NIGERIAN ASSOCIATION OF UROLOGICAL SURGEONS

NAUS

Guidelines For Management Of Benign Prostatic Hyperplasia

FIRST EDITION

NIGERIAN ASSOCIATION OF UROLOGICAL SURGEONS

GUIDELINES FOR MANAGEMENT OF BENIGN PROSTATIC HYPERPLASIA

FIRST EDITION

COORDINATING EDITOR:
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LIST OF ABBREVIATIONS

5-ARIs	5α-reductase inhibitors
AUA-SI	American Urologic Association Symptom Index
BLSA	Baltimore Longitudinal Study of Aging
BoNT-A	Botulinum toxin-A
BOO	Bladder outlet obstruction
BoNT-A	Botulinum toxin-A
BPH/BPE	Benign prostate hyperplasia/ benign prostate enlargement
BPO	Benign prostate obstruction
CKD	Chronic kidney disease
CombAT	Combination of Avodart and Tamsulosin
CT	Computed tomography
DAN-PSS	Danish Prostate Symptom Score
DHT	Dihydrotestosterone
DO	Detrusor overactivity
DRE	Digital-rectal examination
ED	Erectile dysfunction
eGFR	estimated glomerular filtration rate
EjD	Ejaculatory dysfunction
FVC	Frequency volume chart
Ho;YAG	holmium:yttrium-aluminium garnet
HoLRP/ HoLEP	Holium laser resection/ Holium laser enucleation of prostate
HRQoL	Health related quality of life
ICIQ-MLUTS	International Consultation on Incontinence Questionnaire
IFIS	Intra-operative floppy iris syndrome
IGF-1	Insulin Growth Factor
IIEF	International Index for Erectile Function
IPP	Intravesical prostatic protrusion
IPSS	International Prostate Symptoms Score
IVU	Intravenous urography
KTP	Kalium-Titanyl-Phosphat
LBO	Lithium triborate
LSP	Laparoscopic simple prostatectomy
LUTS	Lower urinary tract symptoms
Ly	Lycopene
M1-M5	Muscarinic receptor subtypes 1 to 5
MCS	Urine Microscopy Culture and Sensitivity
MCUG	Micturating cysto-urethrogram

LIST OF ABBREVIATIONS

MISP	Minimal invasive simple prostatectomy
MRI	Magnetic resonance imaging
M-TURP/ B-TURP	Monopolar TURP/ Bipolar TURP
NSAID	Non-steroidal ant-inflammatory drug
OAB	Over active bladder
Pca	Prostate cancer
PCAR	Prostatic configuration using presumed circle area ratio
PDE5Is	Phosphodiesterase 5 inhibitors
PFS	Pressure flow studies
PSA	Prostate Specific Antigen
PUL	Prostatic urethral lift
PV	Prostatic volume
PVR	Post-void residual
Qmax	Maximum flow
QoL	Quality of life
RASP	Robot assisted simple prostatectomy
REDUCE	Reduction by DUtasteride of prostate Cancer Events
RUG	Retrograde urethrography
Se	Selenium
SeR	Serenoa Repens
Tm;YAG laser	Thulium:yttrium-aluminium-garnet laser
TRUS	Transrectal ultrasound
TUMT	Transurethral microwave therapy
TUNA	Transurethral needle ablation of the prostate
TURP	Transurethral resection of prostate
UTI	Urinary tract infections
UUI	Urgency urinary incontinence
VPSS	Visual prostate symptoms score

PREFACE

This guide line has been developed under the auspices of the Nigerian Association of Urological Surgeons (NAUS), the umbrella body of all urologists practicing in Nigeria. NAUS is an affiliate member of the European Association of Urology (EAU). We have thus used the EAU guideline as a template and domesticated it in line with the peculiarities of our environment, while still maintaining standards. It is arranged in a concise well organised manner that will aid the understanding, diagnosis and treatment of benign prostatic hyperplasia (BPH) in our sub region.

Residents in surgery and urology, practicing urologists, family physicians and other physicians will find this guideline very useful in managing patients with BPH. It is also a useful guide for examiners in general surgery and urology. Summary boxes are provided for quick reference.

This is the first edition and may be revised as necessary in the future.

We are immensely grateful to NAUS for giving us the opportunity to develop this guideline, all the contributors for their time and expertise, the reviewers for their invaluable input and to GlaxoSmithKline
(GSK) for their support.

Professor Venyir M Ramyil
President, Nigerian Association of Urological Surgeons
June, 2018.

CHAPTER 1
INTRODUCTION

1.1: THE NEED FOR NATIONAL BPH MANAGEMENT GUIDELINE FOR NIGERIA

Benign prostatic hyperplasia remains a common urological problem in males above 50 years of age.[1,2] Guidelines have been defined as 'systematically developed statements that assist clinicians or patients in making decisions about appropriate treatment for specific conditions'.[3] These could be local, regional, national or supra national. Various countries and international bodies have developed guidelines e.g. AUA (American) guidelines, EUA (European) guidelines, Australian guidelines, to assist attending healthcare personnel in managing these patients who are mainly the older people. There is at present no guideline in Nigeria to guide its health personnel on this vital subject, despite the fact that BPH is a common disease in the practice of urologists and forms a great proportion of cases seen not only in specialist centres but also in non- specialist set ups in this country. Patients are seen by urologists and non-urologists.

This has implication on the outcome of management as the quality may differ widely. Studies have also shown that many of these patients in our environment present to hospital late[5,6], with patients presenting[5] with mean IPSS of 18 and 91% presenting with moderate/ severe symptoms and 56.7% with quality of life scores of ≥5. Another study revealed late presentation with 2.9%, 51.0% and 46.1% of patients presenting with minor, moderate, and severe symptoms, respectively. In these studies, the quality of life also correlated with the IPSS. Studies have also shown that black patients are more likely to present with severe symptoms.[7] The implication is that these patients are more likely to present with complications relating to prostatic enlargement.[8] Our patients present with bothersome symptoms as shown by the high QOL scores. Bothersomeness that affects QOL is what brings patients to the physician and relief of symptoms is more important to the patient, even more than flow rate, detrusor pressure etc.[9] Late presentation is thus quite a burden in Nigeria. This late presentation is usually associated with high cost as the patient may have to be optimized (e.g. treatment for retention, renal impairment, haematuria etc). There is also a higher recourse to surgery for the prostate and its complications. The probability of undergoing surgery over four years is 10%, 24% and 39% in patients with mild, moderate and severe symptoms respectively.[10] There is also a higher possibility of organ damage e.g. renal impairment and such patients with renal impairment are more prone to post-operative complications.[11] The need for guidelines cannot be overemphasised. They are very necessary to help with everyday dilemmas, especially needed in our

peculiar environment. Also, the practice in Nigeria is too varied and needs standardisation.

A situation where we rely on traditional 'policy design' process or idiosyncrasies of individual consultants is outdated. Having guidelines will help us to have high-quality practice relating to the best available evidence and will also help us to change practice for the better, a process of standardisation. This will in the long run improve quality of care and thus positively impact on the outcome of treatment of BPH. As already stated, many patient with BPH are seen by non-urologists, one of the reasons being that there are less than 200 urologists in Nigeria, to about 180million population. Having guidelines will make it easier for other personnel to know what to do and when to refer patients. It will also encourage multi disciplinary approach to the management of patients which is lacking in Nigeria. A situation where the first recourse to treatment is surgery will be minimised as many attending health personnel will now be fully aware of all other options of management and their indications.

1.2: OBJECTIVES

This guideline provides a guide for the management of BPH in Nigeria using the EAU guideline as a template with modifications, and it provides the best available evidence to physicians in the country. It has also been peer reviewed by the most senior urologists in the country. However, following guideline recommendations will not necessarily result in the best outcome. Guidelines can never replace clinical expertise when making treatment decisions for individual patients, but rather help to focus decisions - also taking personal values and preferences/individual circumstances of patients into account. Guidelines are not mandates and do not purport to be a legal standard of care.

1.3: METHODOLOGY

A proposal was written by the project director to seek for sponsorship. This was subsequently approved by the National Association of Urological Surgeons (NAUS). We generally followed internationally suggested steps 12,13,14 for development of guidelines, though with some modifications. This started with the construction of a guideline development group (GDG) composed of 13 urological surgeons drawn from all regions of the country. These included Prof NK Dakum (Project Director), Dr EA Jeje, Prof VM Ramyil, Prof AME Nwofor, Prof H Maitama, Prof CK Oranusi, Dr ON Ekeke, Dr AO Takure, Dr I Lawal, Dr A T

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Meetings was the main modus operandi of the groups. The first meeting was a discussion on BPH, the process of guideline development, various available guidelines available, etc. It also served as the avenue for distribution of responsibilities. Subsequent meetings discussed and developed the guidelines. This started with a determination of guideline scope and critical questions to be answered and the focus for literature review. This was followed by a collation and assessment of the current evidence from the literature. The literature review was mainly of all relevant studies done in Nigeria and similar climes, as well as others all over the world. Evidence was obtained from various databases e.g. Pub Med, African Journals on line, HINARI, Google scholar using search words such as prostate, Nigeria, guidelines etc. Available guidelines from around the world were collected and compared. In view of the fact that we have never had guidelines in the country and the fact that NAUS is a member of EAU, we decided to adopt the EAU guideline as a template and made necessary input to suit our local circumstances. Development of clinical recommendations and guideline text was then done after several meetings and discussions.

Review, comments and approval process: The draft guideline was then circulated to selected experts and stakeholders for their comments. These senior urologists included Prof O.O.Mbonu, Prof J Esho, Prof OB Shittu, Prof N Eke, Prof JC Orakwe, Prof LI Okeke, Dr E Azodoh, Prof I Mungadi and Prof TA Badmus. The draft was then sent via email to all members of the Nigerian Association of Urological Surgeons (NAUS), the umbrella body of all urologists in Nigeria for their input.

Periodic review process: This will be done one year after its distribution, or as may be necessary depending on circumstances. Any necessary modifications will then be done. However, the first major review of the document will be done five years after approval of the document.

1.4 AVAILABLE PUBLICATIONS:

This guideline is available as booklets and pamphlets (pocket guidelines) and will be circulated to doctors in government and private institutions all over the country. It will also be distributed to other stakeholders in the country and will also be posted on the website of NAUS (www.nausonline.org).

1. Yeboah EO. The prostate gland in: Badoe E. A, Archampong EQ Da Rocha – Afodu J.I Principles and practice of surgery including pathology in the tropics 3rd edition Ghana: Ghana Publishing Corporation. 2000;850 – 867
2. Barry M.J. Epidemiology of & Natural history of BPH. Urol clinic North Am. 1990: 17; 495 – 497

3. Eddy D. Assessing health practices and designing Practice policies. Philadelphia: American College of physicians, 1992

4. Dakum, N.K., Ogwuche, E.I., Ojo, E., Longmut, H. (2007).The practice of urology where there is no urologist.
Nigerian Medical Practitioner.52 (5/6):103-8.

5. Ogwuche E.I., Dakum, N.K., Amu CO, Dung DE, Udeh E, Ramyil VM. Problems with administration of International Prostate Symptom Score in a developing community. Annals of African Medicine. 2013. 12(3): 171-173.

6. Amu, O.C., Udeh, E.I., Ugochukwu, A.I., Dakum, N.K., Ramyil, V.M. The value of International Prostate Symptom Scoring system in the management of benign prostatic hyperplasia in Jos, Nigeria. Nigerian Journal of Clinical Practice. 2013. 16: 273-278.

7. Sarma AV, Wei JT, Jacobson DJ, Dunn RL, Roberts RO, Girman CJ, et al. Comparison of lower urinary tract symptom severity and associated bother between community-dwelling black and white men: The Olmsted County Study of Urinary Symptoms and Health Status and the Flint Men's Health Study. Urology 2003;61;1086-1091.Dos Reis RB

8. Rodrigues Neto AA, Reis LO, Machado RD, Kaplan S. Correlation between the presence of inguinal hernia and the intensity of lower urinary tract symptoms. Acta Cir Bras 2011;26(Suppl 2):125-128.

9. Mebust WK, Roizo R, Schroeder F, Villers A. Correlations between pathology, clinical symptoms and the course of the disease. The International Consultation on Benign Prostatic Hyperplasia Proceedings. Paris, 1991; 53:51.
10. Barry MJ, Fowler FJ, Bin L, et al: The natural history of patients with benign prostatic hyperplasia as diagnosed by North American urologists. J Urol

1997;157:10–15.

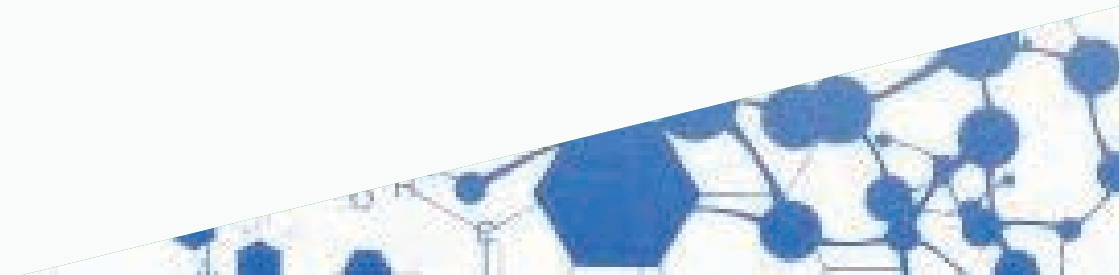
11. Presti JC, Christopher JK, Shinohara K, Carroll PR. Neoplasms of the prostate gland. In: Tanagho EA, McAninch J(Eds). Smith's General Urology, 17th Ed., McGraw Hill Companies, 348-374.

12. The guidelines manual. National institute for care excellence (NICE). http://publications.nice.org.uk/the-guidelines-manual-pmg6. Accessed 03/07/2015

13. Guideline development tool. http://www.guidelinedevelopment.org/. Accessed 03/07/2015

14. Guideline development process. American Academy of Dermatology. https://www.aad.org/education/clinical-guidelines/guideline-development-process. Accessed 03/07/2015

CHAPTER 2
EPIDEMIOLOGY, AETIOLOGY AND PATHOPHYSIOLOGY



2.0: EPIDEMIOLOGY, AETIOLOGY AND PATHOPHYSIOLOGY

Lower urinary tract symptoms can be divided into storage, voiding and post-micturition symptoms[1] Lower urinary tract symptoms (LUTS) are prevalent, cause bother and impair quality of life (QoL).[2-5] An increasing awareness of LUTS and storage symptoms in particular, is warranted to discuss management options that could increase QoL.[6] Lower urinary tract symptoms are strongly associated with ageing[2, 3,] associated costs and burden are, therefore, likely to increase with future demographic changes .[3,7] Lower urinary tract symptoms are also associated with a number of modifiable risk factors, suggesting potential targets for prevention (e.g. metabolic syndrome).[8]Most elderly men have at least one LUTS[3], however, symptoms are often mild or not very bothersome.[5, 6, 19] Lower urinary tract symptoms progress dynamically: for some individuals, LUTS persist and progress over long time periods, and for others they remit.[3] LUTS have traditionally been related to bladder outlet obstruction (BOO), which is often caused by benign prostatic enlargement (BPE) resulting from the histologic condition of BPH.[4] However, recent studies have shown that LUTS are often unrelated to the prostate.[3,10] Bladder dysfunction may also cause LUTS, including detrusor overactivity/OAB, detrusor underactivity/under-active bladder, as well as other structural or functional abnormalities of the urinary tract and its surrounding tissues.10 Prostatic inflammation also appears to play a role in BPH pathogenesis and progression.[11,12] In addition, many non-urological conditions also contribute to urinary symptoms, especially nocturia.[3]

The definitions of the most common conditions related to male LUTS are presented below:

- Acute retention of urine is defined as a painful, palpable or percussible bladder, when the patient is unable to pass any urine.[1]
- Chronic retention of urine is defined as a non-painful bladder, which remains palpable or percussible after the patient has passed urine. Such patients may being incontinent.[1]
- Bladder outlet obstruction is the generic term for obstruction during voiding and is characterised by increasing detrusor pressure and reduced urine flow rate. [1]
- Benign prostatic obstruction is a form of BOO and may be diagnosed when the cause of outlet obstruction is known to be BPE.[1]
- Benign prostatic hyperplasia is a term used (and reserved) for the typical histological pattern, which defines the disease;

- Detrusor overactivity (DO) is a urodynamic observation characterised by involuntary detrusor contractions during the filling phase which may be spontaneous or provoked.[1]
- Overactive bladder syndrome is characterised by urinary urgency, with or without urge.

