally effective. Ejaculatory problems were more in silodosin group. However, in this trial the drugs used were the marketed brands of the drugs. The medications were removed from original packing and repacked, so blinding might be an issue. Moreover, the scale used for sexual function assessment is not clear from the article. In younger sexually active patients, it would be prudent to use drugs with less ejaculatory dysfunction.

Dizziness, Postural hypotension

All alpha blockers cause dizziness and postural hypotension. Terazosin and doxazosin have incidence rates of these adverse events greater than placebo, whereas alfuzosin (ER) and tamsulosin had these rates comparable or slightly greater than placebo. Percentage of patients discontinuing the drugs because of these adverse events was also more with terazosin and doxazosin than tamsulosin and alfuzosin (50).

Patients who are very old, or those with cardiovascular co-morbidities and the patients with mobility issues or high fall risks should be monitored meticulously while on alpha blocker treatment (61). A meta-analysis regarding vascular-related safety profile of alpha blockers found that the risk of vascular-related adverse events were least with tamsulosin (comparable to placebo) when compared to terazosin, doxazosin, alfuzosin (51). In a structured literature review Capitanio et. al. (55) reported that there is no increased risk of orthostatic hypotension in patients receiving silodosin and concomitant antihypertensive medications. As the patient population in whom these drugs are used are old, drugs which have less vasodilatory adverse events may be preferred.

Concomitant use of two alpha blockers or other antihypertensive drugs

Selective alpha1 blockers like prazosin are sometimes used as antihypertensive medicines. Such patients might be prescribed selective alpha 1a blockers (silodosin, tamsulosin) for LUTS. Additive pharmacodynamic effects might be experienced in these patients. There is a possibility of increased risk/ severity of adverse events. (65)(66). Co-administration of tamsulosin with nifedipine or enalapril or atenolol has been studied in a randomized placebo-controlled study. No significant effects on the action of antihypertensive drugs or blood pressure or adverse events were seen (67). There is no clinical data

available regarding the co-administration of two alpha blockers. Panel feels that it is better to avoid concomitant prescription of two alpha blockers.

How long can alpha blockers be given? How to monitor the treatment?

Several studies have demonstrated sustained efficacy of alpha blockers over six years. Since these drugs do not decrease prostate size and do not alter the disease progression, the patients on alpha blocker therapy should be regularly monitored when alpha blockers are used as a monotherapy. This is quite relevant for men with high risk of disease progression without bothersome symptoms (68). In an opinion regarding the use of alpha blockers, KT Foo has opined that the alpha blockers should be used for short periods and may be withheld when the LUTS are not bothersome (68). Panel also feels that the alpha blockers can be withheld if the LUTS are not bothersome.

Intra-operative floppy iris syndrome (IFIS)

IFIS is poorly dilating iris during cataract surgery. It has been reported in patients receiving alpha blocker treatment for BPH. Tamsulosin is maximally associated with this complication. But IFIS has been reported after alfuzosin, doxazosin and saw palmetto too. The exact mechanism is not known. It is not clear whether tamsulosin withdrawal reduces the risk of IFIS. If a patient is scheduled for cataract surgery in recent future, it would be prudent not to start him on Tamsulosin (or other alpha blockers) (69).

Alpha blockers prior to Trial of voiding without catheter (TWOC) for acute urinary retention

Fisher and colleagues(70) published a Cochrane review of nine randomized trials regarding the use of alpha blockers for successful resumption of voiding following catheter removal for acute retention. Alfuzosin, tamsulosin, silodosin and doxazosin have been studied in this regard. There is some evidence to suggest that alpha blockers increase the success of TWOC. Moderate quality statistically significant evidence was noted in favor of alfuzosin, tamsulosin and silodosin, though not for doxazosin. The drugs were given for one to three days or for eight to 32 days prior to TWOC in various trials included in this review. It is generally suggested that the drugs should be given for at least three days.

Recommendation	Recommendation Level

Offer Alpha blockers to men with moderate to severe LUTS	Strong
Alpha blockers can be prescribed irrespective of prostate volume	Strong
Silodosin may be prescribed preferentially in patient with nocturia*	Conditional / Selective
Tamsulosin or Silodosin may be the preferred drugs in patients receiving concomitant antihypertensive drugs and at higher risk of orthostatic hypotension*	Conditional / Selective
Alfuzosin may be preferred in young sexually active patients who wish to preserve antegrade ejaculation*	Conditional / Selective
Alpha blockers, especially tamsulosin, might be avoided in patients scheduled for cataract surgery in near future till the cataract surgery is performed*	Conditional / Selective
Concomitant use of two alpha blockers should be avoided*	Conditional / Selective
Silodosin may be considered a second line drug in patients not satisfied with other alpha blockers either because of efficacy or tolerability*	Conditional / Selective
Naftopidil may be considered in patients with predominant storage symptoms*	Conditional / Selective
Use alpha blockers for three or more days prior to trial of voiding without catheter in acute retention due to BPH	Optional

*Low quality evidence regarding these statements.

5 Alpha Reductase Inhibitors (5ARI)

The 5ARIs available for clinical use are Finasteride and Dutasteride. Finasteride inhibits only 5 alpha reductase type 2. Dutasteride inhibits both the type 1 and type 2 isoforms of the enzyme. Compared with finasteride, dutasteride provides more complete and sustained inhibition of serum dihydrotestosterone (DHT)(71).

The greatest risk factor for progression of BPH is the prostate size. Compared with men with prostate size less than 30 mL, men with prostate volumes of more than 30 mL have 3-4 times higher likelihood of moderate to severe LUTS, 2-3 times higher risk of decreased Qmax and 3-4 times more risk of developing AUR(72). Of all the medications available for BPH treatment only 5ARIs have shown to decrease the prostate volume (73). In MTOPS trial (74), the baseline predictors of increased risk of BPH progression were: prostate volume > 30 g, PSA >1.5 ng/mL, Qmax <10 mL/s, PVR >38 mL, and age >62 years. 5ARIs act by reducing the prostate size thereby improving symptoms and increasing the flow rates. They decrease the prostate size by 18-28% and decrease the circulating PSA by around 50% after six to twelve months of treatment (71). It takes at least six to twelve months to demonstrate beneficial clinical effects relative to placebo. In trial of > 1 year duration, finasteride consistently improved the IPSS and decreased the risk of BPH progression (75).

