

Available online at www.sciencedirect.com

**ScienceDirect** 

journal homepage: www.elsevier.com/locate/ajur

Review

# Management of BPH then 2000 and now 2016 – From BPH to BPO



CN 31-01047 609 321 + 3852 (2114) 609 331 + 3852 (2114)

**@** 

ASIAN JOURNAL OF

Johan Braeckman<sup>a</sup>, Louis Denis<sup>b,\*</sup>

<sup>a</sup> Department of Urology, UZ Brussel, Brussels, Belgium <sup>b</sup> Oncology Center Antwerp (OCA), Antwerp, Belgium

Received 25 August 2016; received in revised form 24 January 2017; accepted 22 February 2017 Available online 30 March 2017

## **KEYWORDS**

Benign prostate hyperplasia; Benign prostatic obstruction; Lower urinary tract symptoms; Pharmacological treatment; Transurethral resection of the prostate; Laser prostatectomy; Minimal invasive treatment **Abstract** The diagnosis and treatment of benign prostatic obstruction (BPO) is based on a number of well-known lower urinary tract symptoms (LUTS) feared by all ageing males with functional testes. The ascent of modern urology turned this disease from lethal into an annoying but treatable health problem in the previous century. We are able to relieve the great majority of patients from their bothersome symptoms to a respectable quality of life by medication or removal of the obstructive part of the enlarged prostate. We can be proud of some progress made in the new millennium to reach a correct diagnosis and subsequent choice of treatment aiming for quality of life and cost-efficiency for public health. Still it remains symptomatic treatment and we expect the new generation of urologists to close some gaps in our knowledge on the regulation of prostatic growth to focus on prevention and elimination of the disease in the foreseeable future.

© 2017 Editorial Office of Asian Journal of Urology. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

## 1. Introduction

One of the biggest challenges for practicing physicians is to recognize, understand and implement new innovative procedures and complete insight in disease processes for the benefit of their patients. The study and treatment of benign prostatic hyperplasia (BPH) is no exception. Its presence is a common finding in the ageing male and its bad reputation as first a nuisance and later a nightmare for the affected males is based on its obstruction of the urethra causing prostatism leading to acute urinary obstruction and subsequent renal failure in the end stages of the disease.

It is fair to state that the development of urology as a recognized speciality finds its origin in the surgical ability of

\* Corresponding author.

E-mail address: louis.denis@skynet.be (L. Denis).

Peer review under responsibility of Second Military Medical University.

http://dx.doi.org/10.1016/j.ajur.2017.02.002

<sup>2214-3882/© 2017</sup> Editorial Office of Asian Journal of Urology. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

an august line of medical pioneers to reduce the operative mortality to near zero by the end of the previous century. A herculean task greatly aided by the evolution of modern anaesthesia, effective anti-infectious treatment and a widely increased knowledge on early diagnosis and renal physio-pathology [1].

By the end of the century the scientific research, clinical trials and innovative pharmacological and health technology became so complex and at the same time so variable in the different regions and nations of the world that an urgent need for collaboration and standardization became a scientific and social priority in health care. Under the impulse of French urology, Professor Saad Khoury supported by Professor Rene Kuss, took the initiative in 1991 to start the International Consultation on Urological Diseases (ICUD) with the support of the World Health Organization (WHO).

The background idea was to prepare multidisciplinary and multiprofessional guidelines for various urological disorders by urologists and relevant specialists around the world. Its purpose was to bring researchers and clinicians together to speed up translational research and support for randomised clinical trials leading to evidence-based medicine. The ICUD would also provide consensual guidelines for the study and treatment of urological diseases from basic gold standard to research leading practice in relation to the economic means available. This idea emerged at the right time, parallel to the explosion of our knowledge on (i) the patho-physiology of the prostate, with adequate relief by new medications such as finasteride and the  $\alpha$ -blockers; (ii) innovative health technology; (iii) a social approach to involve other professions including nursing focussing on the specific needs of the patients in general, and the importance in comprehensive health care in particular.

The enthusiastic collaboration of all involved stakeholders from health authorities to simple patients groups resulted in a truly global consultation where all important urological associations, international and national, met every 2 years to compare their respective progress in the field as well as to colour outside their respective boxes. They remained modest enough to call it a consultation and not a consensus.

The results of these meetings were published in proceedings co-sponsored by WHO and the Union Internationale Contre le Cancer (French name) (UICC). In the scope of this contribution, we felt that the proceedings published on the start of the new millennium was a solid platform to summarize where we were, and watch the progress made on all aspects of BPH until 2015. That even the term BPH is now replaced by more appropriate terminology, is in the tradition of urology. We just are no linguists and we will keep talking about prostatectomy when we mean adenomectomy and radical prostatectomy when we attempt to perform a perfect anatomical prostatectomy [2].

It is clear that these contributions and the final recommendations are the compiled work and credit of the 124 authors and thousands of collaborators. The network is still active in the activities of the European Association of Urology (EAU), but the global approach on vision and mission has been replaced by the International Society of Urology (SIU). BPH surgery was still a lethal challenge in the first half of the 20th century. An explosion of progress in health care changed this situation in the second half. Antibiotics, anaesthesia and improved surgical procedures, especially the transurethral resection of the hyperplastic tissue of the diseased prostate (TURP) made BPH and its complications into an unpopular but non-lethal disease.

