Abstract

Objective: To establish guidelines for the diagnosis, treatment, and follow-up of BPH.

Methods: A search of published work was conducted using Medline. In combination with expert opinions recommendations were made on the usefulness of tests for assessment and follow-up: mandatory, recommended, or optional. In addition, indications and outcomes for the different therapeutic options were reviewed.

Results: A digital rectal examination is mandatory in the assessment for the diagnosis of BPH. Recommended tests are the International Prostate Symptom Score, creatinine measurement (or renal ultrasound), uroflowmetry, and postvoid residual urine volume. All other tests are optional. The aim of treatment is to improve patients’ quality of life, and it depends on the severity of the symptoms of BPH. The watchful waiting policy is recommended for patients with mild symptoms, medical treatment for patients with mild-moderate symptoms, and surgery for patients who failed medication or conservative management and who have moderate-severe symptoms, and/or complications of BPH which require surgery. Regarding non-surgical treatments, transurethral microwave thermotherapy is the most attractive option. These treatments should be reserved for patients who prefer to avoid surgery or who no longer respond favourably to medication. Finally, recommendations for follow-up tests and a recommended follow-up time schedule after BPH treatment are provided.

Conclusions: Recommendations for assessment, possible therapeutic options, and follow-up of patients with BPH are made.
Symptom Scores

Several urinary symptom score systems such as the International Prostate Symptom Score (I-PSS), the Clinical Prostate Score, and the Danish Prostate Symptom Score describe and quantify BPH symptoms. They were developed to compare the patient status before and after BPH treatment. The I-PSS system is recommended here and consists of 8 questions, 7 of which explore urinary symptoms and 1 of which investigates the quality of life.

Prostate-Specific Antigen (PSA) Measurement

The conclusions of the 1997 International Consensus Meeting are recommended here [7].

- PSA measurement should be offered to men with LUTS and a life expectancy of over 10 years in whom the diagnosis of prostate cancer, once established, would change the treatment plan.
- The benefits and risks, including the likelihood of a false-positive or false-negative PSA test and the potential need for a transrectal ultrasonography (TRUS) guided biopsy, should be discussed with the patient.
- It has been suggested that newer concepts, such as PSA density, PSA velocity, and age-specific reference ranges, may enhance the statistical performance of PSA as a cancer-screening test. Until the results of definite studies are available, physicians must use clinical judgement to determine which patient should or should not undergo TRUS and TRUS-guided biopsy.
- New assays separating free and complexed PSA are being developed. These are believed to enhance the statistical performance of PSA as a cancer-screening test in the critical range of total PSA values between 2.0 and 10.0 ng/ml.

PSA density, PSA velocity, and PSA free/total ratio might offer valuable information in a subgroup of patients.

Creatinine Measurement

Bladder outlet obstruction due to BPH may cause hydronephrosis and renal failure [8]. A recent study of 264 men presenting with BPH symptoms found that approximately 1 in 10 (11%) had renal insufficiency [9]. While it is difficult to select those BPH patients with renal insufficiency, these guidelines recommend the measurement of serum creatinine levels in all BPH patients. Proper therapy can be provided and the costs of long-term renal damage and postsurgical complications avoided.

Digital Rectal Examination (DRE)

A DRE has to be performed, as it helps determine the presence of prostate cancer and the size of the prostate gland.

Table 1. Recommended assessments for the diagnosis of BPH

<table>
<thead>
<tr>
<th>Assessment</th>
<th>EAU recommendations</th>
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<tbody>
<tr>
<td>Digital rectal examination</td>
<td>mandatory</td>
</tr>
<tr>
<td>International prostate symptom score</td>
<td>recommended</td>
</tr>
<tr>
<td>Creatinine measurementa</td>
<td>recommended</td>
</tr>
<tr>
<td>Flow rates</td>
<td>recommended</td>
</tr>
<tr>
<td>Post void residual urine volume</td>
<td>recommended</td>
</tr>
<tr>
<td>Prostate-specific antigen</td>
<td>optional</td>
</tr>
<tr>
<td>Renal ultrasound</td>
<td>optional</td>
</tr>
<tr>
<td>Bladder ultrasound</td>
<td>optional</td>
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<tr>
<td>Transrectal ultrasonography</td>
<td>optional</td>
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<tr>
<td>Voiding charts</td>
<td>optional</td>
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<tr>
<td>Urodynamicsb</td>
<td>optional</td>
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<tr>
<td>Endoscopy</td>
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a Or renal ultrasound.

b Straightforward cases.