The prevalence of BPH varies with the definition used. Various definitions have been used depending on presence of symptoms, DRE findings, uroflowmetry or histopathological criteria. Berry et al summarising data from five previous studies shows that no men younger than 30years have BPH, whereas the prevalence was 8% in the fourth decade. They also showed that 50% of men had evidence of histologic BPH between the ages 50 and 60 years. [13]

In Nigeria, community based studies report that one-in-four men older than 40 years have symptoms suggestive of BPH.[14] The DRE and ultrasound prevalence of enlarged prostate were 68.3% and 64.9% respectively based on the definition of prostate volume of >30ml.[15] The overall prevalence of LUTS due to BPH is 57.4% in the fifth decade of life.[15] The age-specific prevalence of BPH is 104 per 1000 men in the fifth decade of life and increased to the highest prevalence of 429 per 1000 men in the ninth decade.[15]

2.1: RISK FACTORS FOR BPH AND LUTS

On a population level, there are two broad categories of risk factors associated with BPH and LUTS: Non-modifiable (age, geography and genetics) and modifiable factors (sex steroid hormones, the metabolic syndrome, obesity, diabetes, physical activity, and inflammation).

2.1.1: AGE

The prevalence of BPH rises markedly with age. Autopsy studies have observed a histological prevalence of 8%, 50% and 80% in the 4th, 6th and 9thdecades of life, respectively.[16] Worldwide observational studies have demonstrated older age to be a risk factor for BPH onset and clinical progression by several different metrics.[17,18,19]

Prostate volume also increases with age, with data from the Krimpen and Baltimore Longitudinal Study of Aging (BLSA) cohorts suggesting a prostate

growth rate of 2.0% to 2.5% per year in older men. Although prostate volume does not directly correlate with symptom severity, prostate growth is a risk factor for LUTS progression and larger volume prostates are associated with increased risks of BPH clinical progression, urinary retention and need for prostate surgery.[20,21] LUTS incidence also increases among older men. In the osteoporotic fractures in men study cohort, in a prospective study of 6000 community dwelling men over the age of 65 years in the US, 29% of those without LUTS at baseline developed clinically significant LUTS within two years of follow-up; among those ≥ 80 years, this proportion increased to 34%.22 In the US Olmsted County cohort, 14% of men without LUTS at baseline subsequently reported moderate or severe symptoms within 18 months of follow-up and 22% reported moderate or severe symptoms within 42 months of follow-up.23 Similarly, 21% of Japanese, 26% of black American and 20% of Austrian men with no or mild LUTS at baseline reported worsened symptoms after three, four and five years of follow-up, respectively.[24,25,26] A study by Platz et al., followed 9628 men for progression of LUTS over 18 years based on IPSS and observed that the incidence and progression rates of LUTS increased steeply as the men aged, with progression rates being higher than incidence rates.[27]

2.1.2: GEOGRAPHY

International studies have demonstrated geographic heterogeneity in prostate volume and LUTS prevalence. Significantly lower prostate volumes have been observed in men from Southeast Asia compared to Western populations. However, smaller volume did not always correlate with a decreased prevalence of LUTS: Ganpule, et al., demonstrated lower prostate volume, but higher mean IPSS values in a population of 2406 Asian men compared to men in Western world.[28]

2.1.3: GENETICS

Evidence suggests that there are genetic components to both BPH and LUTS. One case control analysis, in which cases were men less than 64 years of age who underwent surgery for BPH, noted 4-fold and 6-fold increase in the age-specific risks of BPH surgery among all male relatives and brothers of cases respectively. These investigators further estimated that 50% of men undergoing surgery for BPH less than 60 years of age had an inheritable form of the disease.[29] These

findings and those of others have suggested an autosomal dominant pattern of inheritance.[30] Men with inherited forms of BPH tend to have larger volume prostates and earlier age of onset of clinical symptoms then men with sporadic BPH.[31]

Monozygotic twin concordance rates of 63% and 26% have been observed for LUTS and BPH respectively, with one study estimating that genetic factors may contribute as much as 72% to the risk of high-moderate or severe LUTS among older men.[32,33]

Gene polymorphisms have also been implicated in the development of BPH. Deletions of Glutathione S-transferase enzyme genes, thought to confer cellular resistance to oxidative stress, are significantly associated with an increased risk of symptomatic BPH.[34]

2.1.4: SEX STEROID HORMONES:

(Testosterone, dihydrotestosterone and estrogen)

In prostatic secretory cells, the hormone 5-alpha reductase converts testosterone to DHT, a potent stimulator of prostate growth that, in addition to being necessary for prostate development, appears to play a central role in BPH pathogenesis. Multiple studies have explored associations of endogenous sex steroid hormones – namely testosterone, DHT and estrogen – with BPH and LUTS.Several observational studies have reported no associations and occasionally inverse associations of serum testosterone (total, bioavailable, or free) with BPH or LUTS.35,36,37 Furthermore, data from a subset of men in the Proscar long-term efficacy and Safety trial demonstrate low testosterone (<300 ng/dl) in 21.7% of aging men with BPH.38 A salient, but theoretical, concern of testosterone replacement therapy is the potential for it to exacerbate BPH, BOO and LUTS.39 These observations, however, imply that higher serum testosterone concentrations do not promote BPH and even are potentially protective.Several studies have noted an increased risk of BPH with increased serum concentrations of DHT and its metabolites. In one prospective study of community men, those with the highest midlife levels of DHT had nearly three times the risk of subsequent BPH compared with those with the lowest levels.[40]

These results are consistent with prior studies of serum concentrations of two DHT metabolites: 17b-diol-glucuronide and androstnediol glucuronide. These metabolites are surrogate markers for DHT activity, with higher concentrations indicating increased and lower concentrations decreased levels of DHT. Two

cross-sectional and one prospective study have shown direct associations of these DHT metabolites with BPH or LUTS.[41,42] Five-alpha reductase inhibitors (finasteride and dutasteride) decrease serum concentrations of DHT[43] and prevent clinical progression of BPH and LUTS.[44]

NON-MODIFIABLE RISK FACTOR FOR BPH/LUTS

Non-modifiable risk factors for BPH	Comments
Age	· Prevalence of BPH/LUTS increases with age · Prostate volume increases with age · Volume do not correlate with symptoms
Geography	· lower volumes among Asian men · Bigger volume among Nigerians (Badmus et al,2013)
Genetics	· Men with BPH who underwent surgery < 60years, inheritable disease · Higher concordance rates of BPH/LUTS in monozygotic twins · Gene polymorphism implicated in BPH (deletion Glutathione S-transferase enzyme)

Modifiable risk factors for BPH	Comments
Serum testosterone	· BPH / LUTS not related to high serum testosterone
DHT/metabolites	· Increased risk of BPH/LUTS
Diabetes	· IGF-1, increased risk for BPH/LUTS
Physical activity	· Increased physical activity reduce BPH/LUTS by 25%
Inflammation	· Strong links between BPH and histological inflammation.

2.1.5: OBESITY

A preponderance of evidence also demonstrates that obesity increases the risks of BPH surgery, initiation of BPH medical therapy and LUTS[45,46,47] and decreases the efficacy of finasteride[48] and dutasteride[49] for the treatment of BOO

2.1.6: DIABETES AND DISRUPTIONS IN GLUCOSE HOMEOSTASIS

Disruptions in glucose homeostasis at multiple different levels – from alterations in serum insulin growth factor (IGF) concentrations to diagnosis of clinical diabetes – are associated with higher likelihoods of BPH, BPE and LUTS. Higher serum concentrations of IGF-1 and insulin-like growth factor binding protein 3 have been associated with increased risk of clinical BPH and BPH surgery.[50] cross-sectional and one prospective study have shown direct associations of these DHT metabolites with BPH or LUTS.[41,42] Five-alpha reductase inhibitors (finasteride and dutasteride) decrease serum concentrations of DHT[43] and prevent clinical progression of BPH and LUTS.[44]

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2.1.7: PHYSICAL ACTIVITY

Increased physical activity and exercise have been robustly and consistently linked with decreased risks of BPH surgery, clinical BPH, histological BPH and

LUTS.[45,47] A meta-analysis of 11 published studies (n= 43,083 men) indicated that moderate to vigorous physical activity reduced the risk of BPH or LUTS by as much as 25% relative to a sedentary life-style, with the magnitude of the protective effect increasing with higher levels of activity.[53]

2.1.8: INFLAMMATION

A majority of observational studies suggests that inflammation is linked to the development of BPH and LUTS. The mechanisms underlying this relationship are unclear. One potential explanation is that the metabolic syndrome, which promotes systemic inflammation and oxidative stress, mediates the connection. Inflammation has been implicated as a primary stimulus for prostate carcinogenesis and it is possible that BPH represents a non-malignant proliferative pathway promoted by oxidative stress and inflammatory mediators.[54,55]

There are strong links between BPH and histological inflammation in surgical specimens, with the extent and severity of the inflammation corresponding to the magnitude of prostate enlargement and BPH area.[56,57] Data from the REDUCE trial suggest that more severe inflammation detected in prostate biopsy core specimens is correlated with higher IPSS scores.[58] Men with LUTS are more likely to have higher serum C-reactive protein, a marker of systemic inflammation59 while prior gonorrhoeal infection or prostatitis increase the likelihoods of BPH surgery and LUTS.[60] A history of infection with gonorrhoea, chlamydia or trichomonosis increases the risk of elevated PSA;[61] high serum IgG antibody titres to cytomegalovirus, herpes virus, human papilloma virus and hepatitis are associated with LUTS.[62].

Conversely, inhibition of inflammatory pathways potentially attenuates BPH risk. In one community cohort, men who reported daily non-steroidal anti-inflammatory (NSAID) use experienced significantly decreased risks of LUTS, low urinary flow rate, increased prostate volume and elevated PSA.[61]

1. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, van Kerrebroeck P, Victor A, Wein A. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. American Journal of Obstetrics & Gynecology. 2002 Jul 1;187(1): 116-126.

2. Martin SA, Haren MT, Marshall VR, Lange K, Wittert GA. Prevalence and factors associated with uncomplicated storage and voiding lower urinary tract symptoms in community-dwelling Australian men. World journal of urology. 2011 Apr 1;29(2):179-184.

3. Société Internationale d'Urologie (SIU), Lower Urinary Tract Symptoms (LUTS) : An International Consultation on Male LUTS. C. Chapple & P. Abrams, Editors. 2013. http://www.siuurology.org/themes/web/assets/files/ICUD/pdf/

4. Kupelian V, Wei JT, O'Leary MP, Kusek JW, Litman HJ, Link CL, McKinlay JB. Prevalence of lower urinary tract symptoms and effect on quality of life in a racially and ethnically diverse random sample: the Boston Area Community Health (BACH) Survey. Archives of Internal Medicine. 2006 Nov 27;166(21): 2381-2387.

5. Agarwal A, Eryuzlu LN, Cartwright R, Thorlund K, Tammela TL, Guyatt GH, Auvinen A, Tikkinen KA. What is the most bothersome lower urinary tract symptom? Individual-and population-level perspectives for both men and women. European urology. 2014 Jun 1;65(6):1211-1217.

6. De Ridder D, Roumeguere T, Kaufman L. Urgency and other lower urinary tract symptoms in men aged≥ 40 years: a Belgian epidemiological survey using the ICIQ-MLUTS questionnaire. International journal of clinical practice. 2015 Mar 1;69(3):358-365.

7. Taub DA, Wei JT. The economics of benign prostatic hyperplasia and lower urinary tract symptoms in the United States. Current urology reports. 2006 Aug 1;7(4):272-281

8. Gacci M, Corona G, Vignozzi L, Salvi M, Serni S, De Nunzio C, Tubaro A, Oelke M, Carini M, Maggi M. Metabolic syndrome and benign prostatic

enlargement: a systematic review and meta analysis. BJU international. 2015 Jan 1;115(1):24-31.

9. Kogan MI, Zachoval R, Özyurt C, Schäfer T, Christensen N. Epidemiology and impact of urinary incontinence, overactive bladder, and other lower urinary tract symptoms: results of the EPIC survey in Russia, Czech Republic, and Turkey. Current medical research and opinion. 2014 Oct 1;30(10):2119-2130.

10. Chapple CR, Wein AJ, Abrams P, Dmochowski RR, Giuliano F, Kaplan SA, McVary KT, Roehrborn CG. Lower urinary tract symptoms revisited: a broader clinical perspective. European urology. 2008 Sep 1;54(3):563-569.

11. Ficarra V, Rossanese M, Zazzara M, Giannarini G, Abbinante M, Bartoletti R, Mirone V, Scaglione F. The role of inflammation in lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) and its potential impact on medical therapy. Current urology reports. 2014 Dec 1;15(12):463.

12. He Q, Wang Z, Liu G, Daneshgari F, MacLennan GT, Gupta S. Metabolic syndrome, inflammation and lower urinary tract symptoms: possible translational links. Prostate cancer and prostatic diseases. 2016 Mar;19(1):7.

13. Berry SJ, Coffey DS, Walsh PC, Enwing LL. The development of benign prostate hyperplasia with age. J Urol 1984; 132(3):474-479

14. Ezeanyika, L.U.S., Ejike, C.E.C.C., O. Obidoa, O, Elom, S.O.. Prostate disorders in an apparently normal Nigerian population 1: Prevalence. Biokemistri. 2006 18: 127-132.

15. Ojewola RW, Oridota ES, Balogun OS, Alabi TO, Ajayi AI, Olajide TA, Tijani KH, Jeje EA, Ogunjimi MA, Ogundare EO. Prevalence of clinical benign prostatic hyperplasia amongst community-dwelling men in a South-Western Nigerian rural setting: A cross-sectional study. African Journal of Urology. 2017 Jun 30;23(2):109-115.

16. Barry MJ, Fowler FJ, Jr, Bin L, Pitts JC, 3rd, Harris CJ, Mulley AG., Jr The natural history of patients with benign prostatic hyperplasia as diagnosed by North American urologists. J Urol. 1997;157:10–14.

17. Taylor BC, Wilt TJ, Fink HA, Lambert LC, Marshall LM, Hoffman AR, et al. Prevalence, severity, and health correlates of lower urinary tract symptoms among older men: The MrOS study. Urology. 2006;68:804–809.

18. Wei JT, Calhoun E, Jacobsen SJ. Urologic diseases in America project: Benign prostatic hyperplasia. J Urol. 2005;173:1256–1261.

19. Kok ET, Schouten BW, Bohnen AM, Groeneveld FP, Thomas S, Bosch JL. Risk factors for lower urinary tract symptoms suggestive of benign prostatic hyperplasia in a community based population of healthy aging men: The Krimpen study. J Urol. 2009;181:710–716.

20. Bosch JL, Bangma CH, Groeneveld FP, Bohnen AM. The long-term relationship between a real change in prostate volume and a significant change in lower urinary tract symptom severity in population-based men: The Krimpen study. Eur Urol. 2008;53:819–825.

21. Roehrborn CG. BPH progression: Concept and key learning from MTOPS, ALTESS, COMBAT, and ALF-ONE. BJU Int. 2008;101(Suppl 3):17–21.

22. Parsons JK, Wilt TJ, Wang PY, Barrett-Connor E, Bauer DC, Marshall LM, et al. Progression of lower urinary tract symptoms in older men: A community based study. J Urol. 2010;183:1915–1920.

23. Jacobsen SJ, Girman CJ, Guess HA, Rhodes T, Oesterling JE, Lieber MM. Natural history of prostatism: Longitudinal changes in voiding symptoms in community dwelling men. J Urol. 1996;155:595–600.

24. Masumori N, Tsukamoto T, Rhodes T, Girman CJ. Natural history of lower urinary tract symptoms in men – Result of a longitudinal community-based study in Japan. Urology. 2003;61:956–960.

25. Sarma AV, McLaughlin JC, Jacobsen SJ, Logie J, Dolin P, Dunn RL, et al. Longitudinal changes in lower urinary tract symptoms among a cohort of black American men: The Flint Men's Health Study. Urology. 2004;64:959–965.

26. Temml C, Brössner C, Schatzl G, Ponholzer A, Knoepp L, Madersbacher S, et

al. The natural history of lower urinary tract symptoms over five years. Eur Urol. 2003;43:374–380.

27. Platz EA, Joshu CE, Mondul AM, Peskoe SB, Willett WC, Giovannucci E. Incidence and progression of lower urinary tract symptoms in a large prospective cohort of United States men. J Urol. 2012;188:496–501.

28. Ganpule AP, Desai MR, Desai MM, Wani KD, Bapat SD. Natural history of lower urinary tract symptoms: Preliminary report from a community based Indian study. BJU Int. 2004;94:332–334.