Further increased knowledge of the patho-physiology of the bladder in obstruction including urodynamics, defining "prostatism" in terms of lower urinary tract obstruction (LUTS) improving symptomatic therapy resulted in two kinds of management. The first was reassuring the patient on the condition and just observe or treat the condition with "alternative" medication and adapted life style. The second was the reassurance that in case of acute retention or crippling symptoms surgery, endoscopic or open, was available for most patients as a gold standard of cure. In the 1980's and 1990's rapid progress was noted; correct diagnosis by ultrasound imaging, urodynamic investigations and improved medical treatment in the early phases of the disease by the introduction of  $\alpha$ -blockers and finasteride. In general it was accepted that not all islands of hyperplastic tissue up to the false (surgical) capsule had to be removed. A bladder neck incision was to be considered in small, sclerotic prostates while BPH masses were reserved for open surgery. Minimal invasive procedures became a clinical research topic as well. Simultaneously we should consider the clinical introduction of the marker prostate specific antigen (PSA) and the painless biopsy as a revolution to exclude the presence of cancer in BPH management.

We do not claim that the urologists were the champions to increase the mean human lifespan in the developed countries from 60 years in 1940, to over 72 years in 1980, 77 in 2000 and last to 80 in 2012. However, the public in general and our patients in particular were so satisfied with our services that we earned the nickname, plumbers. An honour well deserved but earned by the labour of our teachers while each new generation is responsible to keep this standard and reputation of urology to ensure optimal services to our fellow men.

The 5th International Consultation in 2000 represented talent from all continents and decided under the sponsorship of WHO to develop recommendations on LUTS and BPH for the standard patient seeking relief with his general practitioner and his urologist. It should be noted that we recommend multidisciplinary evaluation and treatment for cancer patients. However it is clear that no patient with prostate cancer can expect optimal treatment without the expertise of an urologist available.

The total publication involved depended on 14 focused committees. Their report is presented to all participants for questions and answers. The resulting report, the product of literature search, the committee experience and peer review by an open presentation and comment, was then finalised by the scientific committee. The scientific committee consisted of the chairmen of all committees. The committees were multiprofessional including relevant specialities in medicine, general practitioners, nursing experts and patients. The final recommendations on symptoms, diagnosis and treatment of BPH were specifically focused on a standard patient. This standard (usual) patient is a 50-year-old male consulting a qualified health care provider for LUTS. These symptoms may or may not include bladder outlet obstruction (BOO) or histological BPH. Patients with prostate cancer, previous invasive treatment, diabetes, neurological disorders, sexually transmitted diseases and a history of trauma, fall out of these recommendations.

The age-old wisdom that something that walks like a duck, quacks like a duck and flies like a duck should be a duck is challenged by the observed discordance between anatomical and histological confirmed abnormalities and LUTS emanating from bladder functional disorders. In simple terms a huge prostate felt on digital rectal examination (DRE) may have few non-bothering LUTS while a small middle lobe prostate may cause acute retention.

The recommendation, next to defining terms and abbreviations for clinical use and specific advice to develop and evaluate new investigational drugs and devices, aimed to improve clinical practice. Diagnostic tests were classified as recommended, to be done on every standard patient, or optional for selected patients. Here the popular International Prostate Symptom Score (IPSS) for patient selfadministration is still widely used, together with physical examination and DRE. Urine analysis and a voiding diary form the base for an initial diagnosis.

The PSA test is recommended in the initial evaluation of patients with an anticipated life expectancy of over 10 years, and in whom the diagnosis of prostate cancer once established would change the treatment plan. Note that the presence of curable prostate cancer has no relation and is not the cause of LUTS in these patients.

Optional tests are part of the subsequent urological evaluation and include flow rate recording, residual urine, pressure flow studies and imaging by transabdominal or transrectal ultrasound to assess prostatic size and shape [3].

An identical classification was proposed for management by general practitioners (Fig. 1). If the initial evaluation demonstrates LUTS only without a suspicious DRE for cancer, then treatment depends on the bother score. Reassuring the patient and watchful waiting are appropriate if the symptoms are not bothersome. If bothersome, life style changes and pharmacological treatment are advised. If there is no improvement then referral to the specialist is appropriate for further assessment.

Specialised management is also indicated in the presence of infection, haematuria, suspicious DRE, abnormal PSA, palpable bladder and neurological disease (Fig. 2). If the condition is suggestive of obstruction eg.  $Q_{max} < 10 \text{ mL/s}$  intervention can be discussed. For the standard patient, TURP is in 2000 the gold standard for BPH, with overall benefit and reasonable side-effects of retrograde ejaculation. Unfortunately it requires experience and expertise to become "star resectionist" and adequate training for the next generation is not always available as the indication for surgery becomes more restricted.

Fortunately the urological sciences are engaged in clinical and basic research leading to a new wave of insight into prostatic growth, new pharmaceuticals and innovative devices.