Boyle et. al. (76), in a meta-analysis of six trials pooling 2601 men, reported that men with larger baseline prostate size benefitted most from finasteride. PLESS (77), a multicenter randomized controlled trial enrolled 3040 men with average prostate size of 55 gram followed over four years, found reduced prostate volume by 18%, 2.6 point improvement in IPSS, improvement in Qmax by finesteride. The most important finding of this study was significant reduction in the risk of AUR and BPH related surgery in finasteride group vs placebo. ARIA trial (78), wherein 4325 men with IPSS>12, Qmax <15mL/s, prostate volume >30gm, PSA 1.5-10.0 ng/mL on dutasteride vs placebo followed for 24 months, reported reduction in prostate volume, symptoms, improvement in flow rates. There was significant reduction in the risk of AUR and BPH related surgery. Further continuation of this trial (79), wherein 1188 men were enrolled in open labelled two year continuation, reported a very low rate of AUR and BPH related surgery in dutasteride group. Surprisingly, dutasteride alone (and not finasteride) is approved for clinical use in Japan (80), so Japanese guidelines do not recommend use of finasteride.

Both these drugs are well tolerated. Number of withdrawals from treatment are similar to placebo group. The side effects reported with finasteride are impotence, low libido, decreased ejaculate volume, ejaculation disturbance, breast engorgement, breast tenderness (77). Similar effects are noted with dutasteride. In the 4 year trial of Dutasteride (79), although the rate of gynecomastia was relatively constant, the rate of newly reported sexual disturbances decreased with time. Compared with doxazosin and terazosin, finasteride has significantly lower risk of dizziness, asthenia, postural hypotension (75). Although these drugs are for use in men, women who are pregnant or likely to become pregnant should not handle crushed tablets of finasteride or dutasteride due to potential risk to male fetus (81)(82). These drugs should not be used in men without prostatic enlargement(83).

Recommendation	Recommendation Level
Offer 5 alpha reductase inhibitors to patients with moderate to severe LUTS with prostatic enlargement	Strong
Inform patients about the delayed onset of action (3-6 months)	Strong
Do not use 5 alpha reductase inhibitors in patients with LUTS without prostatic enlargement	Strong

Combination therapy (Alpha Blockers and 5 alpha reductase inhibitors)

Alpha blockers have a quick onset of action as compared to 5ARI. On the other hand, 5ARI are the drugs which decrease prostate size and reduce risk of disease progression like AUR and BPH related surgery. MTOPS (74) trial, which studied doxazosin alone vs finasteride alone vs combination therapy, reported that the risk of clinical progression was less by 66% with combination therapy. Whereas it was less by 39% with doxazosin alone and by 34% with finasteride alone. In this trial the risk of clinical progression was defined as IPSS increase of > 4 points, AUR, incontinence, renal insufficiency, or recurrent urinary tract infections. Similarly Combination of Avodart and Tamsulosin (CombAT) trial (84) was reported in 2010. This trial examined the effect of dutasteride and tamsulosin in combination and alone. In CombAT, 4844 men were enrolled and 3195 were followed through for 4 years. The primary endpoints evaluated were AUR and need for BPH related surgery. In this trial also, combination therapy reduced the risk AUR or BPH related surgery by 66% compared to tamsulosin alone. When compared to dutasteride alone the risk reduction was by 20%. In addition, the combination therapy did show significant reduction in IPSS compared to either drug alone.

In contrast VA (85) trial (terazosin vs finasteride vs combination) as well as PREDICT (86) trial (doxazosin vs finasteride vs combination) did not show superiority of the combination therapy over alpha blocker monotherapy. But these trials included patients with smaller prostates where finasteride may not show desired benefits. In VA trial the mean prostate volume was 37 cc. In PREDICT trial the baseline prostate volume just 36 cc. The study duration was one year. The end points did not include disease progression (risk of AUR and BPH related surgery). In this situation, the finasteride would not have any meaningful chance to show improvement. Both VA and PREDICT trials enrolled all men with clinical BPH. Whereas MTOPS and CombAT trials included men with clinical BPH and large prostates, a subset likely to respond to 5ARI. This observation has been argued in another way by Lepor (60). According to him, to prevent one man from needing invasive therapy for BPH, we have to treat 29 men with combination therapy for 4.5 years. To prevent one man from developing AUR, we have to treat 56 men with combination therapy for 4.5 years. And to prevent one man from developing symptom progression, we have to teat 12 men with combination therapy for 4.5 years.

A meta-analysis of RCTs of tamsulosin vs combination of tamsulosin + dutasteride was reported by Zhou (87). Five studies including total of 4384 patients followed for one year or more were included. The combination therapy demonstrated a preferable therapeutic effect. Sexual side effects were higher with

combination therapy. As expected, combination therapy markedly reduced the disease progression in form of AUR and BPH related surgery.

In Indian setting, if a clinician feels that follow up of the patient is unlikely to be regular, it would be prudent to put a patient with high risk of disease progression on combination therapy rather than putting him on alpha blockers alone (panel's opinion)

Recommendation	Recommendation Level
Offer combination therapy (alpha blocker + 5 ARI) to all men with moderate to severe symptoms and large prostates (> 30 gm or >40 gm) and poor flow rates i.e. men with high risk of disease progression	Strong
Inform patients about ability of this treatment to reduce the disease progression and risk of sexual side effects	Strong
Offer combination therapy to men with high risk of progression where follow up is likely to be poor	Conditional / Selective

Is Discontinuation of alpha blockers possible? If yes when?

Henk van der Worp (88) and colleagues published a systematic review and meta-analysis on this issue. The review included 10 studies comprising 1081 participants. There was worsening (increase in symptom score and decrease in peak flow rates) after stopping the alpha blocker monotherapy at 3 and 6 months but not at 12 months. In contrast discontinuation of alpha blocker after combination (alpha blocker + 5ARI) did not have significant short term or long-term effects. 5ARIs do not have significant improvement in LUTS severity after the initiation of therapy, but their continuation seems to be beneficial in protection against symptom worsening after alpha blocker withdrawal in combination therapy. However, the evidence in this regard is low quality. For frail elderly patients or with concomitant illnesses it may be appropriate to discontinue alpha blockers. Moreover, it may be a measure to reduce the drug intake in polypharmacy. EAU guidelines mention discontinuation of alpha blockers after six to nine months of combination therapy. However the studies on which this recommendation is based are of short duration and the follow up period after discontinuation is also short (3). Some of the studies in the above mentioned review (88) suggested restarting alpha blockers if the PVR was > 100 ml or if the symptoms worsened.