29. Sanda MG, Beaty TH, Stutzman RE, Childs B, Walsh PC. Genetic susceptibility of benign prostatic hyperplasia. J Urol. 1994;152:115–119.

30. Pearson JD, Lei HH, Beaty TH, Wiley KE, Isaacs SD, Isaacs WB, et al. Familial aggregation of bothersome benign prostatic hyperplasia symptoms. Urology. 2003;61:781–785.

31. Sanda MG, Doehring CB, Binkowitz B, Beaty TH, Partin AW, Hale E, et al. Clinical and biological characteristics of familial benign prostatic hyperplasia. J Urol. 1997;157:876–879.

32. Rohrmann S, Fallin MD, Page WF, Reed T, Partin AW, Walsh PC, et al. Concordance rates and modifiable risk factors for lower urinary tract symptoms in twins. Epidemiology. 2006;17:419–427.

33. Partin AW, Page WF, Lee BR, Sanda MG, Miller RN, Walsh PC. Concordance rates for benign prostatic disease among twins suggest hereditary influence. Urology. 1994;44:646–650.

34. Konwar R, Manchanda PK, Chaudhary P, Nayak VL, Singh V, Bid HK. Glutathione S-transferase (GST) gene variants and risk of benign prostatichyperplasia: A report in a North Indian population. Asian Pac J Cancer Prev. 2010;11:1067–1072.

35. Trifiro MD, Parsons JK, Palazzi-Churas K, Bergstrom J, Lakin C, Barrett-Connor E. Serum sex hormones and the 20-year risk of lower urinary tract

symptoms in community-dwelling older men. BJU Int. 2010;105: 1554–1559.

36. Parsons JK, Palazzi-Churas K, Bergstrom J, Barrett-Connor E. Prospective study of serum dihydrotestosterone and subsequent risk of benign prostatichyperplasia in community dwelling men: The Rancho Bernardo Study. J Urol. 2010;184:1040–1044.

37. Kristal AR, Schenk JM, Song Y, Arnold KB, Neuhouser ML, Goodman PJ, et al. Serum steroid and sex hormone-binding globulin concentrations and the risk of incident benign prostatic hyperplasia: Results from the prostate cancer prevention trial. Am J Epidemiol. 2008;168:1416–1424.

38. Kaplan SA, O'Neill E, Lowe R, Hanson M, Meehan AG. Prevalence of low testosterone in aging men with benign prostatic hyperplasia: Data from the Proscar Long-term Efficacy and Safety Study (PLESS) Aging Male. 2013;16:48–51.

39. Bhasin S, Singh AB, Mac RP, Carter B, Lee MI, Cunningham GR. Managing the risks of prostate disease during testosterone replacement therapy in older men: Recommendations for a standardized monitoring plan. J Androl. 2003;24:299–311.

40. Amory JK, Wang C, Swerdloff RS, Anawalt BD, Matsumoto AM, Bremner WJ, et al. The effect of 5alpha-reductase inhibition with dutasteride and finasteride on semen parameters and serum hormones in healthy men. J Clin Endocrinol Metab. 2007;92:1659–1665.

41. McConnell JD, Roehrborn CG, Bautista OM, Andriole GL, Jr, Dixon CM, Kusek JW, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. N Engl J Med. 2003;349:2387–2398.

42. Parsons JK, Schenk JM, Arnold KB, Messer K, Till C, Thompson IM, et al. Finasteride reduces the risk of incident clinical benign prostatichyperplasia. Eur Urol. 2012;62:234–241.

43. Kumar R, Verma V, Sarswat A, Maikhuri JP, Jain A, Jain RK, et al. Selective

estrogen receptor modulators regulate stromal proliferation in human benign prostatic hyperplasia by multiple beneficial mechanisms - Action of two new agents. Invest New Drugs. 2012;30:582–593.

44. Haffner S, Taegtmeyer H. Epidemic obesity and the metabolic syndrome. Circulation. 2003;108:1541–1545.

45. De Nunzio C, Aronson W, Freedland SJ, Giovannucci E, Parsons JK. The correlation between metabolic syndrome and prostatic diseases. Eur Urol.2012;61:560–570.

46. Parsons JK, Sarma AV, McVary K, Wei JT. Obesity and benign prostatic hyperplasia: Clinical connections, emerging etiological paradigms and future directions. J Urol. 2013;189:S102–106.

47. Parsons JK. Modifiable risk factors for benign prostatic hyperplasia and lower urinary tract symptoms: New approaches to old problems. J Urol.2007;178:395–401.

48. Parsons JK, Messer K, White M, Barrett-Connor E, Bauer DC, Marshall LM, et al. Obesity increases and physical activity decreases lower urinary tract symptom risk in older men: The Osteoporotic Fractures in Men study. Eur Urol. 2011;60:1173–1180.

49. Muller RL, Gerber L, Moreira DM, Andriole G, Jr, Hamilton RJ, Fleshner N, et al. Obesity is associated with increased prostate growth and attenuated prostate volume reduction by dutasteride. Eur Urol. 2013;63:1115–1121.

50. Sarma AV, Parsons JK, McVary K, Wei JT. Diabetes and benign prostatic hyperplasia/lower urinary tract symptoms – What do we know? J Urol.2009;182:S32–37.

51. Parsons JK, Bergstrom J, Barrett-Connor E. Lipids, lipoproteins and the risk of benign prostatic hyperplasia in community-dwelling men. BJU Int.2008;101:313–318.

52. Gupta A, Gupta S, Pavuk M, Roehrborn CG. Anthropometric and metabolic

factors and risk of benign prostatic hyperplasia: A prospective cohort study of Air Force veterans. Urology. 2006;68:1198–1205.

53. Parsons JK, Kashefi C. Physical activity, benign prostatic hyperplasia, and lower urinary tract symptoms. Eur Urol. 2008;53:1228–1235.

54. Nickel JC, Downey J, Young I, Boag S. Asymptomatic inflammation and/or infection in benign prostatic hyperplasia. BJU Int. 1999;84:976–981.

55. Anim JT, Udo C, John B. Characterisation of inflammatory cells in benign prostatic hyperplasia. Acta Histochem. 1998;100:439–449.

56. Nickel JC, Roehrborn CG, O'Leary MP, Bostwick DG, Somerville MC, Rittmaster RS. The relationship between prostate inflammation and lower urinary tract symptoms: Examination of baseline data from the REDUCE trial. Eur Urol. 2008;54:1379–1384.

57. Rohrmann S, De Marzo AM, Smit E, Giovannucci E, Platz EA. Serum C-reactive protein concentration and lower urinary tract symptoms in older men in the Third National Health and Nutrition Examination Survey (NHANES III) Prostate. 2005;62:27–33.

58. Sutcliffe S, Giovannucci E, De Marzo AM, Willett WC, Platz EA. Sexually transmitted infections, prostatitis, ejaculation frequency, and the odds of lower urinary tract symptoms. Am J Epidemiol. 2005;162:898–906.

59. Sutcliffe S, Zenilman JM, Ghanem KG, Jadack RA, Sokoll LJ, Elliott DJ, et al. Sexually transmitted infections and prostatic inflammation/cell damage as measured by serum prostate specific antigen concentration. J Urol. 2006;175:1937–1942.

60. Sutcliffe S, Rohrmann S, Giovannucci E, Nelson KE, De Marzo AM, Isaacs WB, et al. Viral infections and lower urinary tract symptoms in the third national health and nutrition examination survey. J Urol. 2007;178:2181–2185.

61. St Sauver JL, Jacobson DJ, McGree ME, Lieber MM, Jacobsen SJ. Protective association between nonsteroidal antiinflammatory drug use and measures of

benign prostatic hyperplasia. Am J Epidemiol. 2006;164:760–768.

62. Parsons JK. Lifestyle factors, benign prostatic hyperplasia, and lower urinary tract symptoms. Curr Opin Urol. 2011;21:1–4.

CHAPTER 3
DIAGNOSTIC EVALUATION

3.0: DIAGNOSTIC EVALUATION

A common consequence of aging is benign prostatic enlargement (BPE), clinically or histologically proven benign prostatic hyperplasia (BPH). It may manifest with features of benign prostatic obstruction (BPO) in some men and usually as lower urinary tract symptoms (LUTS). The diagnosis can be made in most instances with good clinical history and physical examination, including digital rectal examination (DRE) to exclude other causes of bladder outlet obstruction (BOO). However, laboratory tests are useful for confirmation of diagnosis/exclusion of other causes of LUTS, assessing disease severity, risk of disease progression, complications, treatment planning and monitoring of treatment outcomes. In order to offer appropriate care to patients, the objectives of clinical evaluation of BPE/LUTS include:

I. To assess the clinical status of patients with LUTS, risks of progression and the presence of associated complications .

II. To rule out differential diagnosis, because LUTS in men are not specific for BPO, but often multifactorial.

3.1: MEDICAL HISTORY

The diagnosis of BPO requires a detailed and comprehensive medical history in order to identify the characteristics of the symptoms, risk factors, complications and relevant comorbidities (diabetes, hypertension, including neurological diseases) . Other relevant history should include medications, lifestyle and patients' perception of disease including emotional and psychological factors . Whenever possible, the following should also be explained or discussed with the patient in simple language or in the patient's first language:

1. LUT/BPO are age related and are treatable
2. The reason for treatment is not due to the size of the prostate but the presence/severity of LUTS .
3. Reassuring the patient that there is no definite link between LUTS and prostate cancer (Pca).

The need to seek medical attention by men with LUTS is often initiated by their subjective perception of worsening symptoms and/or the development of complications. In order to objectively quantify the severity of the LUTS, a validated symptom questionnaire should be applied. The commonest tool in use today for LUTS quantification is the international prostate symptoms score (IPPS) .Voiding diaries have been shown to be particularly beneficial when

assessing patients with predominant nocturia and/or storage symptoms; however, there are no local data to support the routine use of voiding diaries for routine evaluation of patients with BPO at the moment.

Sexual function should be deliberately assessed, because a number of men assume that ED is a consequence of normal aging and are often too embarrassed to talk about it. Therefore, it is useful to fill a validated symptoms questionnaire such as the International Index for Erectile Function (IIEF) when ED is present.

Recommendation: Take a complete medical history from men with LUTS, including erectile function and symptoms quantification with validated questionnaires.

3.2: SYMPTOM SCORE QUESTIONNAIRES

There are several questionnaires which are currently routinely used in urology and they are recommended by all guidelines . They were designed to objectively assess symptoms (LUTS) severity, characteristics and as a measure of treatment outcome. The common ones include the International Prostate Symptoms Score (IPSS) or the American Urologic Association Symptom Index (AUA-SI), the International Consultation on Incontinence Questionnaire (ICIQ-MLUTS) and the Danish Prostate Symptom Score (DAN-PSS). More recently the Visual prostate symptoms score (VPSS) was introduced by Chris Heyns.

3.2.1: THE INTERNATIONAL PROSTATE SYMPTOM SCORE (IPSS)

The IPSS is an 8-item self-administered questionnaire, consisting of seven symptom questions and one quality of life (QoL) question. The IPSS score is categorized as 'asymptomatic' (0 points), 'mildly symptomatic' (1-7 points), 'moderately symptomatic' (8-19 points), and 'severely symptomatic' (20-35 points) . There are a number of limitations to the use of IPSS; which have been observed generally, and they include lack of assessment of:

- Incontinence,
- Post-micturition symptoms
- Bother caused by each separate symptom.

Local studies in Nigeria have established the usefulness of IPSS and recommended its use in the management of BPO. In a study on 104 newly diagnosed patients with BPO by Amu et al in Jos; in which they sought to find the value of IPSS in the management of BPO, they observed a mean change in IPSS

scores of +2.3 for the minor symptom category, -8.1 ($P < 0.001$) for IPSS and -1.7 ($P < 0.001$) for QOLS in the moderate symptom category, and -24.6 ($P < 0.001$) for IPSS and -4.0 ($P < 0.05$) for QOLS in the severe symptom category. They concluded that IPSS is valuable in the initial evaluation of patients and outcome assessment. Similar studies in other centres in Nigeria corroborated their findings. Studies in Ibadan and Nnewi , which compared IPSS with uroflowmetry in patients with BPO, found a strong correlation. However there are some peculiar limitations to the use of IPSS in our setting as observed by Ogwuche et al . They found that only about 25.7% of the patients were literate enough in English to read, understand and complete the IPSS questionnaire. Thus they concluded that low literacy level and the absence of translated and validated IPSS in our local languages were strong limitations to its use and they recommended that validated translated versions of IPSS in our local languages be made available.

The severity of LUTS is often thought to correlate with the size of the prostate. However some studies in Nigeria have not demonstrated a correlation between prostate size and the severity of LUTS. Thus IPSS and prostate size are independent surrogates of severity of BPO.

3.2.2: THE INTERNATIONAL CONSULTATION ON INCONTINENCE QUESTIONNAIRE (ICIQ MLUTS)

The ICIQ-MLUTS was created from the International Continent Society (ICS) Male questionnaire. It is a widely used and validated patient completed questionnaire. It contains 13 items, with subscales for nocturia and overactive bladder (OAB), and is available in 17 languages. However, there are presently no local studies to support its use in Nigeria.

3.2.3: THE DANISH-PROSTATE SYMPTOM SCORE (DAN-PSS)

The Danish-Prostate Symptom Score (DAN-PSS) is a symptom score used mainly in Denmark and Finland. It is currently not used in Nigeria and there are no local studies to support its use at the moment.

3.2.4: THE VISUAL PROSTATE SYMPTOM SCORE (VPSS)

The visual prostate symptoms score (VPSS) was developed in South Africa by Chrys Heyns, to obviate the language barrier associated with the use of the IPSS among native South Africans. It was designed to address the limitations of the

traditional IPSS in societies with great language diversity and limited education. VPSS uses pictograms to assess the force of the urinary stream, daytime urinary frequency, nocturia and QoL. A study by Onowa in Jos, validated the usefulness of VPSS among patients with BPO in Jos, and they concluded that VPSS is simple and effective in assessing the severity of LUTS among patients with limited education or unable to complete the IPSS questionnaire.[19]

Recommendation: Use a validated symptom score questionnaire including quality of life assessment (IPSS) during the evaluation of men with LUTS. Because of the observed limitations of the IPSS, we recommend that in men who are literate enough the standard self-administered questionnaire should be utilized while for men with limited or no education, the questionnaires may be administered by the attending physician pending the translation and availability of the questionnaire in local languages. An alternative is the use of the VPSS for patients with limited education.

Research should be encouraged in translating and validating existing questionnaires or developing local alternatives altogether to meet our needs.

3.3: FREQUENCY VOLUME CHARTS AND BLADDER DIARIES

The recording of volume and time of each void by the patient is referred to as a Frequency Volume Chart (FVC). It is of value in patients with predominant nocturia and or polyuria. Inclusion of additional information such as fluid intake, use of pads, activities during recording, or symptom scores is termed a bladder diary. Parameters that can be derived from the FVC and bladder diary include:

- Daytime and night-time voiding frequency
- Total voided volume
- The fraction of urine produced during the night (nocturnal polyuria index) and volume of individual voids.

Recommendation: We did not find any relevant local studies or data to support its use, however, in the evaluation of patients with predominant nocturia, obtaining a bladder diary from the patient is advised. The patient should be told to complete a bladder diary for the duration of at least three days based on recommendations from other guidelines.

HISTORY TAKING

Recommended

- A detailed and comprehensive medical history
- The characteristics of LUTS
- Risk factors
- Complications and relevant comorbidities
  Diabetes, Hypertension and Neurological diseases.
- Medication history, lifestyle habits (smoking, alcohol)
- Patients' perception of disease
- Sexual history and erectile function
- Symptom quantification with IPSS and Bother Score
- Visual Prostate Symptoms Score (VPSS) for patients with limited education.

Optional

- Frequency Volume Chart (FVC)/Bladder Diary in patients with predominant nocturia
- Complete IIEF-5 in patients with ED

3.4: PHYSICAL EXAMINATION AND DIGITAL-RECTAL EXAMINATION (DRE)

BPO is a diagnosis of exclusion; therefore, a thorough physical examination is required to exclude other potential causes/factors that may affect the manifestation of LUTS. Attention should be focused on:

- The suprapubic area for tenderness and a distended bladder,
- The external genitalia for mental stenosis, urethral discharge, phimosis, urethral induration that may suggests urethral stricture and testicular swelling or tenderness when there is epididymoorchitis
- The perineum for sensation and reflexes or lower limbs weakness or paralysis as pointers to a neurogenic cause of LUTS.
- A thorough nervous system examination to exclude neurologic diseases like dementia, Parkinson's disease, multiple sclerosis and other neuropathies.