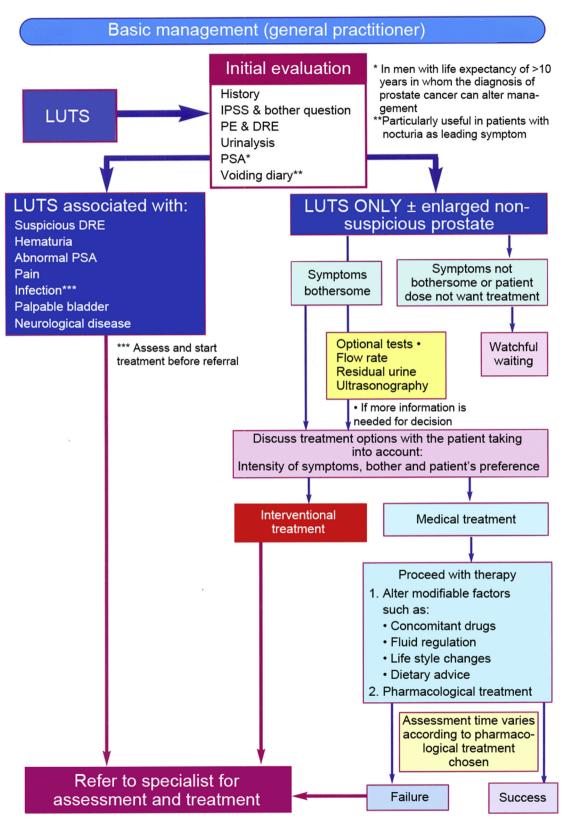
#### 3. BPH 20 years later...BPO

Our diagnostic tools for evaluation of men supposed to suffer from BPH with BOO or benign prostatic obstruction (BPO) did not really change very much over the last decades. Thanks to the work of national and international consultation groups, gathering together worldwide recognized experts, we learned to make better use of them. Even so important is that we should share this information with general practitioners, our partners in first line in the prostate disease management. The therapeutic approach of this disease, with medication or with conventional or socalled minimal invasive surgical treatment alternatives, is changing almost daily. No other medical specialisation was overwhelmed with so many new therapeutic developments over the last 20 years than prostate diseases. That is mainly because we gained new insights about the origin of this condition. This could and should have a positive impact on the prevention of the condition or at least on the onset of symptoms. Like for example, life style advice to avoid or to slow down what is called the metabolic syndrome. This better knowledge of what BPO is, also generated multiple usually multicentre randomized clinical trials to evaluate several new medical treatment agents. Combining some of those compounds can guarantee a long time and sometimes lifelong protection against bothering symptoms, resulting in less surgical procedures. Let's not forget that, after cataract, TURP is the most frequently performed surgical intervention in male patients worldwide. Surgical treatment options are also in a "switch condition" towards less invasive procedures with laser based interventions at the head for the moment.

## 4. BPO causalities

BPH is considered to be a natural process in the "aging prostate" but the development of BPO and urinary symptoms is probably linked to variable and interconnected pathophysiological processes. A complex pathological condition named "the metabolic syndrome", resulting from bad food habits, a sedentary behaviour and excessive alcohol use, among other possible causal factors like genetics, was identified in epidemiological studies to play a major role in the onset of LUTS and also erectile dysfunction in the ageing male [4]. Whether there is a direct link between this metabolic syndrome and changed activity of the androgen receptors in the prostate, a key factor in the development of BPH, is not known yet. Epidemiological data also strongly support a common pathophysiological mechanism for BPO and erectile dysfunction [5]. Three hypothetical mechanisms were identified to explain these concordant symptoms. An alteration of the NO-cGMP pathway and autonomic hyperactivity lead to a reduced vascular perfusion and reduced smooth muscle relaxation in the bladder neck, the prostate and the penis. The third mechanism, pelvic atherosclerosis, reduces pelvic perfusion.

More recently, in Europe [6] and in China [7], it was observed that chronic prostatic inflammatory processes result more frequently in symptomatic BPH. Clinically apparent prostatitis probably renders the external capsule



**Figure 1** Basic management (general practitioner) (Courtesy Prof. S. Khoury). DRE, digital rectal examination; IPSS, international prostate symptom score; LUTS, lower urinary tract symptoms; PE, physical examination; PSA, prostate specific antigen.