Recommendation	Recommendation Level

Consider discontinuation of alpha blocker after combination therapy of six months or more	Conditional / Selective

Antimuscarinic agents (alone or in combination with alpha blockers)

Muscarinic receptor antagonists used for treating overactive bladder (OAB) / storage symptoms are darifenacin, fesoterodine, oxybutynin, propiverine, solifenacin, tolterodine and trospium. Antimuscarinics as a single agent have been used mainly for OAB symptoms without BOO. These drugs can significantly reduce the urgency incontinence, daytime and 24-hour frequency and OAB questionnaire scores. The adverse events commonly found are dry mouth, constipation, micturition difficulties, nasopharyngitis and dizziness. Of these, dry mouth is the commonest one and other adverse effects are rare. Drug withdrawal rates are similar to placebo. In men without BOO, increase in PVR in patients taking antimuscarinic agents is similar to placebo (3). The main philosophy of using antimuscarinic agents is persistence of storage symptoms in patients on alpha blockers alone. Alpha blocker monotherapy does not have significant effect on OAB symptoms. Moreover the storage symptoms of frequency, urgency, nocturia and urge incontinence are more bothersome (89). There has been concern about the risk of AUR in patients with BOO when they are prescribed antimuscarinic agents. A placebo-controlled trial of tolterodine in men with BOO and confirmed detrusor overactivity was reported. Short term treatment with antimuscarinic agents in patients with mild to moderate BOO is safe. Tolterodine when given to men with mild to moderate BOO increased the PVR but not the incidence of AUR. Urodynamic assessment showed unchanged Qmax. But larger bladder volume at first sensation, higher maximum cystometric capacity and decreased bladder contractility index was documented (90). Long term studies about these agents in ageing population are lacking. Caution should be exercised in prescribing these medicines to patients with high PVR and patients should be made aware to discontinue these drugs in case of worsening symptoms (3). The question remains as to when to start antimuscarinics in patients with BOO and OAB, either as an initial combination with alpha blocker or as a serial addition after maintenance or induction treatment with alpha blockers. A meta-analysis regarding this aspect (89) suggested initial combination therapy of alpha blockers with antimuscarinics. The OAB symptoms must be treated with initial combination therapy as initial monotherapy would not address OAB symptoms. However, the exact role of antimuscarinics either alone or in combination with alpha blockers has been questioned. A meta-analysis and review of newer medicines compared to traditional alpha blockers and 5ARIs was published in 2016 (91). This meta-analysis included various trials comparing darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine

and trospium either alone or in combination with alpha blockers. None of the newer drugs were found to be superior to the traditional alpha blocker therapy alone. Improvements in mean IPSS scores were similar, withdrawals due to adverse events were more

Recommendation	Recommendation Level
Use antimuscarinic agents (either alone or in combination with alpha blockers) in patients with predominant storage symptoms	Strong
Avoid antimuscarinic agents in men with PVR > 150 mL	Conditional / Selective
Initial combination of alpha blockers with antimuscarinic agents is preferable in men with moderate to severe LUTS with predominant storage symptoms	Strong

Phosphodiesterase 5 Inhibitors (either alone or in combination with alpha blockers, 5ARI)

Phosphodiesterase 5 inhibitors (PDE5Is) act by reducing smooth muscle tone of the detrusor, prostate and urethra, altering reflex pathways in the spinal cord and neurotransmission in the urethra, prostate, or bladder and also increasing the blood perfusion and oxygenation in the LUT. Tadalafil is the only molecule approved for the treatment of male LUTS.

A Cochrane review by Patanaik et. al. (92) included sixteen RCTs comparing effects of PDE5i versus placebo or other drugs. Compared with placebo a small improvement in IPSS total score (mean difference (MD) 1.89 lower, 95% confidence interval (CI) 2.27 lower to 1.50 lower; n = 4293; low-quality evidence) and slight reduction in BPHII (Benign Prostatic Hyperplasia Impact Index) (MD 0.52 lower, 95% CI 0.71 lower to 0.33 lower; n = 3646; low-quality evidence) was found. Rates of adverse events may be increased (risk ratio (RR) 1.42, 95% CI 1.21 to 1.67; n = 4386; low-quality evidence). The symptom improvements (IPSS scores and BPHII scores) with PDE5i and alpha blockers are similar. The combination of PDE5i and alpha blockers, when compared to alpha blockers alone or PDE5i alone, provided a small improvement in IPSS total score. Similar outcomes were found with combination of PDE5i and 5ARI. Most of the studies were of short duration up to 12 weeks. Another meta-analysis by Wang et. al. (93) reported improvements in IPSS as well as IIEF (International index of erectile function) score with tadalafil but no improvement in Qmax. One of the interesting observation about use of tadalafil for LUTS is its improved efficacy in younger men and less obese men (94). PDE5i are associated with adverse effects like flushing, headache, dyspepsia, nasal congestion leading to discontinuation rates up to 2%. PDE5i are contraindicated in patients using nitrates and potassium channel openers, patients with

unstable angina pectoris, recent myocardial infarction and with significant hepatic or renal insufficiency(3).

Recommendation	Recommendation Level
Phosphodiesterase 5 Inhibitors may be offered to men who have moderate to severe LUTS especially in younger men with low body mass index	Selective
Phosphodiesterase 5 inhibitors should not be used in patients using nitrates and potassium channel openers, patients with unstable angina pectoris, recent myocardial infarction and with significant hepatic and renal insufficiency	Strong

Beta 3 Agonists

Beta 3 receptors are expressed in smooth muscles cells of detrusor, stimulation of which induces detrusor relaxation. Mirabegron has been shown to significantly alleviate symptoms of storage failure i.e. urge incontinence, urgency and frequency (95). Discontinuation rates because of side effects are significantly less as compared to antimuscarinics (96). Mirabegron does not result in significant increase in PVR and thus carries no increased risk of AUR. Mirabegron is contraindicated in patients with uncontrolled hypertension. Most of the studies of Mirabegron were conducted in women. In a long term safety trial by Chapple (97), mirabegron has been shown to be safe, effective and well tolerated in patients with overactive bladder. Around one fourths of the patients in this study were males.

Recommendation	Recommendation Level
Beta 3 Agonists may be offered to men who have moderate to severe LUTS especially in men presenting predominantly with bladder storage symptoms	Optional

Phytotherapy

None of the phytotherapeutic drugs have been conclusively proven to be beneficial in management of LUTS due to BPH.

Serenoa repens: A Cochrane review (98) published in 2012 including 32 randomized trials involving 5666 men did not find any improvement in nocturia, peak urine flow, and symptom scores prescribed with Serenoa repens at double and triple doses, when compared to placebo.

Pygeum africanum: A Cochrane review (99) on pygeum africanum concluded that it might be effective, however there is a lack of high quality large studies on this agent.

Beta Sitosterols: Herbal medicines containing beta sitosterols may improve urinary symptoms. But data regarding long term effectiveness, safety and ability to prevent BPH complications is lacking(100).