3.4.1: DIGITAL RECTAL EXAMINATION AND PROSTATE SIZE EVALUATION

Digital rectal examination (DRE) assesses the prostate gland in terms of the size and characteristics. Though the correlation to prostate volume is poor, most studies suggest that DRE under estimates prostate size [21]. However, it offers useful

information to guide subsequent investigations and even treatment especially where ultrasound scan is not readily available. Ultrasound scan particularly the transrectal ultrasound (TRUS) is more accurate in determining prostate volume than DRE. .

Recommendation: Perform a physical examination including digital rectal examination (DRE) in the assessment of men with LUTS/BPE.

EXAMINATION

- Examine the suprapubic area for tenderness and a distended bladder,
- The external genitalia for;
  - I. Meatal stenosis, Urethral discharge, phimosis,
  - II. Urethral induration
  - III. Testicular swelling or tenderness
- The perineum for sensation and reflexes
- Lower limbs weakness or paralysis
- A thorough nervous system examination to exclude neurologic diseases (Dementia, Parkinson's disease, Multiple sclerosis).
- DRE and prostate size estimation

3.5: URINALYSIS

Urinalysis (dipstick or sediment) must be included in the primary evaluation of any patient presenting with LUTS to identify conditions such as:

- Urinary tract infections (UTI),
- Microscopic haematuria and
- Diabetes mellitus.

If abnormal findings are detected further tests should be conducted.

Recommendation: Urinalysis (by dipstick or urinary sediment) is recommended by all guidelines in the assessment of male LUTS, although, we could not find local studies that specifically address its value in patients with LUTS/BPE.

3.6: URINE MICROSCOPY CULTURE AND SENSITIVITY (MCS)

Bladder outlet obstruction due to BPO and other causes leads to stasis of urine and progressive post void residual (PVR) urine; this is often accompanied with bacterial colonization and urinary tract infection (UTI). The incidence of UTI mirrors the severity and duration of BOO and presence or absence of catheter. This observation was confirmed in a study by Agbugui et al in Benin on 94 patients

with LUTS due to BPO in which the incidence of UTI was compared between patients with and without indwelling urethral catheter. They found an overall prevalence of 42 (44.7%) of the patients with positive urine cultures, and Escherichia coli was the commonest organism isolated (47.6%). A similar study in Bida by Akobi et al on 536 patients with BPH showed a high incidence of UTI among patients with BPO and the prevalence was highest among patients with indwelling catheter (62.5%). They also found Escherichia Coli [247(67.7%)] as the most prevalent uropathogen and the most susceptible antimicrobial agent was Nitrofurantoin (61.9%) and Levofloxacin (44.1%). The results of studies in other parts of Nigeria showed similar findings.

There are advantages in performing routine MCS in the primary evaluation of LUTS. While on one hand the presence of UTI often worsens the symptoms of BPO, and thus the need for concurrent treatment, on the other hand it guides the appropriate choice of prophylactic perioperative or therapeutic antibiotics. Ensuring that urine is "sterile" will significantly improve surgical outcomes.

Recommendation: Urine MCS should be done routinely in the primary evaluation of patients with LUTS/BPO.

3.7: PROSTATE-SPECIFIC ANTIGEN (PSA)

3.7.1: PSA AND THE PREDICTION OF PROSTATIC VOLUME.

There is an established relationship between prostate epithelial proliferation and level of PSA. A number of studies have analyzed this relationship among Nigerian men. In one of these studies, the PSA level was correlated with the size of the prostate among patients with histologically proven BPH and they found a strong correlation between PSA and the size of the prostate, however, age did not correlate well with BPH. In another study which involved a large community of men dwelling in Lagos, 4032 men were studied with a mean age of 51.6 (range 40–70) years. There was a strong correlation between serum PSA levels and age ($r = 0.097$, $P < 0.001$). The PSA isoform, PSA density (PSAD) was studied among patients with BPH and the cutoff level generated for Nigerian men in this study was 0.04 which is relatively different from international consensus. This PSAD cutoff level has a positive correlation with histology and could detect patients with CaP who have PSA in the "grey zone".

Recommendation: Prostate-specific antigen (PSA) should be routinely measured in the evaluation of patients with LUTS/BPE

3.7.2: RENAL FUNCTION MEASUREMENT

A dreaded consequence of unrelieved obstructive uropathy due to BPO is renal impairment (obstructive nephropathy), which can progress to end stage renal failure as a terminal event. Obstructive nephropathy is sometimes a consequence of BPO. In a study of men with chronic urinary retention in Zaria, BPO was found to be the commonest cause of renal impairment and the incidence of obstructive nephropathy rose with the duration
of obstruction. The likelihood of renal impairment may be suspected based on history, clinical examination and upper urinary tract ultrasound, in which hydronephrosis is observed. Renal function may be assessed by serum creatinine or estimated glomerular filtration rate (eGFR). Ayokunle et al in a study on men with BPO demonstrated an association between BPH and chronic kidney disease (CKD) in men whose symptoms were bothersome. They noted that the degree of bother (QoL) could be used as the determinant for requesting serum creatinine to assess the renal status of patient with BPH and estimation of GFR among these patients with BPH will offer a rapid method of renal function assessment at presentation and avert possible renal complications. There were no other local studies found on this subject.

Recommendation: Assess renal function if renal impairment is suspected based on history, clinical examination, or in the presence of hydronephrosis on ultrasound, or as part of preoperative preparation of patients scheduled for surgical treatment of BPO.

3.8: POST-VOID RESIDUAL URINE (PVR)

One of the non-invasive surrogates of BPO is post-void residual (PVR) urine; it can be assessed with transabdominal US or catheterization. PVR is not necessarily associated with BOO, since high PVR volumes can either be a consequence of obstruction and/or poor detrusor function (detrusor underactivity). PVR has been established to increase with degree and duration of LUTS and when the volume exceeds 300ml chronic urinary retention is said to ensure. There are currently no relevant local studies on the value of PVR in the management of patients with BPO, there is also no PVR threshold for treatment decision, and thus research is required in this aspect to guide management.

Recommendation: Measure post-void residual (PVR) in the assessment of men with BPO when the diagnosis of BOO is doubtful. PVR measurement should be an integral part of ultrasound evaluation of all patients with BPO/BPH.

3.9: UROFLOWMETRY

Urine flow rate is an objective non-invasive urodynamic measurement of severity of BOO often employed in the evaluation of patients with BPO. However PFR is not diagnostic of BOO as both BOO and detrusor dysfunction (underactivity) can lead to a build-up of PVR. Therefore, it is limited as a diagnostic test as it is unable to discriminate between the underlying mechanisms. The key parameters are maximum flow (Qmax) and flow pattern. Uroflowmetry parameters should preferably be evaluated with voided volume > 150 mL . In a study by Oranusi et al on 51 patients with BPO, they found a mean Qmax of 15.6ml/s, which is non-obstructive, despite clinical evidence of BOO. On the contrary Malomo et al in Ibadan studied 136 patients and found a strong correlation between the severity of symptoms measured on IPSS and Qmax. Uroflowmetry can be used for monitoring treatment outcomes and correlating symptoms with objective findings.

Recommendation: Uroflowmetry in the initial assessment of male LUTS may be performed, when available, in patients in whom there is a doubt about BOO, or for monitoring treatment outcomes.

3.10: IMAGING

3.10.1: UPPER URINARY TRACT

Imaging of the upper urinary tract is required in the routine evaluation of patients with BPO. This is especially relevant in our environment because of delay in presentation, at which time most have developed complications (urinary retention, hydronephrosis and obstructive nephropathy). Ultrasound scan has replaced intravenous urography (IVU) in the evaluation of patients with BPO because of its several advantages. Ultrasound scan is cheap, devoid of radiation and readily available in most Nigerian hospitals and cities. Ultrasound scan allows for simultaneous evaluation of the kidneys, bladder, measurement of PVR and assessment of the prostate. Contrast imaging of the upper tract may be done for patients with haematuria.

Recommendation: Perform ultrasound of the upper urinary tract in men with LUTS due to BPE.

3.10.2: PROSTATE

Benign prostatic enlargement is common in aging men and is often associated with the onset of LUTS, though the size of the prostate correlates poorly with the severity of LUTS. However, patients with larger prostates are more likely to present with symptoms and or complications of BPO. Imaging of the prostate can be performed by transabdominal US, TRUS, computed tomography (CT), and magnetic resonance imaging (MRI). However,the routine practice in Nigeria is the use of ultrasound (transabdominal or TRUS) in the evaluation of the prostate.

3.10.2.1: PROSTATE SIZE AND SHAPE

Assessment of prostate size is important for the selection of appropriate treatment, i.e. open prostatectomy, endoscopic, or minimally invasive modalities. It is also important prior to treatment with 5α-reductase inhibitors (5-ARIs). Evidence from some studies have shown that Black men have mean prostate volumes that are relatively larger than those in Caucasians and Asians. ,31 Several studies among Nigerian men with symptomatic BPH show the mean prostate sizes range between 42cm3 and 214cm3 with an overall median volume of 68.7cm3 (table 1). Prostate volume predicts symptom progression and the risk of complications.

TABLE 1. STUDIES ON MEAN PROSTATE VOLUME AMONG NIGERIA MEN WITH LUTS/BPE

Study	Study Method	No. Patients	Mean Age ± SD	Mean prost. Vol. ± SD
Badmus *et al31*	TRUS	105	64.4 ±	8.8883.5 ± 37.7
Ibinaiye *et al33*	TRUS	98	64.1 ±	45.93 ± 21.46
Ibinaiye *et al33*	Abdominal	98	"	42.62 ± 21.56
Ma'aji & Adamu34	Abdominal	117	67.1 ± 9.25	214.0 ± 8.49
Ahmed *et al21*	TRUS	317	62.5 ± 13.70	68.7 ± 47.2

Some studies among Nigerian men with BPE found transrectal ultrasound (TRUS) to be superior to transabdominal US in the measurement of prostate volume . However, some studies did not find any difference and rather, it is thought to depend on the experience of the sonographer. Intravesical prostatic protrusion (median lobe enlargement) when present may guide treatment choice.

Recommendations: Perform imaging of the prostate with ultrasound preferably

by the transrectal route (TRUS) when available. The transabdominal route is an alternative.

3.10.3: MICTURATING CYSTO-URETHROGRAM/RETROGRADE URETHROGRAM (RUG)

Micturating cysto-urethrogram (MCUG) and retrograde urethrography (RUG) are not required for the routine evaluation of patients with BPE in our current setting. However, in patients with suspected coexisting urethral stricture, RUG/MCUG should be done.

3.11: URETHROCYSTOSCOPY

Patients with a history of microscopic or gross haematuria, urethral stricture, or bladder cancer will require urethrocystoscopy during diagnostic evaluation. BPE is a common cause of haematuria, however, malignant urothelial pathologies must be excluded.

Recommendation: Perform urethrocystoscopy in men with BPE and haematuria or suspected urothelial malignancy.

3.12: URODYNAMIC STUDIES

Urodynamic studies for BOO, which are either cystometry or pressure flow studies (PFS) are required when the cause of BOO is unclear and unlikely to be due to BPE or when comorbid conditions (Diabetes mellitus and neurologic diseases) that are associated with functional BOO are present.

Recommendations: We did not find relevant studies to support routine performance of PFS. However, based on the established value of PFS in certain circumstances, pressure-flow studies (PFS) may be performed in individual patients with specific indications prior to invasive treatment when evaluation of the underlying pathophysiology of LUTS is unclear.

3.13: NON-INVASIVE TESTS IN DIAGNOSING BLADDER OUTLET OBSTRUCTION INMENWITH BPO/LUTS

Though not routine, the following assessments have been added to the armamentarium of evaluation of BPO:

1. Prostatic configuration using presumed circle area ratio (PCAR)
2. Intravesical prostatic protrusion (IPP)
3. Bladder/detrusor wall thickness and ultrasound-estimated bladder weight.

Recommendation: These non-invasive tests are currently not routinely used in Nigeria and there are scanty or no local studies that explored their value in the management of LUTS/BPE. Research is required in this field.

3.13.3: NON-INVASIVE PRESSURE-FLOW TESTING

1. The penile cuff method
2. Prostatic urethral angle

Recommendation: These have been proposed but they are still experimental. There is a need to conduct research on their value particularly because of their low cost, which is a significant factor in our health care.

INVESTIGATIONS

Recommended

- Abdominopelvic Ultrasound scan
- Transrectal ultrasound (TRUS)
- PSA
- Urinalysis and Urine MCS
- Uroflowmetry
- Kidney function tests
- Pressure flow studies (Urodynamics)

Optional

- Urethrocystoscopy
- RUG/MCUG

1. Bock-Oruma A, Dienye P, Oghu I. Prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia in primary care, Port Harcourt, Nigeria. South African Family Practice. 2013. p. 467–72.

2. Udoh E, Ukpong A. Causes of Bladder Outlet Obstruction in Adult Males , Relative Frequency and Mean Age at Diagnosis. 2016;4(4):156–60.

3. Pattern A, Bladder OF, Obstruction O, In A, Abdulkadir A. Aetiological Pattern of Bladder Outlet Obstruction Admissions in. 13(2):125–31.

4. Tela UM, Abubakar BM, Abubakar A, Adamu SA, Waziri MA. Community Based Survey of lower Urinary Tract Symptoms among Men. 2017;5(5):21254–7.

5. Owoaje E, Ladipo M, Fadimu O, Adedeji T. Frequency And Pattern Of Lower Urinary Tract Symptoms In A Screened Population Of Men ABbove 40 Years In Ibadan , Southwestern Nigeria. 2015;5(4).

6. Adegun PT, Adebayo PB, Areo PO. Severity of lower urinary tract symptoms among middle aged and elderly Nigerian men: Impact on quality of life. Adv Urol. 2016;2016.

7. Ejike CECC, Eze KC. Prevalence of symptoms of benign prostatic hyperplasia in Umudike and its relationship with measures of obesity. Asian J Clin Nutr. 2015;7(1):1–8.

8. Badmus TA, Asaleye CM, Badmus SA, Takure AO, Ibrahim MH, Arowolo OA. Benign prostate hyperplasia: average volume in southwestern Nigerians and correlation with anthropometrics. Niger Postgrad Med J. 2012;19(1):15–8.

9. Temi AP, Akande AO, Idris SA, Olufemi AP, Olusanmi EJ, Ayokunle DS. Effect of body mass index and age on international prostate symptom score : on men attending urology clinic in a tertiary institution in Nigeria. Glob Adv Res J Med Med Sci. 2015;4(4):200–6.

10. Pethiyagoda AUB, Pethiyagoda K. Correlation between prostate volume and Lower Urinary Tract Symptoms (LUTS) as measured by International Prostate

Symptom Score (IPSS). 2016;6(4):45–7.

11. Amu OC, Udeh EI, Ugochukwu AI, Dakum NK, Ramyil VM. The value of international prostate symptom scoring system in the management of bph in jos, Nigeria. Niger J Clin Pract. 2013;16(3):273–8.
12. Adegun PT, Areo PO, Solomon A, Dada SA, Adebayo PB. Erectile Dysfunction in Men with and without Lower Urinary Tract Symptoms in Nigeria. World J Mens Health. 2017;35(2):107.

13. Kevin T. McVary, MD, Chair; Claus G. Roehrborn, MD, Co-Chair; Andrew L. Avins, MD, MPH; Michael J. Barry, MD; Reginald C. Bruskewitz, MD; Robert F. Donnell, MD; Harris E. Foster, Jr., MD; Chris M. Gonzalez, MD; Steven A. Kaplan, MD; David R. Penson, MD; J M. American Urological Association Guideline: Management of Benign Prostatic Hyperplasia (BPH). 2010.

14. Oelke M, Bachmann A, Descazeaud A, Emberton M, Gravas S, Michel MC, et al. Guidelines on the Management of Male Lower Urinary Tract Symptoms Benign Prostatic Obstruction (BPO). Eur Assoc Urol 2012. 2012;64:118–140.

15. Heyns CF, Chb MB, Urol M, Urol F, Steenkamp BA, Chb MB, et al. Evaluation of the visual prostate symptom score in a male population with great language diversity and limited education : A study from Namibia. 2014;104(5):353–357.

16. Malomo TA, Adebayo SA, Takure AO, Anegbe A, Shittu OB, Okeke LI, et al. Correlation of the IPSS and quality of life with MMS ® uroflowmetry in patients with LUTS in Ibadan, Nigeria. African J Urol. Pan African Urological Surgeons' Association.; 2014;20(2):111–120.