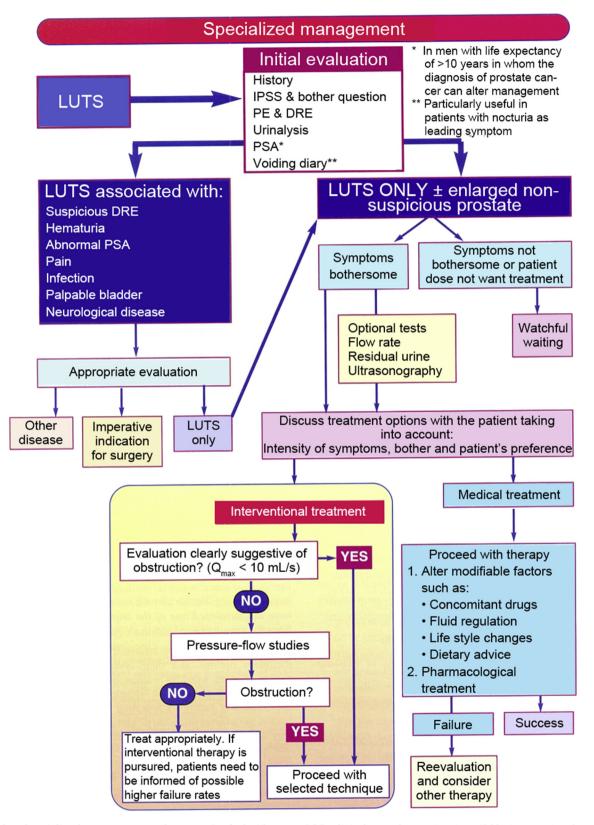


Figure 2 Specialized management (Courtesy Prof. S. Khoury). DRE, digital rectal examination; IPSS, international prostate symptom score; LUTS, lower urinary tract symptoms; PE, physical examination; PSA, prostate specific antigen;  $Q_{max}$ , maximal urinary flow rate.

of the prostate more rigid and this should logically increase the risk for a higher intra prostatic urethral resistance when the prostate gland becomes enlarged from BPH. Clinically unidentified prostatitis is also thought to be a possible cause of BPH and/or BPO, and this may be explained as an auto immune chain reaction in the stromal cells.

## 5. BPO symptoms and diagnosis

Symptoms from BPO are called "LUTS in the aging male" and they are listed together with symptoms from nocturnal polyuria, overactive bladder, underactive bladder, bladder tumours, urinary stones, urinary tract infection and all other causes of infravesical obstruction like urethral stricture. The minimal requirements for optimal diagnosis of this condition, and thus for excluding these other possible causes, are listed in regularly updated international directives like the EAU guidelines [8]. Some of these requirements, like digital rectal palpation of the prostate, urine microscopic and bacteriological analysis and measurement of residual urine are easily accepted by most health care professionals because they were established many years before the guidelines. Others, like symptom score questionnaires and voiding diaries, gain only slow acceptance, although their usefulness was extensively confirmed in national and international studies and in real life. These questionnaires, sometimes of self interrogation, interrogate the patient about urinary symptoms and about the impact of his complaints on his quality of life. They simplify our ability to recognize true BPO related LUTS, help us to differentiate storage from voiding symptoms and to stratify the extent and to monitor the subjective impact of the problem. Voiding diaries are very handy to identify patients with isolated nocturnal polyuria, who do not necessarily need treatment for BPO, from those with solely or predominantly BPO or overactive bladder. It is not always easy to obtain full collaboration from a patient and his environment to fill in the questionnaires properly, these are often older and sometimes mentally disabled men. Results from a recent international European study on nocturia and nocturnal polyuria presented at EAU16 in Munich suggest that patients self-reporting on the volumes of urine at night and in the daytime could serve as well as a voiding diary [9].

Considering the frequent concurrency of LUTS and erectile dysfunction it is considered good policy to ask patients with LUTS about their sexual function.

There is agreement among most urologists that patients who seek help for urinary symptoms do not routinely need PSA measurement. This test is only meaningful in patients in whom the presence of a possible prostate cancer would have a clear impact on the selected treatment. For example a young patient with moderate or severe LUTS who does not respond well to medical treatment and who is scheduled for transurethral resection or another surgical treatment of the prostate, which could render a radical prostatectomy on a later date far more difficult. A PSA based but well informed screening test is certainly acceptable in all patients with a life expectancy above 10 years and a confirmed BPO leading to a possible intervention.

All these tests can be done by a general practitioner and urologists should ideally stand by for more comprehensive evaluations like urinary flow, imaging and endoscopic examinations for abnormal conditions like haematuria or for patients who do not respond well to initial medical treatments.

Even urinary flow measurement, readily performed in the urological office in a urinary flow meter, might be replaced in some instances by visual flow scores on pictograms [10]. The measurement of residual urine can be done with any simple ultrasound device or with a bladder scan. This is an easy procedure that can be done outside the urological office by general practitioners, using second hand equipment disposed off by the radiologists or by any health care assistant.

Apart from measurement of urinary flow and residual urine, urodynamic evaluation is not routinely performed by most urologists. A full urodynamic examination with pressure flow study, the only test to unequivocally objectivise BOO, is only applied in patients considered too young, patients with a history or suspicion of neurological disease or patients with contradicting test results regarding the outcome of surgery.

Many patients are referred to urologists and radiologists requesting transrectal ultrasound (TRUS) of the prostate to assess BPH. TRUS is in fact negligible for the diagnosis of BPO, which is based on the anamnestic and urodynamic data. But it is a reliable way to assess the volume of BPH. The volume measurement is performed in what is called the transition zone of the prostate, surrounding the anterior prostatic urethra. Although the most accurate way to determine prostate volumes is the step section method, the ellipsoid volume measurement (length  $\times$  height  $\times$ width  $\times \pi/6$ ) provides sufficient reliability and may serve as a triage test to determine who may benefit from treatment with  $5\alpha$  reductase inhibitors, or from surgical enucleation rather than transurethral resection of the prostate. There is no cutoff threshold value for deciding who would need adapted treatment for a big prostate, that would depend on other factors like age, weight, comorbidity, experience and habits of the urologist.