Recommendation	Recommendation Level
In the absence of convincing evidence on the use of phytotherapy, the panel does not recommend the use of these agents	Conditional / Selective

Alternative Medicines, Ayurveda, Homoeopathy

Panel members performed a PubMed and google scholar search regarding the utility of various alternative medicines. But there is lack of reliable trustworthy evidence regarding these therapies. Some of the studies that panel members found on literature search had lacunae like no randomization, no control or placebo group, physician selected use of a particular drug (101); quite small number of subjects or individual case reports which can be passed off as anecdotes (102)(103)(104), short follow up period (105) and animal trials (106)

Recommendation	Recommendation Level
In the absence of convincing evidence on the use of Ayurvedic and Homoeopathic medicines, the panel does not recommend the use of these agents	Conditional / Selective

Surgical Treatment

Indications for surgery

Surgical treatment is the most effective of all treatment modalities. With the advent of medical therapy, the number of patients needing surgical treatment of BPH is decreasing. The patients coming for surgery are older, have tried medical options and may have co-morbidities (107)(108). The standard indications for surgical therapy are: (109)

- Renal insufficiency secondary to BPH
- Refractory urinary retention secondary to BPH

- Recurrent UTIs
- Recurrent bladder stones due to BPH
- Gross recurrent and persistent hematuria due to BPH
- LUTS attributed to BPH refractory to medical treatment
- LUTS attributed to BPH in a patient unwilling to use other therapies.

Recommendation	Recommendation Level
Surgery should be offered as a primary modality for patients presenting with complications arising secondary to BPH like renal insufficiency, refractory urinary retention, recurrent urinary tract infections, recurrent bladder stones and gross hematuria	Strong
Surgery shall be offered as an alternative to patients presenting with moderate to severe LUTS who failed to respond to medical management and who are not tolerant or compliant to medical management.	Optional

Open Prostatectomy

Open prostatectomy is the oldest surgical treatment for moderate to severe LUTS attributable to BPH. It is performed by transvesical (Freyer) and retropubic (Millin) routes. Currently it is performed mainly for large (>80-100 gram) glands. It has the best long term outcomes and lowest retreatment rates (110). Open prostatectomy reduces LUTS by 63-86%, improves QoL score by 60-87%, increases Qmax by 375%, and reduces PVR by 86-98% (3). With the advent of newer endoscopic enucleation techniques, the open surgery is taking a backseat (111). A RCT of open prostatectomy vs HOLEP with follow up periods up to five years reported comparable improvements in mean AUA symptom score, PVR urine volumes and late complications like urethral strictures, bladder neck contractures and reoperation rates (112). A systematic review of open prostatectomy versus transurethral enucleation (TUEP) reported similar functional outcomes in the TUEP arm (113). Open prostatectomy is an invasive procedure with its associated morbidity in the form of prolonged convalescence, longer hospital stay, prolonged catheterization time and higher blood transfusion rates (114). Bladder neck contracture and urethral stricture rates are comparable to TUEP techniques.

Recommendation	Recommendation Level

Open prostatectomy shall be offered for treatment of moderate to severe LUTS in men with prostate size >80-100ml if endoscopic enucleation techniques are not available or are deemed unsuitable for the patient	Selective

Transurethral Resection of Prostate (TURP)

Monopolar TURP (MTURP)/ TUIP

MTURP has been the cornerstone of surgical treatment of BPH for over eight decades. It has been considered the reference standard for surgical treatment of BPH. It is the only surgical therapy about which most substantial long-term data is available (115). Ahyai and colleagues published a meta-analysis of 27 publications about different transurethral procedures for BPH management. TURP resulted in a substantial improvement of mean Qmax (+162%) and a significant reduction of mean IPSS (−70%), mean QoL scores (−69%), and mean PVRU (−77%)(116). Secondary procedure (secondary TURP, urethrotomy, and bladder neck incision) after initial TURP happened in 5.8%, 12.3%, and 14.7% at one, five, and eight years follow-up (110).

The mortality and short-term morbidity has been reported to be 0.1% and 11.1% respectively. The complications reported are failure to void (5.8%), surgical revision (5.6%), significant urinary tract infection (3.6%), bleeding requiring transfusions (2.9%) and transurethral resection syndrome (1.4%) (117). The complication rates have decreased over time (118). MTURP is deemed unsuitable for prostates larger than 80 gm. The complication rates after TURP increase with increasing surgical duration. From a retrospective data of 31813 patients, longer operative time was associated with a greater risk of postoperative sepsis or shock, transfusion, reoperation, and deep vein thrombus or pulmonary embolism. (119)

TUIP

Transurethral incision of the prostate involves (TUIP) is used in selected cases with prostate sizes < 30 mL without a middle lobe. It has been proposed as an ideal treatment option in younger sexually active men. The efficacy is comparable or somewhat inferior to TURP. Blood transfusion rates (0.4% Vs 8.6%) and retrograde ejaculation rates (18.2% vs. 65.4%) are lower than TURP. (115)

Bipolar TURP (BUTRP)

One major fundamental flaw of MTURP is resection needs hypo-osmolar irrigation. BTURP is performed in normal saline thereby eliminating the risk of TUR syndrome. The BTURP systems are of two types. In true bipolar system, the passive pole of the system is situated on the resectoscope tip. Whereas in quasi

bipolar system it is through the resectoscope sheath. BTURP has been shown to have similar short-term efficacy as that of MURP with lower rates of perioperative complications. Results from a Cochrane review (120) of 59 RCTs including 8924 patients with longest follow up of 12 months reported no clinically relevant differences in short-term efficacy (IPSS, QoL score and Qmax) of MTURP and BTURP. BTURP reduces TUR syndrome events corresponding to 20 fewer TUR syndrome events per 1000 participants. In this review, there were 83/3412 TUR syndrome events in MTURP group, whereas there was none out of 3333 in the BTURP group. There is similar risk of incontinence, slightly reduced blood transfusion requirements, similar rates of Re-TURPs and similar erectile function as compared to MTURP.

There have been some concerns regarding the use of quasi-bipolar systems (TURIS, Olympus) wherein the return electrode is in the resectoscope sheath. Earlier RCT of MTURP vs BTURP (TURIS) reported higher urethral stricture rates in BTURP-TURIS group. The incidence of stricture was 1/52 in MTURP and 3/48 in BTURP groups. These differences was not statistically significant (121). The higher incidence of urethral strictures in TURIS group has been considered a drawback of quasi-bipolar system as the resectoscope serves as the return electrode and the higher current densities for all bipolar techniques are possible (122). NICE guidelines (122) comprising meta-analysis of 10 studies including 1870 patients reported no statistically significant differences between TURis and monopolar TURP in procedure time, time to catheter removal, the incidence of clot retention and incidence of urethral stricture or bladder neck contracture. However, in addition to the above mentioned RCT(121), Komura et. al. (123) have reported higher incidence of strictures in TURIS group in patients with larger preoperative prostate volumes. Stucki et. al. (124) have reported higher incidence of bladder neck strictures in BTURP group. In this RCT, BTURP was performed Gyrus PK SuperPulse generator.