17. Oranusi CK, Nwofor AE, Mbonu O. Correlation between international prostate symptom score and uroflowmetry in patients with benign prostatic hyperplasia. Niger J Clin Pract. 2017;20(4):454–458.

18. Ogwuche E, Dakum N, Amu C, Dung E, Udeh E, Ramyil V. Problems with administration of international prostate symptom score in a developing community. Ann Afr Med. 2013;12(3):171.

19. Onowa, VE. Relationship between IPSS, VPSS and Uroflowmetry in Men with Symptomatic Benign Prostatic Enlargement at the Jos University Teaching Hospital. Being a dissertation for the National Postgraduate College of Nigeria, for the award of the Fellowship in Surgery. 2016

20. Udeh EI, Ozoemena OFN, Ogwuche E. The relationship between prostate volume and international prostate symptom score in Africans with benign prostatic hyperplasia. Niger J Med. 2012;21(3):290–295.

21. Mohammed A, Bello A, Maitama H, Ajibola H, Lawal A, Isah M, et al. Determination of prostatic volume and characteristics by transrectal ultrasound among patients with lower urinary tract symptoms in Zaria, Nigeria. Arch Int Surg. 2014;4(1):31–35.

22. Agbugui J, Obarisiagbon E, Osaigbovo I. Bacteriology of urine specimens obtained from men with symptomatic benign prostatic hyperplasia. Niger J Surg. 2016;22(2):65.

23. Akobi OA, Inyinbor HE, Akobi EC, Emumwen EG, Ogedengbe SO. Lower Urinary Tract Infections among Patients Diagnosed of Benign Prostate Hyperplasia in Federal Medical Centre , Bida , North Central , Nigeria. Br J Med Med Res. 2016;14(7):1–9.

24. Oshodi AJ, Nwabuisi C, Popoola AA, Edungbola LD, Agbede OO, Akanbi Ii AA, et al. Bacterial Uropathogen among Benign Prostatic Hyperplasia Patients at a Tertiary Hospital in Nigeria. Open J Med Microbiol. 2015;5(5):22–7.

25. Udeh E, Dakum N, Amu O, Ramyl V. Correlation between Serum Prostate Specific Antigen and Prostate Volume in Nigerian Men with Biopsy Proven Benign Prostatic Hyperplasia: (A prospective study). J Urol Internet J Urol. 2009;7(2):1–5.

26. Ikuerowo SO, Omisanjo OA, Bioku MJ, Ajala MO, Nonyelim Mordi VP, Esho JO. Prevalence and characteristics of prostate cancer among participants of a communitybased screening in Nigeria using serum prostate specific antigen and digital rectal examination. Pan Afr Med J. 2013;15:1–7.

27. Ahmed M, Abubakar A, Lawal AT, Bello A, Maitama HY, Mbibu HN. Rapid and complete decompression of chronic urinary retention: a safe and effective practice. Trop Doct. 2013;43(1):13–6.

28. Ekiti A. Estimated Glomerular Filtration Rate in Patients with Lower Urinary Tract Symptoms / Benign Prostatic Obstruction in an ... Estimated Glomerular Filtration Rate in Patients with Lower Urinary Tract Symptoms / Benign Prostatic Obstruction in an Emerging Te. 2016;9(January 2015):1–7.

29. Salako AA, Badmus TA, Owojuyigbe AM, David RA, Ndegbu CU, Onyeze CI. Open Prostatectomy in the Management of Benign Prostate Hyperplasia in a Developing Economy. Open J Urol. 2016;6(12):179–89.

30. Fowler Jr. JE, Bigler S a, Kilambi NK, Land S a. Relationships between prostate-specific antigen and prostate volume in black and white men with benign prostate biopsies. Urology. 1999;53(99):1175–8.

31. Kaplan SA, Reis RB, Staimen VB, Te AE. Is the ratio of transition zone to total prostate volume higher in African-American men than in their Caucasian or Hispanic counterparts? Br J Urol. 1998;82(6):804–7.

32. Badmus TA, Asaleye CM, Badmus SA, Takure AO. Benign Prostate Hyperplasia : Average Volume in Introduction : Niger Postgrad Med J. 2013;20(1):56–60.

33. Ibinaiye PO, Adeyinka AO, Obajimi MO. Comparative Evaluation Of Prostatic Volume By Transabdominal And Transrectal Ultrasonography In Patients With Prostatic Hypertrophy In Ibadan. Eur J Sci Res. 2005;10(1):6–14.

34. Ma'aji S.M., B. A. Transabdominal ultrasonographic assessment of prostate size and volume in Nigerians with clinical diagnosis of benign prostatic hyperplasia. Niger J Clin Pract. 2013;16(3):404.

35. Ajayi I, Aremu A, Olajide A, Bello T, Olajide F, Adetiloye V. Correlation of transrectal and transabodominal ultrasound measurement of transition zone volume with post-operative enucleated adenoma volume in benign prostatic hypertrophy. Pan Afr Med J. 2013;16:1–5

CHAPTER 4
MEDICAL TREATMENT OF BPH

4.0: MEDICAL TREATMENT OF BPH

4.1: CONSERVATIVE TREATMENT

Conservative management of LUTS-BPH plays an important role in the management of patients with BPH after an initial assessment to rule out other possible causes of LUTS. Studies have shown that the natural history of BPH is not well defined1,2, therefore, watchful waiting, behavioral and dietary modifications can play vital roles in the initial management of patients with LUTS-BPH.

4.1.1: WATCHFUL WAITING

Studies have shown that untreated LUTS due to BPH does not necessarily progress. 1,2 A policy of watchful waiting is, therefore, an appropriate choice in patients with mild to moderate LUTS symptoms on IPSS. Local studies on this method of treatment are unavailable but it is practiced by most urologist in Nigeria. Isaac3 in a meta-analysis of contemporary reports showed that 16% of those with BPH had no changes in symptoms, 38% felt better, under a policy of watchful waiting with a follow up period of 2.6-5 years. The mean probability of symptomatic improvement with watchful waiting is estimated at 42%.4Patients elected for watchful waiting must be reviewed at regular intervals with monitoring of IPSS, PVR and urine flow rate (Qmax) to detect worsening conditions and complications.

WATCHFUL WAITING/BEHAVIORAL/LIFESTYLE CHANGES

Offer in patients with

1. Mild to moderate symptoms on IPSS with
2. minimal bothersomeness of symptoms

Institute lifestyle modifications.

Monitor IPSS, PVR, urine flow rate (Qmax).

4.1.2: BEHAVIOURAL AND DIETARY MODIFICATIONS.

Patient as well as caregiver education on the disease condition has been shown to allay anxiety and significantly impact on any choice of therapy chosen for the patient. Discussions on modalities for treatment and possible complications must also be considered and discussed whenever the diagnosis of BPH is made. This allows for a better informed consent when a mode of therapy is taken. However, low patient education and awareness of disease conditions in the elderly impacts significantly on patient management in our environment.

Behavioral changes that have been recommended include:

- Reduction in fluid intake especially at nights to improve nocturia.
- Reduction of alcohol/caffeine intake.
- Control of co-morbid diseases like diabetes, Parkinson's disease, Alzheimer's disease which may worsen LUTS.
- Alteration or optimization of time of administration of medications that could worsen LUTS like diuretics in patients with hypertension, renal disease, or heart failure.
- Use of voiding diary (timed voiding schedules)

4.1.3: PRACTICAL CONSIDERATION

Recommendations

1. Patients with mild to moderate symptoms on IPSS with minimal bothersomness of symptoms can be offered watchful waiting as part of initial treatment, provided they are well educated enough on the disease and the need for regular reviews to detect complications.
2. Behavioral as well as dietary modifications can be included to better improve the treatment.

4.2: PHARMACOLOGICAL TREATMENT

4.2.1: α1-ADRENOCEPTOR ANTAGONISTS (α1-BLOCKERS)

Mechanism of action: The principal action of α1-adrenoreceptor(α1AR) antagonists in BPH has been attributed to a neurally mediated relaxant action on prostatic, bladder neck and urethral muscles.[5]Smooth muscles account for 40% of

the area density of the hyperplastic prostate[6] By blocking the agonist effect of norepinephrine on prostate smooth muscles, α1AR antagonists produce relaxation of the prostate smooth muscles, thus overcoming the dynamic component of benign prostatic obstruction. An additional mechanism has been postulated, in particular, the induction of apoptosis in BPH cells[7] However, it remains unclear whether this potential beneficial effect is a drug-specific effect associated with one drug, or a class specific action attributable to α1-adrenoreceptor blockade[7]

α1-adrenoreceptors (α1AR) are the predominant receptor subtype located within the prostate.[8] α1- antagonist subtypes (α1A ,α1B, α1D) are also located outside the prostate (bladder neck, ureter, central nervous system and blood vessels) and thus mediate potential adverse effects of α1AR.Older α1- blockers initially reported for use in BPH include Prazosin and Terazosin. Newer, and more selective α1- receptor blockers include Tamsulosin, Doxazosin, Alfuzosin and Silodosin.

Efficacy: Systemic analysis of placebo-controlled studies show that commonly used antagonists (Tamsulosin, Doxazosin and Alfuzosin) are similarly effective and better than placebo in improving urine flow rate and reducing symptoms.[9] The effects on flow rate and symptoms are prompt within days of commencing treatment and their effects are well maintained over time and there is no evidence of tolerance or tachyphylaxis to α1AR blockade with prolonged use after six months.[7]

α1AR blockers have become an effective initial treatment for patients with mild to moderate symptoms of BPH and in those with severe symptom opting out of surgery, before progression to acute retention and need for surgery. α1AR blockers do not affect the prostate volume.[10]

Tamsulosin has a rapid onset of action of one week, while Alfuzosin works within 2-3weeks. Alfuzosin, additionally improves sex drive in elderly men with erectile dysfunction.[10] The maximum improvement is felt at six months (24weeks) but may continue to 18months(64 weeks).[11] The effects of these α1AR blockers are greater in younger patients (<60years) and smaller prostate volume(<30cc). Treatment failures are associated with baseline prostate volume >40cc.[10]

Tolerability and Safety: The most frequent adverse effect of α1 AR blockade are asthenia, dizziness and orthostatic hypotension.[12] A systematic review concluded that α1-blockers do not adversely affect libido, have a small beneficial effect on

erectile function, but sometimes cause abnormal ejaculation.[13] Originally, abnormal ejaculation was thought to be retrograde, but more recent data demonstrate that it is due to a decrease or absence of seminal fluid during ejaculation, with young age being an apparent risk factor. In a recent meta-analysis, ejaculatory dysfunction (EjD) was significantly more common with α1-blockers than with placebo (OR 5.88). In particular, EjD was significantly more commonly related with tamsulosin or silodosin (OR: 8.57 and 32.5) than placebo, while both doxazosin and terazosin (OR 0.80 and 1.78) were associated with a low risk of EjD.[14]An adverse ocular event termed intra-operative floppy iris syndrome (IFIS) was reported in 2005, affecting cataract surgery.[15] A meta-analysis on IFIS after alfuzosin, doxazosin, tamsulosin or terazosin exposure showed an increased risk for all α1-blockers.16 However, the OR for IFIS was much higher for tamsulosin. It appears prudent not to initiate α1-blocker treatment prior to scheduled cataract surgery, and the ophthalmologist should be informed about α1-blocker use.

Practical consideration: α1 blockers are a good initial treatment for LUTS-BPH in patients with moderate to severe symptoms. They have the advantage of a rapid onset of action, good efficacy, and low levels of adverse effects. However, they do not have any effect on prostate volume and do not prevent the occurrence of acute urinary retention or need for surgery. Young patients who have need to preserve sexual function should be placed on Alfuzocin. Potential adverse effects must be explained to patients before commencing therapy especially orthostatic hypotension and patients going for cataract surgery must inform their ophthalmologist of the use of α1 blockers especially Tamsulosin.

PHARMACOLOGICAL TREATMENT.

α1-ADRENOCEPTOR ANTAGONISTS (α1-BLOCKERS).

α1 blockers are a good initial treatment for LUTS-BPH in patients with moderate to severe symptoms. They have the advantage of a rapid onset of action, good efficacy, and low levels of adverse effects. Young patients who have need to preserve sexual function should be placed on Alfuzocin. Adverse effects which include asthenia, dizziness and orthostatic hypotension,EjD, IFIS, should be explained to patients.

4.2.2: 5 α-REDUCTASE INHIBITORS (5-ARIs)

Mechanism of action: The more potent androgen known as dihydrotestosterone (DHT) which acts on the prostate is derived from testosterone after conversion to DHT by the nuclear bound enzyme known as 5α-reductase. Within the prostate, 90% of testosterone is converted to DHT.[17] 5α-reductase has two isoforms, each encoded by a separate gene.[18]

Type 1 isoenzyme is highly expressed in the liver and skin. Type 2 is responsible for virilisation of the male fetus, and is the predominant form in the prostate and genitals.

Two 5-ARIs are available for clinical use: dutasteride and finasteride. Finasteride was the first 5α-reductase inhibitor to be studied. Finasteride competitively inhibits the type 2 5α-reductase. Finasteride shrinks the prostate by inducing prostatic epithelial apoptosis and atrophy, with few stromal changes[19] leading to prostate size reduction of about 18-28% and a decrease in circulating PSA levels of about 50% after six to twelve months of treatment.[20] Adverse effects associated with its use including reduction of libido and gynaecomastia encouraged the discovery of a second 5-ARI, dutasteride.[21] The latter, launched in 2002, is a potent dual inhibitor and inhibits both the iso-enzyme type 1 and type 2. The suppression of DHT by dutasteride is 95% within the first month of its use. This suppression is reversible when dutasteride is discontinued.[19] The intra prostatic DHT suppression has been reported as 89.3% at two weeks, 92.4% at four weeks, and 98.9% at four months.[22] This reduction of DHT levels has a significant effect on prostatic volume (PV) and reduction reaches 95% clearance in six (6) months in blood. The prostatic volume shrinkage is about 24-25% by the second year of continuous taking of the drug dutasteride[23] This leads to symptom and flow rate improvement by over 65% with effect maintained over four years.

Efficacy: The long term safety and efficacy of finasteride has been well established in several controlled trials.[24,25,26] Significant differences were apparent after four months of treatment in ProscarLong Term Efficacy and Safety Study (PLESS).$_{27}$ In the 487 patients treated for five years the AUA symptom score decreased four points, the median prostate volume decreased by 24% and the mean maximum urinary flow (Qmax) increased by 2.9ml/s. Dutasteride has a dual 5α-reductase inhibitor action with a 60-fold greater inhibition of type 1 isoenzyme than does finasteride, as well as being potent against the type 2 isoenzyme. Biochemically, dutasteride achieves a rapid, near complete and consistent suppression of DHT. The efficacy results suggest that this agent is

similar to finasteride and the net improvement with dutarsteride over placebo increased with increasing total prostate volume, transition zone volume, and serum PSA levels.[7] Patients with larger prostate and higher PSA levels are most likely to have the greatest improvements with dutasteride. Dutasteride has also demonstrated efficacy in reducing the risks for AUR and BPH related surgery. Finasteride might reduce blood loss during transurethral prostate surgery, probably due to its effects on prostatic vascularisation.[28]

Tolerability and Safety: 5-ARIs are well tolerated, with a similar adverse effect profile, including erectile dysfunction, altered libido, ejaculatory disorders and gynecomastia.[29]

Practical Consideration: 5-ARIs are indicated in patients with moderate to severe symptoms. Its effects usually can be felt after four weeks of use and can be sustained for up to four years. Their effect on the serum PSA concentration needs to be considered in relation to PCa screening.

5 α-REDUCTASE INHIBITORS(5-ARIs)

5ARIs are indicated in patients with moderate to severe symptoms. Its effects usually can be felt after four weeks of use and can be sustained for up to four years. Their effect on the serum PSA concentration needs to be considered in relation to PCa screening.

Adverse effect include: erectile dysfunction, altered libido, ejaculatory disorders and gynecomastia.

4.2.3: MUSCARINIC RECEPTOR ANTAGONISTS

It has now become understood that primary or secondary bladder dysfunction are important components to LUTS. Men like women have overactive bladder (OAB) with advancing age but most published literature on antimuscarinics were mainly tested in females in the past, as it was believed that LUTS in men were caused by the prostate. The OAB componets of LUTS explains why prostate-directed therapies are not universally effective in reducing LUTS.

Five muscarinic receptor subtypes (M1-M5) have been described, of which M2 and M3 are predominant in the detrusor. M2 are more numerous, but the M3 subtype is functionally more important in bladder contractions. Antimuscarinic

agents inhibit muscarinic receptors in detrusor muscle, thereby decreasing the OAB components of LUTS.