Intravesical prostatic protrusion (IPP) is a readily measurable marker for BPO by a non-invasive approach with transabdominal ultrasound [11]. It is measured on a sagittal abdominal ultrasonogram of the prostate from the tip of the protrusion to the base of the prostate at the circumference of the bladder. IPP can be graded 1 (0–5 mm), 2 (>5–10 mm) or 3 (>10 mm) and may be helpful to predict the outcome and thus the necessary treatment, i.e. medical or surgical treatment, in patients with BOO, be it together with other subjective (bothersome) and objective (residual urine) findings [12]. This could be particularly interesting in places with minimal diagnostic resources.

Renal ultrasonography is only advised in patients with impaired renal function (azotemia), overflowing incontinence or very large amounts of residual urine. Abdominal CT scans are useful in patients with urinary tract infection or gross haematuria.

Cystoscopy is quoted optional in the guidelines, because like transrectal ultrasound, one does not need endoscopy to diagnose BPO. When there is doubt whether BPO is causing the LUTS, for example when uroflow measurement suggest a urethral stricture, urethrocystoscopy is useful. With the flexible cystoscope this previously feared examination is now a patient-friendly test that may help to exclude other problems and to appreciate the configuration of the BPO. This is especially so in the presence of IPP, an independent parameter for predicting the outcome in patients undergoing TURP [13].

#### 6. Conventional conservative treatment

The first treatment option for patients with well tolerated and uncomplicated LUTS should be life style advice. Key points of this approach are a reduced fluid intake, especially for caffeine and alcohol, relaxed and if possible double voiding, specific bladder training, maximal avoidance of constipation and timed intake of medication like diuretics. Patients complaining of nocturia, be it from BPO or nocturnal polyuria, who are on diuretic treatment for heart failure, hypertension, renal impairment or other reasons, are advised to take their pill in the late afternoon. That way most of the diuretic effect will take place in the hours before bedtime resulting in less urine production during the night. A limited number of, obviously non placebo controlled, clinical trials on self-management for BPO show a significant benefit expressed in the symptom score questionnaire in favour of an adapted life style [14].

Plant extracts were already and extensively prescribed many years before the arrival of the modern drugs for BPO and LUTS in general. In spite of some positive reports in the 1990s, they do not seem to be able to offer more than a placebo effect for BPH related symptoms and urodynamic findings. However, this is not necessarily inappropriate, especially in the group of patients mentioned above. In those days the decision whether to operate or to wait could be psychologically softened by prescribing a botanical medicine. The most popular products were and still are Serenoa repens (saw palmetto extract from the American dwarf palm), Hypoxis rooperi (African potato), Secale cereale (rye), Pygeum africanum (from the bark of the red stinkwood tree), Urtica dioica (stinging nettle) and Curcubita pepo (pumpkin seeds). One clear advantage of those herbal medicines over other drugs is the absence of any side-effect in most patients, except placebo side-effects of course [2].

 $\alpha$ 1A Receptor blocking agents and  $5\alpha$  reductase inhibitors are in the true sense of the word "established values" among medicines against BPO. Their mechanisms of action are well understood, documented and appreciated.  $\alpha 1A$ Blocking agents provide a quick symptomatic relief of BPO symptoms, unfortunately passing after a few (in average 4) years. 5a Reductase inhibitors provoke a slow but sustained reduction of the volume of the prostate, resulting in less symptoms, less risk of urinary retention and less risk for progression to surgery. The side-effects of those drugs are also well documented and rarely lead to withdrawal of the pills. Few men on  $\alpha$  blockers are affected by orthostatic hypotension and with the prolonged release preparations it is now exceptional. Retrograde ejaculation or even anejaculation is a regular side-effect and a substantial number of patients cannot accept this. With  $5\alpha$  reductase inhibitors the main problem is loss of libido, and here again patients may withdraw from the treatment for that reason. It is not clear whether changes in erectile and ejaculatory function in patients on these drugs are real or merely nocebo sideeffects. Combining the advantages, and also the sideeffects, of these pills is however a very popular approach today. Apparently the  $\alpha$ 1A receptor blocker can be withdrawn from the combined preparation after half to 1 year of treatment [15], except in patients with initially severe symptoms or with persisting storage dysfunction.

Antimuscarinic drugs, formerly absolutely prohibited in patients with suspicion of BPO, are now also regularly used for patients with BPO and overactive bladder symptoms, be it as part of or in addition to their prostate problem. Of course one must be careful in patients with large amounts of residual urine. This must be excluded before and from time to time reassessed during treatment with anticholinergic pills. These drugs can also be prescribed in combined preparations with an  $\alpha$ 1A receptor antagonist or with a 5 $\alpha$  reductase inhibitor. Whether this combination treatment should be replaced by monotherapy and which one should then be continued after a certain period has not been evidenced in trials.