Recommendation	Recommendation Level
TURP should be offered to treat moderate to severe LUTS in men with prostate size 30-80 ml	Strong
TUIP should be offered to treat LUTS in men with prostate size < 30ml, in absence of a median lobe	Strong
Bipolar TURP may be offered to treat moderate to severe LUTS in men with prostate size 30 - 80ml based on equipment availability, surgeon's experience and patient's choice	Optional

Bipolar Transurethral Vaporization of Prostate (BTUVP)

BTUVP has similar efficacy as compared to TURP in short term but inferior clinical efficacy outcomes at mid-term. Perioperative profile and mid-term safety is comparable to TURP. High quality RCT are needed (3).

Preoperative drug treatment to reduce bleeding during TURP

Androgenic control of prostate growth and angiogenesis has intrigued researchers to try these medicines before TURP with intention to reduce blood loss. Bansal and colleagues reported a randomized trial of 450 patients undergoing TURP. These patients were treated by finasteride, dutasteride or placebo for four weeks before surgery. Both finasteride and dutasteride had similar efficacy and significantly reduced perioperative bleeding during TURP (125). In their meta-analysis Zhu et. al. reported similar outcomes with finasteride, but the beneficial effect of dutasteride was inconclusive (126). Similar findings were reported by Zong (127). On the contrary Ren et. al. in their systematic review and meta-analysis demonstrated beneficial effects dutasteride in reducing surgical bleeding during TURP (128). It is generally accepted that 5ARI generally take around six months for its effect on prostate volume. The role of short term 5ARI treatment in reducing blood loss has been questioned. The available evidence in this regard is conflicting. Bruha et. al. recommended against customary routine use of 5ARI in this setting (129). El-Enen reported reduced bleeding with single dose of goserelin four weeks before TURP (130). Panel recommends to wait for consolidated data on this issue before any recommendation or guideline statement.

Laser Treatments

HOLEP

The results of Holmium laser enucleation of prostate (HOLEP) are comparable to open prostatectomy. It is equally effective, durable with lower blood transfusion rates, shorter catheter time and shorter hospital stay. It is the size independent surgical modality of treatment for BPH (111). Kuntz and colleagues (112) reported comparable micturition results with HOLEP and open surgery. They suggested HOLEP to be the true endourological alternative to open surgery. It has been proposed as the ‘new gold standard’ for the surgical management of BPH by some of the investigators (131). An earlier meta-analysis (132) comparing TURP with HOLEP reported similar symptom improvements with both the modalities. The advantages noted with HOLEP were significantly less blood loss, shorter catheterization time and shorter hospitalization time. The only drawback was HOLEP required more operative time. Yin

and colleagues (133) in a systematic review and meta-analysis of TURP vs HOLEP reported slightly better postoperative results in Qmax and IPSS in HOLEP group with significantly better perioperative results and low complication rates. Similar outcomes were reported by other meta-analyses of trials on HOLEP vs TURP (134)(135).

Gilling et. al. (136) reported long term data on the outcomes of TURP vs HOLEP. At seven year follow up, both the operations yielded equivalent outcomes with regard to Qmax, AUASI, QOL scores, BPHII, IIEF-FF and ICS male voiding and continence scores. There were fewer re-operations in HOLEP group. Elmansy and colleagues (137) reported long term durable results with HOLEP with low rates of complications. The follow up in this study was up to ten years (mean follow up 62 months) in some patients..

HOLEP can be performed in patients receiving anticoagulation or antiplatelet medicines. Except for slight prolongation of duration of bladder irrigation, no adverse outcomes were observed in patients undergoing HOLEP in this group (138). Bishop and colleagues (139) reported their experiences about patients undergoing HOLEP with or without antithrombotic therapy. In this retrospective study they found that HOLEP was safe in these patients. Hospitalization time and transfusion rates were predictably higher in patients on antithrombotic treatment. Another retrospective study from China showed that HOLEP can be safely performed in patients on single or dual antiplatelet therapy (140).

TURP as well as HOLEP, both lower the IIEF orgasmic function due to retrograde ejaculation (141). Ejaculatory hood sparing modification of HOLEP have been claimed to preserve ejaculation. In this technique paracollicular and supracollicular tissue >1cm proximal to verumontanum is preserved. Overall 46.2% success rate of ejaculation preservation is reported with this technique (142).

HOLEP has a steep learning curve (143). Learning requires longer training than standard TURP. It is reported that an operator can become adapt at HOLEP after a mean of twenty supervised procedures (144), although there is sustained improvement in the outcomes with increasing experience (145). Du and colleagues from Hangzhou, China reported that HOLEP is safe even when performed by inexperienced surgeons (146). Mentorship programs and simulators for learning HOLEP are recommended (147)(148).

Recommendation	Recommendation Level
HOLEP can be offered to treat moderate to severe LUTS in men as size independent modality as an alternative to TURP	Strong

HOLEP is especially beneficial offered to treat moderate to severe LUTS in men with prostate size > 80 ml	Strong
HOLEP is an endourological alternative to open surgery	Strong

Greenlight Laser (KTP Laser), Photoselective vaporization (PVP)

Currently available green light laser systems include 80W KTP and 120W HPS (LBO) laser systems that work at wavelength of 532 nm. The LASER energy is absorbed selectively by hemoglobin and not by water, hence vaporization leads to immediate removal of prostatic tissue resulting in relief of bladder outlet obstruction. Greenlight laser is an effective alternative to TURP (149). As compared to TURP, green light laser vaporization of prostate has been demonstrated to have higher intra operative safety profile with regards to hemostatic properties. Other perioperative parameters like catheterization time, hospital stay and bleeding complications are also favorable for Green light laser vaporization of prostate. The operative time and reoperation rates are relatively higher as compared to TURP. A meta-analysis (150) of nine trials was published in 2012. This included 448 patients in PVP (80W & 120W) and 441 in TURP arm. Catheterization time, hospital stay were shorter in PVP, whereas the operative time was longer. Complications like blood transfusion and clot retention were lower in PVP group. Functional outcomes like Qmax, IPSS were comparable in both the groups. Another meta-analysis (151) published in 2015 reported similar outcomes. This meta-analysis included only the 120 w laser in the study arm.

PVP does not provide tissue for histologic diagnosis. The outcomes are comparable to TURP over mid-term follow up periods of 24 months (152). Of course, dilutional hyponatremia is not reported in PVP. One of the reported advantage of PVP over TURP is preservation of ejaculation (152). In one prospective non-randomized study (80W PVP vs TURP) with over five year follow up IPSS, QoL, Q max, and PVR volume were comparable. However, parameters like PSA reduction, risk of urethral stricture, bladder neck contracture, or persisting or recurrent adenoma were favorable in TURP group. Authors suggested that 80-W KTP laser has inferior tissue ablation capacity (153). A small double blind study comparing urodynamic parameters assessed at 2 years reported same results in PVP and TURP (prostate volume <60ml) group except for storage symptoms of limited duration in PVP group (154).