The following muscarinic receptor antagonists are used for treating overactive bladder/storage symptoms: darifenacin hydrobromide (darifenacin); fesoterodine fumarate (fesoterodine); oxybutynin hydrochloride (oxybutynin); propiverine hydrochloride (propiverine); solifenacin succinate (solifenacin); tolterodine tartrate (tolterodine); trospium chloride. Only oxybutynin, tolterodine and solifenacin are readily available in Nigeria.

Efficacy: There is a significant reduction of daytime frequency, nocturia, urge urinary incontinence and IPSS whilst improving patient perception of treatment benefit. Tolerability and Safety: Drug-related adverse events include dry mouth (up to 16%), constipation (up to 4%), micturition difficulties (up to 2%), nasopharyngitis (up to 3%), and dizziness (up to 5%). The withdrawal rates from antimuscarinic drugs is generally similar to that of placebo (3-10%).Increased post-void residual (PVR) in men without BOO is minimal and similar to placebo. Theoretically, antimuscarinics might decrease bladder strength, and hence might be associated with PVR urine or urinary retention. A twelve-week safety study on men with mild to moderate BOO showed that tolterodine increased thePVR (49 mL vs. 16 mL) but not acute urinary retention (3% in both arms).

Recommendation: Antimuscarinic therapy could benefit subset of men with LUTS/BPH with predominantly storage (irritative) symptoms. Caution should be exercised when giving these agents in men with significant PVR or a history of spontaneous urinary retention.

MUSCARINIC RECEPTOR ANTAGONISTS

Could benefit subset of men with LUTS/BPH with predominantly storage (irritative) symptoms.Caution is recommended, however, when considering these agents in men with an elevated residual urine volume or a history of spontaneous urinary retention.

4.2.4: PHOSPHODIESTERASE-5 INHIBITORS

Studies have demonstrated strong relationship between LUTS and erectile dysfunction in elderly men, ED being highly prevalent among men with LUTS. Pathophysiological mechanisms that have been implicated in this interrelationship include: autonomic hyperactivity, alteration in NO levels,

alteration in Rho-kinase and pelvic atherosclerosis.

Mechanism of Action: Phosphodiesterase 5 inhibitors (PDE5Is) increase intracellular cyclic guanosine monophosphate, thus reducing smooth muscle tone of the detrusor, prostate and urethra. Tadalafil 5mg daily is currently the only PDE5 inhibitor that is approved for the treatment of male LUTS.

Efficacy: Several RCTs have demonstrated that PDE5Is reduce IPSS, storage and voiding LUTS, and improve QoL. However, Qmax did not significantly differ from placebo in most trials. In a meta-analysis, PDE5Is were found to improve IPSS and IIEF score, but not Qmax. A combination of PDE5Is and α-blockers has also been evaluated showing that combination therapy significantly improved IPSS score.

Tolerability and Safety: Reported adverse effects include flushing, gastroesophageal reflux, headache, dyspepsia, back pain and nasal congestion. PDE5Is are contraindicated in patients using nitrates, the potassium channel opener nicorandil, or the α1-blockers doxazosin and terazosin. They are also contraindicated in patients who have unstable angina pectoris, have had a recent myocardial infarction (< three months) or stroke (< six months), myocardial insufficiency (New York Heart Association stage > 2), hypotension, poorly controlled blood pressure, significant hepatic or renal insufficiency, or if anterior ischaemic optic neuropathy with sudden loss of vision is known or was reported after previous use of PDE5Is.

Recommendation: Tadalafil (5mg) should be considered for men with mild to moderate LUTS associated with ED.

PHOSPHODIESTERASE-5 INHIBITORS
Tadalafil (5mg) should be considered for men with mild to moderate LUTS associated with ED.

4.2.5: PLANT EXTRACTS - PHYTOTHERAPY

Mechanism of action: Herbal drug preparations are made of roots, seeds, pollen, bark, or fruits. There are single plant preparations (mono-preparations) and preparations combining two or more plants in one pill (combination preparations). The most widely used plants are Cucurbita pepo (pumpkin seeds), Hypoxis

rooperi (South African star grass), Pygeum africanum (bark of the African plum tree), Secale cereale (rye pollen), Serenoa repens (syn. Sabal serrulata (saw palmetto) and Urtica dioica (roots of the stinging nettle).Possible relevant compounds include phytosterols, ß-sitosterol, fatty acids, and lectins. In vitro, plant extracts can have several effects including anti-inflammatory, anti-androgenic and oestrogenic effects. These effects have not been confirmed in vivo, and the precise mechanisms of plant extracts remain unclear.

Efficacy: The extracts of the same plant produced by different companies do not necessarily have the same biological or clinical effects, therefore the effects of one brand cannot be extrapolated to others. In addition, batches from the same producer may contain different concentrations of active ingredients. Thus, the pharmacokinetic properties can vary significantly.
Pygeum africanum (bark of the African plum tree) and Secale cereale (rye pollen) have been reported to lead to treatment improvement compared to placebo. A Nigerian study showed some improvements in LUTS with plant extracts but the study was not a randomized clinical trial (no control group).[49]

Tolerability and Safety: Side-effects during phytotherapy are generally mild and comparable to placebo. Serious adverse events were not related to the study medication. Gastrointestinal complaints were the most commonly reported. In formulations with Hypoxis rooperi, ED was reported in 0.5% of patients.
Practical Considerations: Phytotherapeutic agents are a heterogeneous group and may contain differing concentrations of active ingredients. Hence, meta-analyses may not be justified and results of any analyses have to be interpreted with caution.

Recommendation: There is insufficient evidence to recommend their routine use.

PLANT EXTRACTS – PHYTOTHERAPY
There is insufficient evidence to recommend their routine use.

4.2.6.: BETA-3 AGONIST

Mechanism of Action: Beta-3 adrenoceptors are the predominant beta receptors expressed in the smooth muscle cells of the detrusor and their stimulation is thought to induce detrusor relaxation.

Efficacy: Mirabegron 50 mg is the first clinically available beta-3 agonist with approval for use in adults with OAB. Mirabegron has undergone extensive evaluation in RCTs conducted in Europe, Australia, North America and Japan. Mirabegron demonstrated significant efficacy in treating the symptoms of OAB, including micturition frequency, urgency, urge incontinence and also patient perception of treatment benefit. These studies had a predominantly female study population.

Tolerability and Safety: The most common treatment-related adverse events in the mirabegron groups were hypertension, UTI, headache and nasopharyngitis.

Practical Considerations: Long-term studies on the efficacy and safety of mirabegron in men of any age with LUTS are not yet available. Studies on the use of mirabegron in combination with other pharmacotherapeutic agents for male LUTS are pending.

Recommendation: It may be considered in men with OAB /LUTS, BPH.

BETA-3 AGONIST
May be considered in men with OAB / LUTS, BPH.

4.2.7: COMBINATION THERAPIES

4.2.7.1: α1-BLOCKERS + 5α-REDUCTASE INHIBITORS

Mechanism of Action: Combination therapy consists of an α1-blocker together with a 5-ARI. The α1-blocker exhibits clinical effects within hours or days, whereas the 5-ARI needs several months to develop full clinical efficacy. Finasteride has been tested in clinical trials with alfuzosin, terazosin, doxazosin or terazosin, and dutasteride with tamsulosin.Long-term data (four years) from MTOPS, and Combination of Avodart and Tamsulosin (CombAT) studies showed that combination treatment is superior to monotherapy for symptoms and Qmax, and superior to α-blocker alone in reducing the risk of AUR, progression or need for surgery. A local study by Odusanya et al looked at finasteride, tamsulosin and the combination and showed its effectiveness among Nigerian men.

Tolerability and Safety: Adverse events for both drug classes have been reported with combination treatment. The adverse events observed during combination treatment were typical of α1-blockers and 5-ARIs. The frequency of adverse events was significantly higher for combination therapy.

Practical Considerations: Compared with α1-blockers or 5-ARI monotherapy, combination therapy results in a greater improvement in LUTS and increase in Qmax, and is superior in prevention of disease progression. However, combination therapy is also associated with a higher rate of adverse events. Combination therapy should, therefore, be prescribed primarily in men who have moderate-to-severe LUTS and are at risk of disease progression (higher prostate volume, higher PSA concentration, advanced age, higher PVR, lower Qmax, etc.). Combination therapy should only be used when long-term treatment (more than twelve months) is intended and patients should be informed about this. Discontinuation of the α1-blocker after six months might be considered in men with moderate LUTS.

Recommendation: Combination therapy of alpha blockers and 5 alpha reductase inhibitors is recommended for patients with prostate size >40mls.

COMBINATION THERAPIES

α1-BLOCKERS + 5α-REDUCTASE INHIBITORS
Combination therapy of alpha blockers and 5 alpha reductase inhibitors is recommended for patients with prostate size >40mls.

α1-BLOCKERS + MUSCARINIC RECEPTOR ANTAGONISTS
The choice of agents should depend on the patient's co-morbidities, side effect profiles and tolerance

4.2.7.2: A1-BLOCKERS + MUSCARINIC RECEPTOR ANTAGONISTS

Mechanism of Action: Combination treatment consists of an α1-blocker together with an antimuscarinic aiming to antagonise both α1-adrenoceptors and muscarinic receptors. The possible combinations have not all been tested in clinical trials yet. Combination treatment is more efficacious in reducing urgency, UUI, voiding frequency, nocturia, or IPSS compared with α1-blockers or placebo alone, and improves QoL. Persistent LUTS during α1-blocker treatment can be

reduced by the additional use of an antimuscarinic.

Tolerability and Safety: Adverse events of both drug classes are seen with combined treatment using α1-blockers and antimuscarinics. .
Adverse events of both drug classes are seen with combined treatment using α1-blockers and antimuscarinics. .

Practical Considerations: Class effects are likely to underlie efficacy and QoL using an α1-blocker and antimuscarinic. Trials used mainly storage symptom endpoints, were of short duration, and included only men with low PVR volumes at baseline. Therefore, measuring PVR is recommended during combination treatment.

Recommendation: The choice of agents should depend on the patient's comorbidities, side effect profiles and tolerance.

1. Clarke R. The prostate and the endocrines: A control series. Br J Urol 1937; 9: 254-271.

2. Craigen AA, Hickling JB, Saunders CRG, et al. Natural history of prostatic obstruction. A prospective survey. JR Coll Gen Pract 1969; 18: 226-232.

3. Isaac JT. Importance of the natural history of benign prostatic hyperplasia in the evaluation of pharmacological intervention. Prostatic Supplement 1990; 3: 1-7.

4. Roehrborn CG. The Agency for Healthcare Policy and Research. Clinical guideline for the diagnosis and treatment of benign prostatic hyperplasia. Urol Clin North Am 1995; 22: 445-453.

5. Caine M. The present role of alpha adrenergic blockers in the treatment of benign prostatic hyperplasia. J Urol 1986: 136: 1-6.

6. Shapiro E, Harlanto V, lepor H. Anti-desmin vs anti-actin for quantifying the area density of prostate smooth muscle. Prostate 1992; 20:259-267.

7. Chapple CR. Pharmacological therapy of BPH/LUTS: an overview of the practicing clinician. BJU Int 2004; 94: 738-744.

8. Lepor H, Tang R, Merety K, Shapiro E. Alpha 1 adrenoceptor subtypes in human prostate. J Urol 1993a: 149: 640-642.

9. Chapple CR. Pharmacotherapy of benign prostatic hyperplasia, the potential for alpha1 adrenoceptor subtype specific blockade. Br J urol 1998; 81: 34-42.

10. Jardin A, Besadonn H, Delauche-Cavelier MC, Attah P(BPH-ALF group). Alfuzocin for treatment of benign prostatic hypertrophy. Lancet 1991; 337: 1457-1461.

11. Lepor H, Auerbach S, Puras-bac ZA et al. A randomized placebo controlled multicentre study of the efficacy and safety of terazocin in treatment of benign prostate hyperplasia. J Urol 1992; 148: 1467-1474.

12. Nwofor AME, Dogunro AS. Doxazocin in the treatment of elderly Nigerian men with benign prostate hyperplasia. AJU 2002; 8(2): 56-61.

13. Van Dijk Mm et al. Effect of alpha 1- adrenoceptor antagonists on male sexual function. Drugs 2006; 66: 287

14. Gacci M et al. Impact of medical treatment for male lower urinary tract symptoms due to benign prostatic hyperplasia on ejaculatory function: a systematic review and meta-analysis. J Sex med 2014; 11:1554.

15. Chang DF et al. Intraoperative floppy iris syndrome associated with tamsulosin. J Cataract Refract Surg 2005; 31:664.

16. Chatziralli IP et al. Risk factors for intraoperative floppy iris syndrome: a metanalysis. Ophthalmology 2011: 118: 730.

17. McConnell JD, Wilson JD, George FW et al. Finasteride an inhibitor of 5 alpha reductase suppresses prostatic dihydrotestosterone in men with benign prostatic hyperplasia. J Clin Endocrinol Metab 1992; 74: 505-508.

18. Delakas D, Lianos E, Karyotis L, Cranidis A. Finasteride, a long-term follow-up in the treatment of recurrent hematuria associated with benign prostatic hyperplasia. Urol Int 2001; 67:69-72.

19. Nwofor AME, Oranusi CK. Benign Prostatic hyperplasia. A review of current management strategies. NJU 2011: 1: 23-37.

20. Naslund MJ et al. A review of the clinical efficacy and safety of 5 alpha-reductase inhibitor for the enlarged prostate. Clin Ther 2007;29:17.

21. Lepor H, Williford WO, Barry MJ et al(VACOUP). The impact of medical therapy on bothersome effects due to symptoms, quality of life and global outcome and factors predicting response. J Urol 1998; 160: 358-3567.

22. Andriole GL, Kirby R. Safety and tolerability of dual 5 alpha reductase inhibitor dutasteride in treatment of benign prostatic hyperplasia. Eur Urol 2003;82-88

23. Schulman CC. Long term aspect of medical treatment of benign prostate hyperplasia. Eur Urol 2001;40: 7-12.

24. Gromley GJ, Stoner E, Bruskewitz RC et al . The effects of finasteride in men with benign prostate hyperplasia. New Eng J Med 1992; 327: 1185-1191.

25. Nickel JC, Fradet Y, Boake RL, et al. Efficacy and safety of finasteride therapy for BPH: results of a 2 year randomized controlled trial (the PROSPECT study) Proscar safety plus efficacy Canadian two year study. CMAJ 1996; 155:1251-1259

26. Anderson JT, Ekman P, Wolf H et al. Can finasteride reverse the progress of BPH? A two year placebo controlled study. The Scandinavian BPH study group. Urology 1995; 46: 631-637.

27. McConnel JD, Bruskewitz K, Walsh P et al. The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with BPH. Finasteride long term efficacy and safety study group. N Eng J Med 1998; 338: 557-563.

28. Donohue JF et al. transurethral prostate resection and bleeding: a randomized placebo controlled trial of the role of finasteride for decreasing operative blood loss. J urol 2002; 168:2024.

29. Siami P, Roebrborn CG, Barkin J, Damiao R, et al. Combination therapy with dutasteride and tamsulosin in men with moderate to severe benign prostate enlargement. The combAT (combination of Avodart and Tamsulosin) trial. Rational and trial design. Contemporary clinical trial 2007; 28: 770-779.

30. Michel MC, Schneider T, Krege S, Goepel M. Does gender or age affect the efficacy and safety of tolterodine? The Journal of urology. 2002;168(3):1027-1031.

31. Chapple CR, Roehrborn CG. A shifted paradigm for the further understanding, evaluation, and treatment of lower urinary tract symptoms in men: focus on the bladder. European urology. 2006;49(4):651-658.

32. Matsui M, Motomura D, Karasawa H, Fujikawa T, Jiang J, Komiya Y, et al. Multiple functional defects in peripheral autonomic organs in mice lacking muscarinic acetylcholine receptor gene for the M3 subtype. Proceedings of the National Academy of Sciences of the United States of America. 2000;97(17):9579-9584.

33. Hofner K, Burkart M, Jacob G, Jonas U. Safety and efficacy of tolterodine extended release in men with overactive bladder symptoms and presumed non-obstructive benign prostatic hyperplasia. World journal of urology. 2007;25(6):627-633.

34. Roehrborn CG, Abrams P, Rovner ES, Kaplan SA, Herschorn S, Guan Z. Efficacy and tolerability of tolterodine extended-release in men with overactive bladder and urgency urinary incontinence. BJU international. 2006;97(5):1003-1006.