Double stroke in urology was the motto for introduction of tadalafil, a phosphodiesterase type 5 inhibitor (5PDEI), in the treatment for BPO in 2006 [16], because erectile dysfunction and BPH-associated LUTS are epidemiologically linked and share common pathophysiological pathways. The ability of tadalafil to relief urinary symptom and to improve the urinary stream and bladder emptying is comparable to  $\alpha$ 1A receptor blocking agents. The major advantage is that in a daily dose of 5 mg it also improves erectile function. Other 5PDEI are less suited for this because of their short half life time. Combining tadalafil 5 mg daily with an  $\alpha$ 1A receptor antagonist provides better efficacy but that does not seem to have any clinical importance. Furthermore, prescribing an expensive pill to improve LUTS and erectile dysfunction and associating this with another pill causing anejaculation does not seem to be a good idea. What might be done, but has not been proven to be achievable and equally beneficial for both problems, is to take the pills alternately depending of the plans for the day.

#### 7. New kids on the block

Mirabegron, a  $\beta$ 3 adrenoreceptor agonist, can be used as an alternative to anticholinergics in patients with glaucoma, a condition occurring in approximately 10% of patients with BOO and, unlike BPO, often a contra indication for the intake of antimuscarinic drugs.

Synthetic vasopressin or antidiuretic hormone is sometimes prescribed for patients with severe nocturia, even in the absence of (documented) diabetes insipidus. The recommended dosage is 0.1-0.2 mg at night approximately 1 h before bedtime. Patients' blood pressure and blood sodium levels should be regularly monitored.

Non-steroidal anti-inflammatory drugs (NSAID) are active on BPO LUTS [17] but not indicated for long-term intake because of possible long-time cardiovascular side-effects, called the COX-2 dilemma [18].

Onabotulinumtoxin A also known as Botox, has been injected directly into the obstructive prostate with early apparently promising results in one single arm study. In one other randomized double blind placebo controlled trial [19] there was no difference with the placebo arm. In the recently finished PROTOX randomized trial [20] however treatment with Botox<sup>®</sup> was judged to be equivalent to optimal medical treatment in 127 patients with significant and objectively assessed LUTS from BPO.

## 8. Surgical treatment

TURP, the standard surgical technique for treatment of BPO, previously called the gold standard, is the second most frequently performed intervention in adult male patients worldwide. There are however some drawbacks and restrictions to its use. The personal experience of the "resectionist" is an independent factor in the outcome of this operation. Patients with very large prostate volumes and with excessive risk for perioperative and postoperative bleeding may suffer from major bleeding problems after TURP. Other possible complications like perioperative fluid resorption, postoperative strictures and postoperative incontinence have become less frequent thanks to better operative training and better equipment. A major breakthrough in this field was obtained with the bipolar TURis [21] resection system where the conventional hypotonic irrigation solution is replaced with saline.

For small volume BPO, many also perform transurethral resection of the prostate, although a transurethral incision (TUIP) of the obstructed zone is as efficacious. Today small prostates are also removed with transurethral vaporization (TUVP). The electrode, named vapotrode, heats the target tissue and turns the cells into steam, creating an open space. Occasional tissue debris is washed out by the continuous irrigation system. There is less blood loss during TUVP and the procedure can also be done in patients under anticoagulant treatment. TUVP can also be used for larger prostate volumes but remains unpopular because of the long operative time [22].

For very large prostate volumes open retropubic surgical removal of all adenomatous prostate tissue is still routinely performed in many centres, although intraoperative and postoperative bleeding can be excessive. Bleeding is not always under full control because some procedures do not permit full access to bleeding vessels in the region of the prostatic surgical capsule. Covering the "bloodbath" with a collagen sponge coated with the human coagulation factors fibrinogen and thrombin is one way to try to tackle the blood loss. One alternative to this open surgery is hemi TURP [23], that is resection of the middle lobe, if present, and one lateral lobe. This method provides acceptable results, be it of shorter duration, and is particularly suitable for patients who are not deemed fit for a complete surgical TURP procedure. Hemi TURP is often a spontaneous decision taken by resectionists who notice that their patient is not doing well or bleeds excessively during the intervention.

Minimal invasive techniques to decompress the obstruction like prostatic stents and balloon dilatation of the prostate failed to show acceptable long-term improvement. The same applies to heat based minimal invasive treatments like prostatic hyperthermia, thermo-therapy, transurethral needle ablation (TUNA) of the prostate and high intensity focused ultrasound (HIFU), aiming to

destroy part of the obstructed prostatic tissue by heating and cryoablation where the tissue is ablated by extreme cold. All these techniques never gained widespread popularity and became obsolete in BPO treatment.

Also less invasive than TURP is the recently developed prostatic urethral lift (PUL), registered as Urolift<sup>®</sup>. The procedure consists of the placement of implants that retract obstructing prostate lobes. After 3 years of follow-up it appears to be a valuable alternative with minimal complications, significant patient satisfaction and preservation of sexual function [24]. This intervention can be done under local anaesthesia.