Chung et. al. in a study of 162 men reported that PVP laser prostatectomy is feasible in anticoagulated patients. They were on either warfarin, acetylsalicylic acid, clopidogrel with 7% patients were on two or more anticoagulants. Mean prostate volume was 91 gm. Operative time was longer. There were few complications and significant durable clinical improvement (155). As the surgery with PVP is virtually

bloodless, it can be performed in high risk patients, patients with cardiopulmonary risk, ASA score of 3 or more (156). PVP has been proposed as the preferred procedure for patients with high risk of bleeding (157)(158)(159). Although continued anticoagulation therapy does not cause overall increase in perioperative adverse events, increased rate of Clavien-Dindo events is reported (160). Delayed gross hematuria occurs after PVP but severe hematuria is rare. In a retrospective study, risk factors for delayed gross hematuria were large prostate size and use of anticoagulation. Interestingly, older age and 5ARI were protective(161).

In a Canadian study cost analysis of PVP and TURP was reported. The PVP turned out to be a cheaper and preferable option than TURP or BTURP due to reduced procedure costs and readmission rates (162). However in another study from India (163), wherein PVP and BTUVP were compared, BTUVP was found to be a significantly cheaper option as compared to PVP. Although the study did not include conventional MTURP in cost analysis, the costs can be extrapolated. In Indian situation MTURP would be a significantly cheaper option.

Recommendation	Recommendation Level
Green light LASER (80W, 120W, 180W, KTP, LBO) vaporisation of prostate maybe offered to treat moderate to severe LUTS in men with prostate size < 80 as an alternative to TURP	Optional
Green light LASER vaporisation of prostate maybe offered to treat moderate to severe LUTS in men receiving antiplatelet therapy	Optional
TURP is cheaper than Greenlight LASER in Indian scenario	Conditional / Selective

Diode laser

120 W Diode LASER systems work at wavelength of 980nm producing vaporization of prostate with better hemostatic and perioperative parameters. The tissue necrosis and penetration depth is higher. Intraoperative safety is higher. PVP with diode laser has been shown to be as safe and effective as TURP with shorter hospitalization and indwelling catheter times (164), less risk of hemorrhage and reduced bladder irrigations (165). Comparable IPSS score and flow rate improvement have been demonstrated. Severe storage symptoms and persistent incontinence are significantly higher in comparison with TURP. Retreatment rates are also higher (166). Diode laser vaporization has been shown to be less efficient than TURP at longer follow up (167).

It is also suggested that diode laser vaporization can be performed without discontinuing anticoagulants (164). In one RCT comparing diode laser enucleation of prostate (DiLEP) with plasmakinetic enucleation of prostate (PKEP) in patient with prostates >80gm with 12 months follow up, DiLEP was found to be equally efficacious in improvement in IPSS and Qmax. DiLEP group had lower risk of blood loss, shorter irrigation and catheterization times, shorter hospitalization times but longer operation times (168). Another trial revealed DiLEP to be non-inferior to PKEP in terms of IPSS and Qmax at 12 months follow up (169). Chiang et. al. published a RCT comparing greenlight vaporization vs diode vaporization. They reported superior hemostatic properties but higher irritative symptoms in the diode group (170). Another RCT comparing KTP with high intensity diode laser found increased re-treatment rates, bladder neck stricture and incontinence rates with diode laser (171).

Recommendation	Recommendation Level
Diode laser vaporisation/ enucleation of prostate maybe offered to treat moderate to severe LUTS in men as an alternative to TURP	Optional

Thulium:yttrium-aluminium-garnet laser (Tm:YAG) / Thulium Laser

Thulium LASER (Tm:YAG) is continuous wave LASER with a wavelength of 2013 nm. It has a penetration depth of 0.2 mm which is why a relatively superficial area of ischemia happens leading to sealing of blood vessels and decreased risk of delayed bleeding (166). Thulium laser is also available in wavelength of 1940 nm. Both 1940 and 2013 nm lasers give equivalent and satisfactory improvement and low morbidity (172). As a versatile tool Thulium LASER (Tm:YAG) offers various therapeutic options in the form of vaporization (ThuVP), resection (ThuLRP or TmLRP), enucleation(ThuLEP) , vapoenucleation (ThuVEP) and vaporesection (ThuVaRP) (173). TmYAG vapoenucleation is efficacious for large prostates (174).

A meta-analysis of Thulium laser prostatectomy vs TURP was published by Jiang et al. Thulium LASER (Tm:YAG) had better peri-operative safety profile in terms of reduced hyponatremia, shorter catheterization time, shorter hospital stay, fewer blood transfusions and reduced blood loss (175). Zhu and colleagues published a systematic review and meta-analysis of Thulium laser prostatectomy (TmLRP) vs TURP in 2014. Seven trials, of which four were randomized were included in this review. Of these seven trial two trials included ThuLEP and five trial included ThuVaRP as study arm and TURP as comparator arm. All Thulium procedures were named TmLRP. TmLRP needed longer operative time. The advantages with TmLRP were significantly less serum sodium decrease, shorter catheterization duration,

shorter hospitalization time and less transfusion requirement. With regard to IPSS, QoL, Qmax and PVR TmLRP had similar efficacy to the standard TURP (176).

Xia et. al. reported that compared to TURP, TmYAG resection of prostate (ThuLRP) is almost bloodless procedure with minimal morbidity. The surgical results are comparable at 12 months follow up (177). Dubey et. al. commented on this paper quoting availability of tissue for histopathology, shorter learning curve as the potential advantages of thulium laser prostatectomy (178). Chang et. al. reported comparable outcomes in their RCT of ThuVEP vs TRUP with one year follow up (179).

A meta-analysis comparing Thulium laser resection of prostate (ThuRP) and plasma kinetic resection of prostate (PKRP) reported similar efficacy in both the techniques. Operative time was more with ThuRP. The advantages with ThuRP were less blood loss, shorter hospital stay, irrigation and catheterization times (180). The outcomes of ThuLEP are durable over follow up periods up to 60 months as reported by Yang and colleagues in their RCT comparing ThuLEP vs PKRP (181). Feng et. al. (182) published a RCT comparing ThuLEP vs plasma kinetic enucleation (PKEP). The patients were followed up for 12 months. The hemoglobin decrease and catheter times were lower in ThuLEP group. The authors concluded that these differences might of little clinical significance.

TmYAG vapoenucleation (ThuVEP) is a size independent treatment modality for BPH, as shown by reduction in prostate volume on TRUS and reduction in PSA levels. Complete removal of BPH adenoma can be accomplished with TmYAG vapoenucleation(183). Netsch and colleagues (184) published their comparative study of ThuVEP with 120 watt and 200 watt systems. The clinical outcomes at 12 months follow up were comparable in both the groups, except lower percentage of resected tissue with 200 watt due to higher rate of tissue ablation. Xia and colleagues & Herrmann and colleagues have described a novel technique of ThuLEP with combination of blunt dissection of adenoma and thulium laser use (185).