35. Ikuerowo SO, Akindiji YO, Akinoso OA, Akinlusi FM, Esho JO. Association between erectile dysfunction and lower urinary tract symptoms due to benign prostatic hyperplasia in Nigerian men. Urologia internationalis. 2008;80(3):296-299.

36. De Nunzio C, Roehrborn CG, Andersson KE, McVary KT. Erectile Dysfunction and Lower Urinary Tract Symptoms. European urology focus. 2017;3(4-5):352-363.

37. Oelke M, Giuliano F, Mirone V, Xu L, Cox D, Viktrup L. Monotherapy with tadalafil or tamsulosin similarly improved lower urinary tract symptoms suggestive of benign prostatic hyperplasia in an international, randomised, parallel, placebo-controlled clinical trial. European urology. 2012;61(5):917-925.

38. Abrams P, Kaplan S, De Koning Gans HJ, Millard R. Safety and tolerability of tolterodine for the treatment of overactive bladder in men with bladder outlet obstruction. The Journal of urology. 2006;175(3 Pt 1):999-1004; discussion

39. Roehrborn CG, Chapple C, Oelke M, Cox D, Esler A, Viktrup L. Effects of tadalafil once daily on maximum urinary flow rate in men with lower urinary tract

symptoms suggestive of benign prostatic hyperplasia. The Journal of urology. 2014;191(4):1045-1050.

40. Gacci M, Salvi M, Sebastianelli A, Vignozzi L, Corona G, McVary KT, et al. The use of a single daily dose of tadalafil to treat signs and symptoms of benign prostatic hyperplasia and erectile dysfunction. Research and reports in urology. 2013;5:99-111.

41. Gacci M, Corona G, Salvi M, Vignozzi L, McVary KT, Kaplan SA, et al. A systematic review and meta-analysis on the use of phosphodiesterase 5 inhibitors alone or in combination with alpha-blockers for lower urinary tract symptoms due to benign prostatic hyperplasia. European urology. 2012;61(5):994-1003.

42. Madersbacher S, Berger I, Ponholzer A, Marszalek M. Plant extracts: sense or nonsense? Current opinion in urology. 2008;18(1):16-20.

43. Buck AC. Is there a scientific basis for the therapeutic effects of serenoa repens in benign prostatic hyperplasia? Mechanisms of action. The Journal of urology. 2004;172(5 Pt 1):1792-1799.

44. Levin RM, Das AK. A scientific basis for the therapeutic effects of Pygeum africanum and Serenoa repens. Urological research. 2000;28(3):201-209.

45. Habib FK, Wyllie MG. Not all brands are created equal: a comparison of selected components of different brands of Serenoa repens extract. Prostate cancer and prostatic diseases. 2004;7(3):195-200.

46. Scaglione F, Lucini V, Pannacci M, Caronno A, Leone C. Comparison of the potency of different brands of Serenoa repens extract on 5alpha-reductase types I and II in prostatic co-cultured epithelial and fibroblast cells. Pharmacology. 2008;82(4):270-275.

47. Wilt T, Ishani A, Mac Donald R, Rutks I, Stark G. Pygeum africanum for benign prostatic hyperplasia. The Cochrane database of systematic reviews. 2002(1):Cd001044.

48. Tacklind J, MacDonald R, Rutks I, Wilt TJ. Serenoa repens for benign

prostatic hyperplasia. The Cochrane database of systematic reviews. 2009(2):Cd001423.

49. Omisanjo O, Ikuerowo S, Izuagba E, Esho J, Adegboyega O. Effect of The Plant Extract Pygeum Africanum and Urtica Dioica on Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasi in Nigerian Men. http://ispub.com/IJU/9/2/13825. Accesed March 3, 2018.

50. Chapple CR, Kaplan SA, Mitcheson D, Klecka J, Cummings J, Drogendijk T, et al. Randomized double-blind, active-controlled phase 3 study to assess 12-month safety and efficacy of mirabegron, a beta(3)-adrenoceptor agonist, in overactive bladder. European urology. 2013;63(2):296-305.

51. Herschorn S, Barkin J, Castro-Diaz D, Frankel JM, Espuna-Pons M, Gousse AE, et al. A phase III, randomized, double-blind, parallel-group, placebo-controlled, multicentre study to assess the efficacy and safety of the beta(3) adrenoceptor agonist, mirabegron, in patients with symptoms of overactive bladder. Urology. 2013;82(2):313-320.

52. Khullar V, Amarenco G, Angulo JC, Cambronero J, Hoye K, Milsom I, et al. Efficacy and tolerability of mirabegron, a beta(3)-adrenoceptor agonist, in patients with overactive bladder: results from a randomised European-Australian phase 3 trial. European urology. 2013;63(2):283-295.

53. Nitti VW, Auerbach S, Martin N, Calhoun A, Lee M, Herschorn S. Results of a randomized phase III trial of mirabegron in patients with overactive bladder. The Journal of urology. 2013;189(4):1388-1395.

54. Roehrborn CG, McVary KT, Elion-Mboussa A, Viktrup L. Tadalafil administered once daily for lower urinary tract symptoms secondary to benign prostatic hyperplasia: a dose finding study. The Journal of urology. 2008;180(4):1228-1234.

55. Roehrborn CG, Siami P, Barkin J, Damiao R, Major-Walker K, Nandy I, et al. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the CombAT study. European urology. 2010;57(1):123-131.

56. McConnell JD, Roehrborn CG, Bautista OM, Andriole GL, Jr., Dixon CM, Kusek JW, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. The New England journal of medicine. 2003;349(25):2387-2398.

57. Odusanya BO, Tijani KH, Jeje EA, Ogunjimi MA, Ojewola RW. Short-term Effect of Tamsulosin and Finasteride Monotherapy and their Combination on Nigerian Men with Benign Prostatic Hyperplasia. Nigerian journal of surgery : official publication of the Nigerian Surgical Research Society. 2017;23(1):5-10.

58. Kaplan SA, Roehrborn CG, Rovner ES, Carlsson M, Bavendam T, Guan Z. Tolterodine and tamsulosin for treatment of men with lower urinary tract symptoms and overactive bladder: a randomized controlled trial. Jama. 2006;296(19):2319-2328.

59. Athanasopoulos A, Gyftopoulos K, Giannitsas K, Fisfis J, Perimenis P, Barbalias G. Combination treatment with an alpha-blocker plus an anticholinergic for bladder outlet obstruction: a prospective, randomized, controlled study. The Journal of urology. 2003;169(6):2253-2256.

60. Kaplan SA, McCammon K, Fincher R, Fakhoury A, He W. Safety and tolerability of solifenacin add-on therapy to alpha-blocker treated men with residual urgency and frequency. The Journal of urology. 2009;182(6):2825-2830.

CHAPTER 5
SURGICAL TREATMENT OF BPH

5.1 PREAMBLE

Patients with BPH in Nigeria tend to present late, often with complications because of poverty, ignorance and poor heath seeking behaviour.[1] They may thus require some additional interventions such as urethral or suprapubic catheterization to relieve acute or chronic urinary retention. There may also be the need to stabilize the patients' electrolytes, urea and creatinine. Anaemia and infection should also be corrected and controlled as the case may be.

5.1A. INDICATIONS

Surgical treatment is usually required when patients have experienced recurrent or refractory acute urinary retention, chronic urinary retention, recurrent UTIs, bladder stones or diverticulae, persistent haematuria or dilatation of the upper urinary tract due to BPO with or without renal insufficiency. Surgery is also needed when patients have not obtained adequate relief from LUTS or PVR using conservative or medical treatments.

INDICATIONS FOR SURGERY

- Recurrent or refractory acute urinary retention,
- Chronic urinary retention,
- Recurrent UTIs, bladder stones or diverticula,
- Persistent haematuria
- Dilatation of the upper urinary tract due to BPO with or without renal insufficiency.
- Inadequate relief of LUTS following medical treatment.

5.1B. CHOICE OF SURGICAL PROCEDURE

The choice of surgical procedure depends on prostate size, comorbidities of the patient, fitness for anaesthesia, patient preference, availability of the surgical armamentarium and skills.

CHOICE OF SURGICAL PROCEDURE

GENERAL CONSIDERATIONS

- Prostate size,
- Comorbidities of the patient,
- Fitness for anaesthesia,
- Patients' preference,
- Availability of the surgical armamentarium
- Surgical expertise

5.2. OPEN PROSTATECTOMY (OP).

Approaches: The oldest surgical treatment for moderate to severe LUTS secondary to BPO is open prostatectomy. Approaching the obstructive adenoma can be from either within the bladder (Freyer's procedure) or through the anterior capsule of the prostate (Millin's procedure). Open prostatectomy is the reference point for surgically treating large adenomas (>80 ml).

Efficacy: OP results in improvement in flow rates as early as first week after surgery.[2] Other notable improvements in outcome measures following OP include reduced PVR by 86 – 98%, improved QoL score by 60 -87%, reduced IPSS by as much as 12.5 – 23.3 points. 3-7Some RCTs indicate that open prostatectomy in men with large glands leads to similar outcomes compared to Holmium laser enucleation of the prostate (HoLEP), endoscopic enucleation of the prostate using bipolar circuitry and photo selective vaporization of the prostate. [8-11]

Tolerability and Safety; Mortality associated with OP has decreased significantly over the last two decades in Nigeria. Local retrospective studies show that mortality rates range from 0.4 to 1%. [2, 12, 13] The transfusion and surgical site infections rates following OP are rather high, approximately 30% and 7.5 to 12.1% respectively. [2, 13] Long term complications include transient incontinence (up to 11%), urethral stricture (0.8%) and retrograde ejaculation (up to 7.9%) [2, 13] and bladder neck constriction (2-3.8%). [2,13,14]

Practical Consideration; OP is the most invasive surgical method but it is an effective and durable procedure for the treatment of LUTS/BPO. Endoscopic enucleation of the prostate (EEP) requires experience and relevant endoscopic

skills. In the absence of endourological armamentarium including laser or bipolar system, OP is the surgical treatment of choice for men with prostate > 80ml.

Recommendation: Offer OP to treat moderate to severe LUTS in men with prostate size >80ml. However, attention should be paid to meticulous haemostasis and control of infection.

Efficacy: TURP results in sustained improvements of up to 96.2% in flow rates and PVR over a period of four years.[15] Low transfusion rates of 0.8% following TURP have been reported in local studies.[15] Repeat TUR rate in a retrospective study done over four years was 0.6%. [15] Other complications associated with TURP include TUR syndrome (4.6%) and capsular perforation (4.6%).[16] The incidence of urethral stricture of 12.3% and bladder neck contracture (BNC) of 14.7% over a longer duration of 8 – 20years as reported in foreign literature is significant but not noted in local studies perhaps due to short follow up in those studies.[17]

Practical Consideration: TURP is effective for the treatment of moderate to severe LUTS secondary to BPO. The choice should be based on prostate volume (30 – 80ml), availability of enduorological armamentarium and requisite expertise. No study on optimal cut off value exists but the complication rates increase with prostate size.[18]

5.3. TRANSURETHRAL RESECTION OF THE PROSTATE (TURP)

Mechanism of Action: TURP removes tissue from transitional zone of the gland. TURP is indicated in prostate size 30 – 80ml or <30ml with median lobe enlargement.

Efficacy: TURP results in sustained improvements of up to 96.2% in flow rates and PVR over a period of four years.[15] Low transfusion rates of 0.8% following TURP have been reported in local studies.15 Repeat TUR rate in a retrospective study done over four years was 0.6%.[15] Other complications associated with TURP include TUR syndrome (4.6%) and capsular perforation (4.6%).[16] The incidence of urethral stricture of 12.3% and bladder neck contracture (BNC) of 14.7% over a longer duration of 8 – 20years as reported in foreign literature is significant but not noted in local studies perhaps due to short follow up in those

studies.[17]

Practical Consideration: TURP is effective for the treatment of moderate to severe LUTS secondary to BPO. The choice should be based on prostate volume (30 – 80ml), availability of enduorological armamentarium and requisite expertise. No study on optimal cut off value exists but the complication rates increase with prostate size.[18]

5.3A. MODIFICATION OF TURP; BIPOLAR TURP

Mechanism of Action: Bipolar TURP (B-TURP) takes care of a major limitation of monopolar TURP (M-TURP) by allowing performance in normal saline. Contrary to M- TURP, in B-TURP systems, the energy does not travel through the body to reach a skin pad, bipolar circuitry is completed locally and energy is confined between an active resection loop and a passive pole situated on the resectoscope tip or sheath. B-TURP requires less energy/voltage because there is a smaller amount of interpolated tissue. During coagulation, heat dissipates within vessel wall creating a sealing coagulum and collagen shrinkage.

Recommendation: Offer M- TURP or B-TURP where available to treat moderate to severe LUTS in men with prostate size 30 – 80ml or <30ml with median lobe enlargement.

INDICATIONS

Open Surgery

- Moderate to severe LUTS
- Large adenomas (>80 ml).

Transurethral resection of the prostate (TURP)

- Moderate to severe LUTS
- Prostate size 30 – 80ml
- Prostate size <30ml with median lobe enlargement.

5.4 LASER TREATMENT OF THE PROSTATE

5.4a. HOLMIUM LASER ENUCLEATION OF THE PROSTATE AND HOLMIUM LASER RESECTION OF THE PROSTATE

Mechanism of Action: The holmium:yttrium-aluminium garnet (Ho;YAG) laser (wavelength 2,140nm) is a pulsed solid state laser that is absorbed by water and water containing tissues. Tissue coagulation and necrosis are limited to $\frac{2}{3}$ – 4mm which is enough to obtain adequate haemostasis. Holmium laser resection (HoLRP) or (HoLEP) results in BPO relief and secondarily in LUTS reduction.

Practical Consideration: The experience of the surgeon is the most important factor affecting overall occurrence of complications. [19,20]

5.4b. GREENLIGHT (532NM) LASER VAPORIZATION OF THE PROSTATE

Mechanism of Action: The Kalium-Titanyl-Phosphat (KTP) and the Lithium Triborate (LBO) lasers work at a wavelength of 532nm. The laser energy is absorbed by haemoglobin but not by water. Vaporization leads to immediate removal of prostatic tissue, relief of BPO and reduction of LUTS.

5.5 DIODE LASER VAPORIZATION OF THE PROSTATE.

Mechanism of Action: For prostate surgery, diode lasers with wavelength of 940nm, 980nm, 1,318nm and 1,470nm are marketed for vaporization and enucleation but only a few have been evaluated in clinical trials. Diode laser vaporization leads to immediate improvement of LUTS due to BPO and provide good haemostatic properties. An initial report from Zaria, Nigeria suggests some improvement in LUTS following diode laser vaporization of the prostate.

5.5A. THULIUM: YTTRIUM-ALUMINIUM-GARNET LASER (TM; YAG)

Mechanism of Action: In the Tm; YAG laser, a wavelength between 1,940nm and 2,013nm is emitted in continuous wave mode. The laser is primarily used in front-fire applications. Different applications ranging from vaporisation (ThuVap), vaporesection ThuVaRP), and enucleation (ThuVEP/ThuLEP: similar enucleating techniques) are published.

5.6. TRANSURETHRAL MICROWAVE THERAPY (TUMT)

Mechanism of Action: Microwave thermotherapy works by emitting microwave

radiation through intraurethral antennae that delivers heat into the prostate. Tissue is destroyed (coagulation necrosis) by being heated by temperatures above cytotoxic threshold (> 45o). The heat may also cause apoptosis and denervation of alpha receptors thereby decreasing the smooth muscle tone of the prostatic urethra.

5.7. TRANSURETHRAL NEEDLE ABLATION OF THE PROSTATE (TUNA)

Mechanism of Action: Transurethral needle ablation (TUNATM) device delivers low-level radiofrequency energy to the prostate through needles inserted transurethrally into the parenchyma under direct vision using an attachment to the standard cystoscope. The energy induces coagulation necrosis in the transition zone resulting in reduction of prostate volume and BPO. TUNA of the prostate can be performed as a day case procedure under local anaesthesia or sedation, however TUNA is not suitable for prostates > 75ml or isolated bladder neck obstruction neither can it effectively treat median lobe enlargement.

5.8. PROSTATIC STENTS

Mechanism of Action: The use of an endoprosthesis to preserve luminal patency is a well-established concept. Prostatic stents were primarily designed as an alternative to an indwelling catheter, but have also been assessed as a primary treatment option in patients with significant comorbidities. A prostatic stent requires a functioning detrusor. Permanent stents are biocompatible, allowing epithelialisation. Temporary stents do not epithelialise and may be either biostable or biodegradable. Temporary stents can provide short term relief from BPO in patients temporarily unfit for surgery or after minimally invasive treatment.