After electrocoagulation/resection, laser energy is the most used energy source for prostate surgery today. Different laser delivery procedures have been proposed: with the laser beam some distance away from the target tissue (visual laser ablation of prostate or VLAP), in close contact with the tissue (contact laser vaporization or ablation) or into the tissue (interstitial laser ablation). Today the most used techniques are contact laser for photo selective vaporization of the prostate (PVP) or laser induced enucleation of obstructive prostate tissue. Popular laser vaporization devices for PVP are the 180 Watt GreenLight XPS laser, the Holmium: YAG laser ablation (HoLAP), the thulium laser (Revolix laser) and the Highpower potassium-titanyl-phosphate (KTP) laser. Cutting away excess prostatic tissue or laser enucleation can be done with a Holmium (HoLEP) or a Thulium laser (ThuLEP). In general the main advantage of laser operations for BPO are less bleeding, both after laser vaporization and laser enucleation, avoidance of open surgery plus reduced catheterization and hospitalization length after laser enucleations. Negative points are the actual high cost both for the laser machines and for the fibres and the lack of longterm results. Also after a laser enucleation of BPO a transurethral morcellation device is introduced through a nephroscope to grind up and remove the intravesical mass of separated adenoma. This is a time-consuming and sometimes tedious procedure and in case of big adenomas, impaired visibility through the nephroscope or malfunctioning of the morcellator, the procedure cannot be finished in the same surgical session. Alternatively approaches like mini laparotomy or in situ endoscopic resection of the enucleated adenoma may then be used [25].

Prostatic artery embolization (PAE), performed in the department of interventional radiology under local anaesthesia, is another new technique for treatment of symptomatic BPH. The embolization catheter is introduced through the right femoral artery and the internal iliac artery into selective arterial branches for the prostate. The procedure takes 60–90 min and the early results are encouraging [26]. The efficacy based upon the IPSS score is twice as good compared with conventional medical therapy and as good as with transurethral laser therapy. The complication rate is very low, with only one case of bladder ischemia due to non-targeted embolization among more the 300 procedures. Long-term results are lacking as are comparative studies with standard treatments like TURP.

Another technique for removal of obstructive prostatic tissue without the use of heat is aquablation or ultrasonically guided robot-assisted water jet ablation of the prostate. After registration and programming of the target tissue contour to excise from the prostate with real time ultrasound, a high velocity saline stream is used to ablate the programmed volume. Some focal electrocautery for haemostasis is usually also required. The procedure is done in less than 1 h, appears to be safe and the preliminary results are acceptable [27].

One drawback of all these new technologies, including laser, is that one does not dispose of representative tissue samples for pathological analysis to rule out prostate cancer after the procedure. This is correct but then we must realize that these treatments are intended to relief symptoms and prevent complications of BOO and not diagnose prostate cancer. If this is deemed necessary PSA testing, transrectal ultrasound and/or other imaging techniques like magnetic resonance and prostate biopsies, especially in the peripheral zone that does not take part in the BPO process, can be performed before prostate surgery.

## 9. Conclusion

Despite the fact that relief or removal of tissue in BPO is in fact only symptomatic, palliative treatment it is appreciated as a trophy of urology to serve the need of our ageing male population. There are still too many gaps in our knowledge on the regulation of prostate growth to treat BPH as a disease related to ageing and functioning testes.

We left the idea that we could control symptomatic disease by removal of all tissue up to the surgical capsule as we know from clinical experience that a poorly performed TURP leads to complications and a second TURP. Our first obligation in training the new generation is to ensure that they acquire expertise in the correct performance of the standard interventional treatment just as learning the expertise of open or robotic-assisted surgery.

Aiming for patient satisfaction, the ideal management should include individualised treatment, according to objective facts (size of the BPH, bladder physiology) and holistic care according to the degree of bother.

Functional urology brought us better definitions, better measurements and insight into the true needs of the patient. It is positive to note that in urological practice, attention is given to watchful waiting, life style advice, medical treatments and a search for minimal invasive surgery as compared to TURP/TUIP.

The solution lies in studies that address improvement of symptoms, urodynamic improvement, quality of life and cost-efficiency for our social health care. We expect the young urologists/researchers to proceed carefully and solve the enigma of BPH leaving us primary prevention as an option to prevent this disease.

## **Conflicts of interest**

The authors declare no conflict of interest.

#### References

 Hinman Jr F, Boyarsky S, Caine M, Chisholm GD, Gammelgaard PA, Madsen PO, et al. Benign prostatic hypertrophy. New York: Springer-Verlag New York Inc; 1983.