Hong et. al. reported their experiences with ThuVEP vs HOLEP in non-randomized retrospective study. Both the modalities were found to be safe and effective. The operative time in Thulium arm was shorter (186). Zhang and colleagues (187) reported their experiences in RCT of ThuLEP vs HOLEP with 18 months follow up. Both the modalities had equal efficacy. Blood loss was lower in ThuLEP and operative time was more in HOLEP. These differences although statistically significant, were clinically negligible.

The improvement noted after Thulium LASER (Tm:YAG) in terms of symptom score and uroflowmetry parameters are comparable to TURP and open prostatectomy. The long term complications of TmYAG

resection in terms of bladder neck contracture and urethral stricture are equivalent to TURP. The outcomes of thulium laser resection have been shown to be stable over follow up periods of four years. It has been suggested as a viable option for older high risk BPH patients (188). VapoEnucleation with Tm:YAG is safe and effective. The operative outcomes in form of voiding improvement and bother are durable for follow up periods more than 12 months (189).

A retrospective study by Hauser et. al. (190) concluded that ThuVEP is safe in patients on antiplatelet or anticoagulation medicines. Similarly another case series by Netsch et. al. (191) reported that ThuVEP is safe in patients with high cardiopulmonary risk on antiplatelets and anticoagulation medicines. Re operation rates after Thulium LASER (Tm:YAG) are better as compared to TURP. The learning curve significantly impacts the ability to replicate overall clinical results. There is a need to learn new procedure as morcellation when contemplating enucleation with Thulium LASER (Tm:YAG).

The operative procedures performed with Tm:YAG laser are quite diverse. Terminologies like vaporization, vapo-resection, vapo-enucleation, enucleation and resection have been used in different papers interchangeably. It is difficult to compare one study group with another without actually looking at the laser settings and procedures used in the study protocol. Maruccia et. al. have suggested a standardized nomenclature for the surgical procedures performed with Tm:YAG laser (192). This nomenclature would make comparative assessment of different modalities easier.

Recommendation	Recommendation Level
Thulium LASER (Tm:YAG) enucleation of prostate should be offered to treat moderate to severe LUTS in men as size independent modality as an alternative to HOLEP and TURP	Strong
Thulium LASER (Tm:YAG) vaporization of prostate maybe offered to treat moderate to severe LUTS in men with prostate size < 80 ml	Optional
ThuVEP / ThuVARP may be offered to the patients receiving anticoagulation	Optional

Thulium Fiber Laser

Tm Fiber laser is a new technology with a wavelength of 1940 nm. It has a small portable unit with reduced depth of tissue penetration. Enikeev and colleagues have reported their initial experience with Thulium fiber enucleation of prostate (ThuFLEP). In a retrospective study comparing ThuFLEP with open surgery for prostates larger than 80gm, ThuFLEP arm had shorter hospital stay, shorter catheterization

time and comparable outcomes at six month follow up (193). A prospective study comparing ThuFLEP with conventional TURP in prostates smaller than 80 grams reported comparable outcomes in both the arms. PSA decrease in ThuFLEP arm was substantially more (194). Another publication from the same group reported comparable impact on erectile function in both the groups (195). More data on this novel laser is awaited.

Prostatic Stents

Prostatic stents are offered as an alternative to catheterization in men who fail medical therapy and who are unfit for surgical or minimally invasive treatment. It is necessary to have good functioning detrusor so as to actively empty the bladder. In contrast bladder emptying through catheter is a passive process (196). Prostatic stents are of two types: Permanent or Temporary. Permanent stents are biocompatible. They become embedded in urethral mucosa. Long term follow up studies (197) have shown 40% removal rate, majority of these in the first two years of deployment. Careful case selection is the key for optimum results.

First generation urethral stents (Urolume) were made of steel. These were prone to encrustation. Full epithelialization was not achieved in all cases. Removal of these stents needed general or regional anesthesia, rigid cystoscope and some cutting tool like holmium laser (196). Second generation stents were made up of titanium nickel alloy (Memokath). These stents are thermo-expandable(196). Perry et. al. (198) reported their experiences about 211 patients in whom memokath was inserted. There were around 25% long term failure rates. The stents are suggested as a valuable addition to the different modalities to treat symptomatic BPH especially for elderly or frail men with advanced BOO. Another similar thermosensitive nitinol stent is available by the name of Memotherm. The thermosensitive stents can be removed by instillation of cold saline at $5\text{-}10^0$ Saline under topical anesthesia. To decrease the risk of migration, hourglass shaped and bell shaped nitinol stents were introduced, but these are not suitable for clinical practice. These stents have high migration rates(196).

Temporary stents are made of biodegradable material like polyglycolic acid (PGA). The process of biodegradation is variable and unpredictable. The temporary stents have small lumen that can get blocked by small clots. These stents have been used after thermotherapy or as a therapeutic trial in patients with BPH and severe OAB (196).

In summary, prostatic stents may be looked upon as an alternative to indwelling catheter. Prostatic Stents are subject to misplacement, migration or encrustation. They are associated with persistent perineal pain, bladder storage symptoms or exacerbation of LUTS

Recommendation	Recommendation Level
Prostatic Stents maybe offered as an alternative to catheterisation in men unfit for any invasive / minimally invasive procedure under anaesthesia	Optional

Other less invasive modalities

Aquablation

Aquablation is a minimally invasive water based therapy for BPH. It combines image guidance and robotics for removal of prostate tissue. The symptomatic improvement is probably similar to TURP. Whether it is associated with lower or higher risk of adverse effects (as compared to TURP) and whether it has any effect on erectile function, is uncertain. It offers small improvement with respect to the preservation of ejaculatory function, but the quality of evidence regarding this is quite poor (199). Panel recommends to wait for consolidated data on aquablation before any recommendation or guideline statement.

Prostatic Urethral Lift

Prostatic urethral lift (PUL) is a new minimally invasive alternative to TURP wherein encroaching lateral lobes are compressed by permanent suture based implants delivered under cystoscopic guidance resulting in opening of the prostatic urethra. This creates a continuous anterior channel through prostatic fossa from the bladder neck to verumontanum (200). PUL is based solely on mechanical compression.

In a Cochrane review (201) on PUL, the authors concluded that PUL is less effective than TURP. QOL outcomes may be similar. It is more likely to preserve ejaculatory function then TURP. Effect on erectile function appears to be similar. Short term results in terms of subjective and objective parameters do match other minimally invasive modalities. Roeherborn et. al. reported the first multicenter randomized blinded trial of PUL: the LIFT study (202). The AUA symptom index reduced from 22.1 at baseline to 18.0, 11.0 and 11.1 at 2 weeks, 3 months and 12 months. The symptom improvement in study group was statistically significant. Peak flow rates increased by around 4.0ml/s. The improvements in QOL and flow rates have been shown to be durable for up to five years (203). Chin et. al. (204) reported a cohort of 64

men with moderate to severe LUTS who underwent PUL. Approximately half of the patients did not need a post-operative catheter. The patients were followed up for two years. IPSS reduced by 42-49%, Peak flow rate improved by >30% without compromising sexual function. Only three out of 64 patients in this study had obstructive median lobes. Two patients did not respond to PUL and underwent TURP.