5.9. PROSTATIC URETHRAL LIFT (PUL)

Mechanism of Action: The prostatic urethral lift represents a novel minimally invasive approach under local or general anaesthesia. Encroaching lateral lobes are compressed by small permanent suture based implants delivered under cystoscopic guidance resulting in an opening of the prostatic urethra that leaves a continuous anterior channel through the prostatic fossa ranging from the bladder neck to the verumontanum. An obstructed/protruding median lobe cannot be effectively treated by PUL and the effectiveness of PUL in large prostate glands has not been shown yet.

5.10 NOVEL INTERVENTION

Intra-Prostatic Injections:

Mechanism of Action: Various substances have been injected directly into the prostate in order to improve LUTS. These include Botulinium toxin-A (BoNT-A), NX-1207 and PRX302. The mechanism of action of BoNT-A is through the inhibition of neurotransmitter release from cholinergic neurons via cleavage of synaptosome - associated protein 25 (SNAP-25). However BoNT-A also appears to act at various other levels by modulating the neurotransmitter of sympathetic, parasympathetic and sensory nerve terminals in the prostate, leading to a reduction in growth and apoptosis of the prostate.The detailed mechanism of action for the injectables NX-107 and PRX 302 are not completely understood but experimental data associates apoptosis induced atrophy of the prostate with both drugs.

5.11 MINIMAL INVASIVE SIMPLE PROSTATECTOMY

The term minimal invasive simple prostatectomy (MISP) includes laparoscopic simple prostatectomy (LSP) and robot assisted simple prostatectomy (RASP). The technique for LSP was first described in 2002 while the first RASP was reported in 2008. Both LSP and RASP are performed using different personalized techniques, developed based on the transcapsular (Millins) or transvesical (Freyer) techniques of OP. An extraperitoneal approach is mostly used for LSP while a transperitoneal approach is mostly used for RASP.

OTHER METHODS OF SURGICAL TREATMENT(MINIMALLY INVASIVE):

- Holmium laser enucleation of the prostate and Holmium laser resection of the prostate
- Greenlight (532nm) laser vaporization of the prostate
- DIODE laser vaporization of the prostate.
- Thulium: yttrium-aluminium-garnet laser (Tm; YAG)
- Transurethral microwave therapy (TUMT)
- Transurethral needle ablation of the prostate (TUNA)
- Prostatic stents
- Prostatic urethral lift (PUL)

Novel interventions:

- Intra-prostatic injections
- Minimal invasive simple prostatectomy(MISP)

5.13. FOLLOW-UP

Anybody treated for LUTS will need to be followed up for life. We need to look out for effectiveness of treatment, complications of treatment, recurrence of disease and emergence of other diseases of the lower urinary tract.

FOLLOW UP:

Look out for:

- Effectiveness of treatment.
- Complications of treatment.
- Recurrence of disease
- Emergence of other diseases of the LUTS.

Check at follow up visits:

- IPSS
- DRE
- Prostate scan with PVR measurement
- PSA
- Uroflowmetry (where available).
- FVC or Bladder diaries(may be needed)

Watchful Waiting (Behavioural)

Patients who elect to pursue a WW policy should be reviewed at six months and then annually, provided there is no deterioration of symptoms or development of absolute indications for surgical treatment. The following are recommended at follow-up visits: history, IPSS, DRE, prostate scan with PVR volume, PSA and uroflowmetry where available.

Medical Treatment

Patients receiving α1-blockers, muscarinic receptor antagonists, beta-3 agonists, PDE5Is or the combination of α1-blockers and 5-ARIs or muscarinic receptor antagonists should be reviewed four to six weeks after drug initiation to determine the treatment response. If patients gain symptomatic relief in the absence of troublesome adverse events, drug therapy may be continued. Patients should be reviewed at six months and then annually, provided there is no deterioration of symptoms or development of absolute indications for surgical treatment. The following are recommended at follow-up visits: history, IPSS, uroflowmetry, and

PVR volume. FVC or bladder diaries should be used to assess response to treatment for predominant storage symptoms or nocturnal polyuria.

Patients receiving 5-ARIs should be reviewed after twelve weeks and six months to determine their response and adverse events. The following are recommended at follow-up visits: history, IPSS, uroflowmetry, PVR volume and PSA.

Men taking 5-ARIs should be followed up regularly using serial PSA testing if life expectancy is greater than ten years and if a diagnosis of PCa could alter management. A new baseline PSA should be determined at six months, and any confirmed increase in PSA while on 5-ARIs should be evaluated.

Surgical Treatment

Patients after prostate surgery should be reviewed four to six weeks after catheter removal to evaluate treatment response and adverse events. If patients have symptomatic relief and are without adverse events, no further re-assessment is necessary. The following tests are recommended at follow-up visit after four to six weeks: IPSS, uroflowmetry and PVR volume. Follow up should be six monthly for the first year and yearly for life.

Recommendation

Follow-up for all conservative, medical, or operative treatment modalities is based on routine local practice.

1. Ojewola RW, Oridota ES, Balogun OS, Ogundare EO, Alabi TO. Lower Urinary Tract Symptoms: Prevalence, Perceptions, and Healthcare-Seeking Behavior amongst Nigerian Men. World J Mens Health.2016;34(3):200-208. doi:10.5534/wjmh.2016.34.3.200.https://doi.org/10.5534/wjmh.2016.34.3.200

2. Salako A, Badmus T, Owojuyigbe A , David R , Ndegbu C, Onyeze C. Open Prostatectomy in the Management of Benign Prostate Hyperplasia in a Developing Economy. Open Journal of Urology, 2016; 6:179-189. doi: 10.4236/oju.2016.612029.

3. Kuntz RM, Lehrich K, Ahyai SA. Holmium laser enucleation of the prostate versus open prostatectomy for prostates greater than 100 grams: 5-year follow-up results of a randomized clinical trial. Eur Urol, 2008; 53: 160. https://www.ncbi.nlm.nih.gov/pubmed/17869409

4. Naspro R, Suardi N, Salonia A, Scattoni V, Guazzoni G, Colombo R, et al. Holmium laser enucleation of the prostate versus open prostatectomy for prostates >70 g: 24-month follow-up. Eur Urol, 2006; 50: 563. https://www.ncbi.nlm.nih.gov/pubmed/16713070

5. Skolarikos A, Papachristou C, Athanasiadis G, Chalikopouos D, Deliveliotis C, Alivizatos G. Eighteen-month results of a randomized prospective study comparing transurethral photoselective vaporization with transvesical open enucleation for prostatic adenomas greater than 80 cc. J Endourol, 2008; 22: 2333. https://www.ncbi.nlm.nih.gov/pubmed/18837655

6. Varkarakis I, Kyriakakis Z, Delis A, Protogerou V, Deliveliotis C. Long-term results of open transvesical prostatectomy from a contemporary series of patients. Urology, 2004; 64: 306. https://www.ncbi.nlm.nih.gov/pubmed/15302484

7. Gratzke C, Schlenker B, Seitz M, Karl A, Hermanek P, Lack N, et al. Complications and early postoperative outcome after open prostatectomy in patients with benign prostatic enlargement: results of a prospective multicenter study. J Urol, 2007; 177: 1419. https://www.ncbi.nlm.nih.gov/pubmed/17382744

8. Chen Q, Zhang L, Fan QL, Zhou J, Peng YB, Wang Z. Bipolar transurethral resection in saline vs traditional monopolar resection of the prostate: results of a randomized trial with a 2-year follow-up. BJU Int, 2010; 106: 1339. https://www.ncbi.nlm.nih.gov/pubmed/20477825

9. Fagerstrom T, Nyman CR, Hahn RG. Complications and clinical outcome 18 months after bipolar and monopolar transurethral resection of the prostate. J Endourol, 2011; 25: 1043. https://www.ncbi.nlm.nih.gov/pubmed/21568691

10. Geavlete B, Georgescu D, Multescu R, Stanescu F, Jecu M, Geavlete P. Bipolar plasma vaporization vs monopolar and bipolar TURP-A prospective, randomized, long-term comparison. Urology, 2011; 78: 930. https://www.ncbi.nlm.nih.gov/pubmed/2180212

11. Komura K, Inamoto T, Takai T, Uchimoto T, Saito K, Tanda N, et al. Incidence of urethral stricture after bipolar transurethral resection of the prostate using TURIS: results from a randomised trial. BJU Int, 2015; 115: 644. https://www.ncbi.nlm.nih.gov/pubmed/24909399

12. Ugwumba FO, Ozoemena OF, Okoh AD, Echetabu KN, Mbadiwe OM. Transvesical prostatectomy in the management of benign prostatic hyperplasia in a developing country. Niger J Clin Pract, 2014;17:797-801. Available from: http://www.njcponline.com/text.asp?2014/17/6/797/144402

13. Ahmed Gadam I, Nuhu A, Aliyu S. Ten-Year Experience with Open Prostatectomy in Maiduguri. ISRN Urology, 2012; 1-4. https://doi.org/10.5402/2012/406872

14. Dakum NK, Ramyil VM, Agbo S, Ogwuche E, Malu D, Makama BS. The Malament suture: any role in transvesical prostatectomy? Sahel Medical Journal. 2007. 4:111-114

15. Alhassan SU, Aji SA, Mohammed AZ, Malami S. Transurethral resection of the prostate in Northern Nigeria, problems and prospects. BMC Urol. 2008;8:18. doi: 10.1186/1471-2490-8-18.

16. Chukwujama NO, Oguike T, Azike J. Transurethral resection of the prostate a 3 year experience. Niger J Surg, 2011; 17:15-8. Available from: http://www.nigerianjsurg.com/text.asp?2011/17/1/15/90367

17 . Madersbacher S, Lackner J, Brossner C, Rolhlich M, Stancik I, Willinger M, et al. Reoperation, myocardial infarction and mortality after transurethral and open prostatectomy: a nation-wide, long-term analysis of 23,123 cases. Eur Urol, 2005; 47: 499. https://www.ncbi.nlm.nih.gov/pubmed/15774249

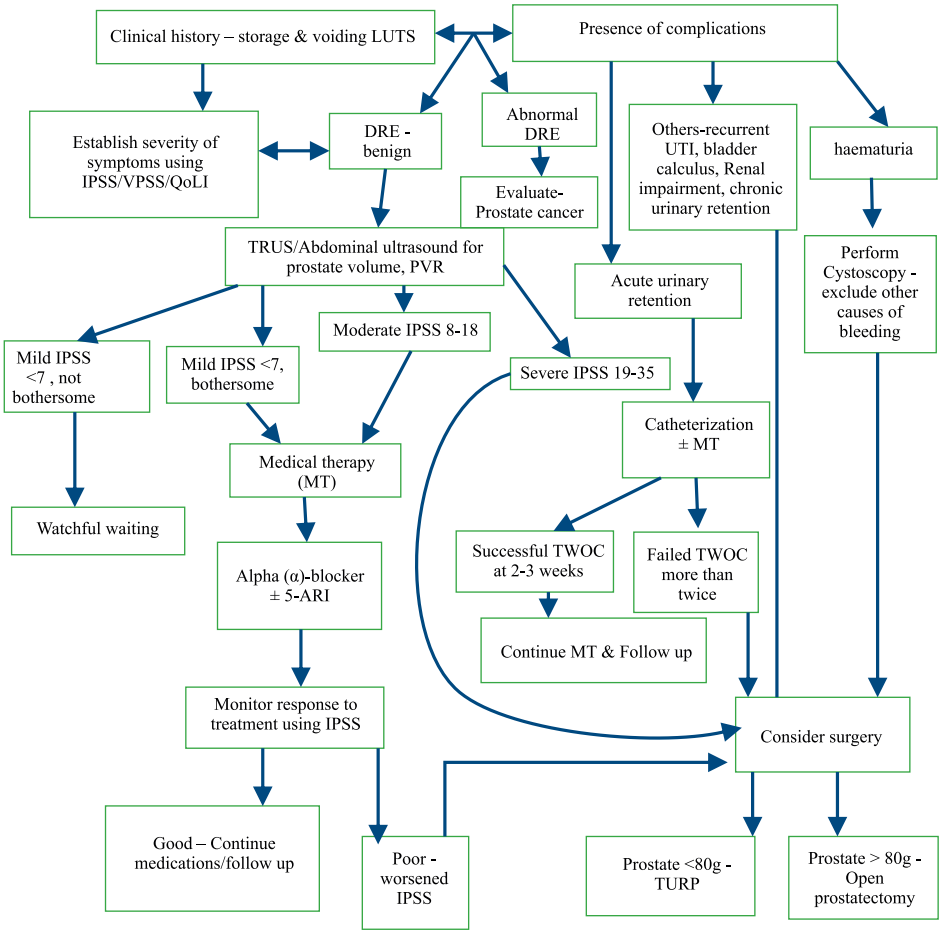
18. Reich O, Gratzke C, Bachmann A, Seitz M, Schlenker B, Hermanek P, et al. Morbidity, mortality and early outcome of transurethral resection of the prostate: a prospective multicenter evaluation of 10,654 patients. J Urol, 2008; 180: 246. https://www.ncbi.nlm.nih.gov/pubmed/18499179

19. Elzayat EA, Elhilali MM. Holmium laser enucleation of the prostate (HoLEP): long-term results, reoperation rate, and possible impact of the learning curve. Eur Urol, 2007; 52: 1465.
https://www.ncbi.nlm.nih.gov/pubmed/17498867

20. Du C, Jin X, Bai F, Qiu Y. Holmium laser enucleation of the prostate: the safety, efficacy, and learning experience in China. J Endourol, 2008; 22: 1031.
https://www.ncbi.nlm.nih.gov/pubmed/18377236

21.Ahmed M, Lawal AT, Bello A, Maitama HY. Short-term report on transurethral diode laser vaporization of the prostate at Ahmadu Bello University Teaching Hospital, Zaria-Nigeria. Arch Int Surg, 2016; 6:32-5. Available from: http://www.archintsurg.org/text.asp?2016/6/1/32/187196

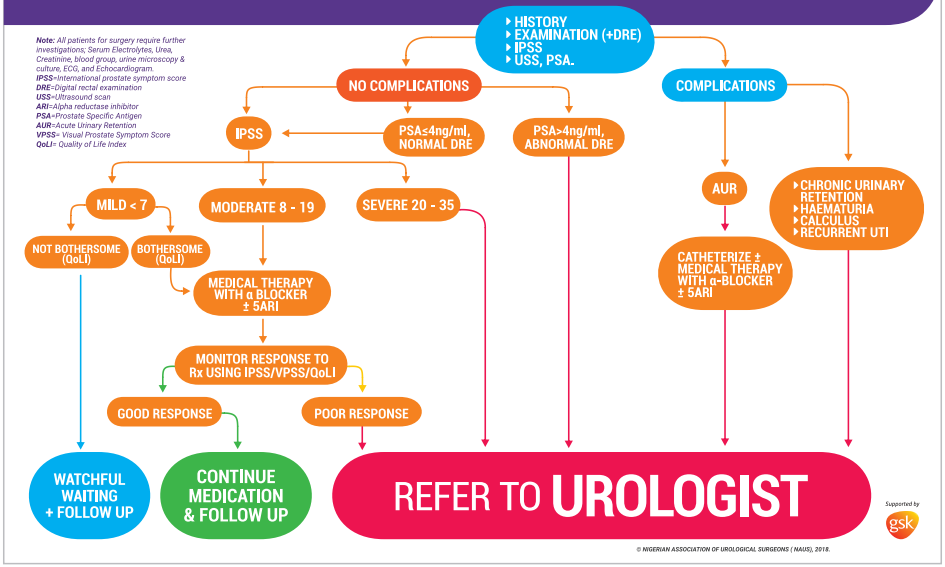
MANAGEMENT ALGORITHM FOR BENIGN PROSTATIC HYPERPLASIA FOR UROLOGISTS



Note: All patients for surgery require further investigations; Serum Electrolytes, Urea, Creatinine, blood group, urine microscopy & culture, ECG, and Echocardiogram.
LUTS = Lower urinary tract symptoms
TURP = Transurethral resection of prostate
IPSS = International prostate symptom score
TWOC = Trial without catheter
DRE = Digital rectal examination
MT = Medical therapy
VPSS = Visual prostate symptom score
QoLI = Quality of life index
ARI = Alpha reductase inhibitor

NIGERIAN ASSOCIATION OF UROLOGICAL SURGEONS (NAUS)

MANAGEMENT ALGORITHM FOR BENIGN PROSTATIC HYPERPLASIA FOR GENERAL PRACTITIONERS



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