- [2] Chatelain C, Denis L, Foo KT, Khoury S, McConnell J. Benign prostatic hyperplasia. UK: Plymbridge Distributors Ltd; 2001.
- [3] Foo KT. Diagnosis and treatment of benign prostate hyperplasia in Asia. Transl Androl Urol 2014;4:478–83.
- [4] Russo GI, Castelli T, Urzi D, Privitera S, La Vignera S, Condorelli RA, et al. Emerging links between non-neurogenic lower urinary tract symptoms secondary to benign prostatic obstruction, metabolic syndrome and its components: a systematic review. Int J Urol 2015;22:982–90.
- [5] Oelke M, Martinelli E. Pharmacological treatment of benign prostatic hyperplasia. Urol A 2016;55:81-94.
- [6] Ficarra V, Rossanese M, Zazzara M, Giannarini G, Abbinante M, Bartoletti R, et al. The role of inflammation in lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) and its potential impact on medical therapy. Curr Urol Rep 2014;15:463.
- [7] Hu J, Zhang L, Zou L, Hu M, Fan J, Cai Y, et al. Role of inflammation in benign prostatic hyperplasia development among Han Chinese: a population-based and singleinstitutional analysis. Int J Urol 2015;22:1138–42.
- [8] Gravas S, Bach T, Bachmann A, Drake M, Gacci M, Gratzke C, et al. Guidelines on the management of non-neurogenic male lower urinary tract symptoms (LUTS) incl. benign prostatic obstruction (BPO). European Assocaition of Urology; 2015. http://uroweb.org/guidelines/compilations-ofall-guidelines/.
- [9] Weiss J, Andersson F, Juul KV. Diagnosing nocturnal polyuria (NP)-based on self-reported nocturnal void volume and fluid intake in clinical practice: results from a real-world treatment survey in Europe and the USA. Munch, EAU16, abstract 536.
- [10] Heyns CF, van der Walt CL, Groeneveld AE. Correlation between a new visual prostate symptom score (VPSS) and uroflowmetry parameters in men with lower urinary tract symptoms. S Afr Med J 2012;102:237–40.
- [11] Foo KT. Decision making in the management of benign prostatic enlargement and the role of transabdominal ultrasound. Int J Urol 2010;17:974–9.
- [12] Luo GC, Foo KT, Kuo T, Tan G. Diagnosis of prostate adenoma and the relationship between the site of prostate adenoma and bladder outlet obstruction. Sing Med J 2013;54:482–6.
- [13] Zheng J, Pan J, Qin Y, Huang J, Luo Y, Gao X, et al. Role for intravesical prostatic protrusion in lower urinary tract symptom: a fluid structural interaction analysis study. BMC Urol 2015;15:86.
- [14] Browne CT, Emberton M. Self-management for men with lower urinary tract symptoms. Curr Urol Rep 2009;10:261–6.
- [15] Barkin J, Guimarães M, Jacobi G, Pushkar D, Taylor S, van Vierssen Trip OB. Alpha-blocker therapy can be withdrawn in the majority of men following initial combination therapy with the dual 5alpha-reductase inhibitor dutasteride. Eur Urol 2003;44:461-6.
- [16] Hatzimouratidis K. A review of the use of tadalafil in the treatment of benign prostatic hyperplasia in men with and without erectile dysfunction. Ther Adv Urol 2014;6:135–47.
- [17] Kahokehr A, Vather R, Nixon A, Hill AG. Non-steroidal antiinflammatory drugs for lower urinary tract symptoms in benign prostatic hyperplasia: systematic review and metaanalysis of randomized controlled trials. BJU Int 2013;111: 304–11.
- [18] Roth SH. Understanding the COX-2/NSAID dilemma. Drugs 2005;65:1915-7.
- [19] Marberger M, Chartier-Kastler E, Egerdie B, Lee KS, Grosse J, Bugarin D, et al. A randomized double-blind placebocontrolled phase 2 dose-ranging study of onabotulinumtoxin A in men with benign prostatic hyperplasia. Eur Urol 2013;63: 496-503.
- [20] Delongchamps N, Descazeaud A, Benard A, Azzouzi R, Saussine C, De La Taille A, et al. A randomized clinical trial

comparing prostatic injection of botulinum neurotoxin type A (Botox<sup>®</sup>) to optimized medical therapy in patients with BPH-related LUTS: end-of-study results of the PROTOX trial. Eur Urol Suppl 2016;15. e1079–e1079a.

- [21] Michielsen DP, Coomans D, Braeckman JG, Umbrain V. Bipolar transurethral resection in saline: the solution to avoid hyponatraemia and transurethral resection syndrome. Scand J Urol Nephrol 2010;44:228–35.
- [22] Narayan P, Tewari A, Garzotto M, Parramore H, Schalow E, Starling E, et al. Transurethral vapotrode electrovaporization of the prostate: physical principles, technique, and results. Urology 1996;47:505–10.
- [23] Agrawal MS, Aron M, Goel R. Hemiresection of the prostate: short-term randomized comparison with standard transurethral resection. J Endourol 2005;19:868–72.

- [24] Roehrborn CG, Rukstalis DB, Barkin J, Gange SN, Shore ND, Giddens JL, et al. Three year results of the prostatic urethral L.I.F.T. study. Can J Urol 2015;22:7772–82.
- [25] Elshal AM, Eldemerdash Y, Mekkawy R, Taha DE, Laymon M, El-Nahas AR, et al. Prostate tissue retrieval after holmium laser enucleation of the prostate; assessment of non-morcellation approaches. Arab J Urol 2016;14:147–55.
- [26] Bagla S, Martin CP, van Breda A, Sheridan MJ, Sterling KM. Early results from a United States trial of prostatic artery embolization in the treatment of benign prostatic hyperplasia. J Vasc Interv Radiol 2014;25:47–52.
- [27] Gilling P, Reuther R, Kahokehr A, Fraundorfer M. Aquablation – image-guided robot-assisted waterjet ablation of the prostate: initial clinical experience. BJU Int 2016;117: 923–9.