PUL can be performed under local anesthesia. The durability of improvement noticed in parameters is questionable. Higher retreatment rates were reported in clinical trials with longer follow up of 2-3 years (205). PUL is associated with short term complication like hematuria, dysuria, urgency, incontinence and urinary tract infections. BPH6 multicenter study compared PUL and TURP. The initial recovery with PUL was more rapid and more extensive, (206) but at 24 month follow up changes in IPSS and Qmax were superior in the TURP group (207). Obstructed or protruding median lobe remains a deterrent to efficacy of PUL. Efficacy in large prostates is not yet proven (3). Cost and availability remains a limiting factor

Recommendation	Recommendation Level
Prostatic Urethral Lift maybe offered to treat moderate to severe LUTS in men with prostate size < 70 ml, with no median lobe especially to men willing to preserve ejaculatory function.	Optional

Intraprostatic Botulinum Toxin injections

Botulinum toxin prevents neurotransmitter release from nerve terminals thereby inhibiting contraction of skeletal and smooth muscles. A recently published systematic review and meta-analysis (208) showed no advantages with botulinum toxin as compared to placebo. Panel recommends to wait for consolidated data on botulinum toxin. Till that time panel recommends against use of botulinum toxin in BPH.

Recommendation	Recommendation Level
Do not use intra-prostatic injections of botulinum toxins (till we get consolidated convincing data supporting its use)	Strong

Other modalities

The panel feels that following modalities are experimental and currently under investigation. Panel recommends to wait for consolidated data on these therapeutic options before any recommendation as a guideline statement.

- Minimally invasive simple prostatectomy
- TIND
- Water vapor therapy (Rezum)
- Prostatic artery embolization

Prostate and associated conditions

BPH and Bladder stones

Bladder stones in elderly male population are usually thought to be the result of bladder outlet obstruction, but in some of the patients enlarged prostate may be an innocent bystander. The etiogenesis of bladder stones in BPH patients may be related to local factors (stasis), systemic factors (metabolic) or multifactorial (209). Most of the guidelines advocate surgery for prostate as well as stone for the patients who have bladder stones due to BPH. The management of BPH and bladder stones should be individualized. Cystolithalopaxy can be performed concomitantly with the surgical procedure used to remove the obstructing prostate tissue. The choice of surgical approach (transurethral, open, or laparoscopic) would depend on the size and number of stones and the size of the prostate.

Recommendation	Recommendation Level
Offer surgery for bladder stones and prostate to the patients who have bladder stones due to BPH	Optional
Approach to each case should be individualised	Optional

BPH and Bladder diverticulum

BPH and bladder diverticulum may co-exist. Most of the bladder diverticula may be asymptomatic. Exact role of bladder diverticulum in LUTS is poorly understood. Icaife and colleagues (210) in their retrospective study of 47 patients found that the diameter of bladder diverticulum was an independent risk factor for acute retention. Diverticulum diameter larger than 5.15 cm was found to be the risk factor

for acute retention. Pressure flow studies in patients with bladder diverticulum may be inaccurate. AUA guidelines suggest that surgery should not be performed solely because of presence of asymptomatic bladder diverticulum (211).

Recommendation	Recommendation Level
Do not offer surgery for BPH patients solely because of presence of asymptomatic diverticulum	Optional
Evaluation for presence of bladder outlet obstruction should be performed	Strong

BPH and Inguinal Hernia

Inguinal hernia and BPH are seen commonly in aged male population. The cause and effect correlation between BPH and hernia is not well understood (212)(213). Combining hernia surgery with TURP is safe and effective (214)(215)(216).

Recommendation	Recommendation Level
BPH and inguinal hernia may co-exist in old people. Cause and effect relationship between these two is not proven	Moderate
Hernia surgery and TURP should be done in same sitting whenever indicated and possible	Strong

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Abbreviations

5ARI	5 alpha reductase inhibitors
AE	Adverse events
ASA	American Society of Anesthesiology score
AUA	American urological association
AUA-SI	American urological association symptom index

AUR	Acute Urinary retention
BiTUEP	Bipolar enucleation of prostate
BOO	Bladder outlet obstruction
BOOI	Bladder outlet obstruction index
BPH	Benign Prostatic Hyperplasia
BPHII	Benign Prostatic Hyperplasia Impact Index
BTURP	Bipolar transurethral resection of prostate
BTUVP	Bipolar vaporization of prostate
CombAT	Combination of Avodart and Tamsulosin (Trial)
CT	Computed Tomography
DHT	Dihydrotestosterone
DiLEP	Diode laser enucleation of prostate
DioLEP	Diode laser enucleation of prostate
DioLVP	Diode laser vaporization of prostate
DRE	Digital rectal examination
DUA	Detrusor underactivity
EAU	European Association of Urology
eGFR	Estimated glomerular filtration rate
FVC	Frequency volume chart
HOLEP	Holmium laser enucleation of prostate
IIEF	International Index of Erectile function
IPP	Intravesical Prostate Protrusion
IPSS	International Prostate Symptom Score
KTP	Potassium-Titanyl-Phosphate
KTP	Potassium titanyl phosphate laser vaporization of prostate
LBO	Lithium triborate
LUTS	Lower urinary tract symptoms
MRI	Magnetic resonance Imaging
MTOPS	Medical therapy of prostate symptoms
MTURP	Monopolar Transurethral resection of prostate
OAB	Overactive Bladder

Pdet	Detrusor pressure
PFS	Pressure Flow Study
PKEP	Plasmakinetic enucleation of prostate
PKEP	Plasmakinetic enucleation of prostate
PKRP	Plasmakinetic resection of prostate
PLESS	Proscar (finasteride) long term efficacy and safety study
PUL	Prostatic urethral lift
PVP	Photoselective vaporization
PVR	Post void residue
Qmax	Maximum flow rate
QOL	Quality of Life
RCT	Randomized controlled trial
TAUS	Trans-abdominal Ultrasound
ThuFLEP	Thulium fiber laser enucleation of prostate
ThuLEP	Thulium Laser enucleation of prostate
ThuLEP	Thulium Laser enucleation of prostate
ThuVEP	Thulium laser vapoenucleation of prostate
TRUS	Trans-rectal Ultrasound
TUEP	Transurethral enucleation of prostate (irrespective of energy used)
TURP	Transurethral resection of prostate (monopolar unless otherwise specified)
TWOC	Trial of voiding without catheter
UDS	Urodynamics / Urodynamic studies
VCUG	Voiding cystourethrography