Background

BPH is a medical condition closely related to ageing [1]. It is not life threatening, but its clinical manifestation as lower urinary tract symptoms (LUTS) reduces patients’ quality of life [2]. Bothersome LUTS can occur in 30% of men older than 65 years [3]. Mild urinary symptoms are very common in men aged over 50 years and generally cause little bother. Moderate and severe urinary symptoms result in higher levels of inconvenience and interference with daily living activities [4]. The same urinary symptoms can cause different bothersome and daily living interferences [5]. There is a relatively low correlation between urinary symptoms, prostate size, and urinary flow rate [6].

The prevalence of clinical BPH remains difficult to determine, and an epidemiological definition of BPH is lacking. The aetiology of BPH is multifactorial, with age and hormonal status being the true factors related to the development of the disease. The need for surgery to treat BPH increases with age and with the degree of clinical symptoms at baseline. Nocturia and changes in the urinary flow stream seem to be the most predictive symptoms.

Diagnosis of BPH

Accurate and early diagnosis of BPH leads to better treatment outcomes and predetermines the treatment choice. These guidelines have defined a series of tests as mandatory, optional, or recommended and not recommended and are presented in table 1.
Imaging of the Urinary Tract

The imaging modality used for patients with LUTS should provide an image of the urinary tract and demonstrate the morphological effects of prostate pathology on the lower and/or upper urinary tract. Intravenous urography (IVU) or sonography and plain films are the procedures routinely used for imaging the upper urinary tract, prior to prostate surgery [10–12]. However, these guidelines recommend a renal ultrasound as the imaging modality for the upper urinary tract. Imaging of the lower urinary tract with a urinary bladder voiding cysto-urethrogram gives limited urodynamic information and is not recommended in the routine diagnostic workup of elderly men with LUTS. A retrograde urethrography gives indirect information on the effect of benign prostatic enlargement on adjacent structures; it is not recommended here.

The prostate is viewed to assess size and shape and the presence of an occult carcinoma and for tissue characterization. Imaging of the prostate can be done by transabdominal ultrasound, TRUS, computed tomography, and magnetic resonance imaging [13]. TRUS has been documented as the most accurate way to calculate the size of the prostate [14, 15]. It is necessary to calculate prostate size when surgery and medical and thermotherapy are considered as treatment options.

Voiding Charts

Voiding charts (diaries) are simple to complete and can provide useful objective clinical information. There is no standard frequency volume chart, but the 7-day chart of Abrams and Klevmark [16] is the simplest. Recording a 24-hour frequency volume chart prior to initial consultation helps identify patients with idiopathic nocturia or excessive fluid intake.

Flow Rates

Uroflowmetry is recommended as a diagnostic assessment in the workup of patients with LUTS and an obligatory test prior to patients receiving surgical treatment. It is a simple, non-invasive test that can reveal abnormal voiding. Flow rate machinery provides information on voided volume, maximum flow (Q_max), average flow (Q_avg) and time to Q_max, and this information should be interpreted by the physician to exclude artefacts [17–19]. Serial flows (two or more) are recommended to get a representative flow test (Q_max). Obstruction can only be diagnosed with a pressure flow test; however, flow rates should be interpreted with caution, as elderly patients with LUTS have age-related urodynamic changes [20].

Postvoid Residual Urine Volume

Postvoid residual urine volume measurement is recommended in these guidelines. It should be calculated by measurement of the bladder height, width, and length obtained by transabdominal ultrasonography. This is a simple, accurate, and non-invasive method [21].

Urodynamic Studies

Pressure-flow studies are regarded as an additional diagnostic test in these guidelines. Flow rates only determine the probability of obstruction, whereas pressure-flow studies can categorize the degree of obstruction and identify patients in whom a low flow rate may be due to a low-pressure detrusor contraction. These guidelines recommend that pressure-flow studies remain optional tests in straightforward cases, presenting for the first time with LUTS. These studies are the most useful investigation available for the purpose of counseling patients regarding the outcome of surgical therapies for BPH. The International Continence Society nomogram should be used for the diagnosis of obstruction in order to standardize data for comparative purposes [22].

Endoscopy

A urethrocystoscopy is the standard endoscopic procedure used for evaluating the lower urinary tract (urethra, prostate, bladder neck, and bladder). It can provide information as to the cause, size, and severity of obstruction, patency of bladder neck, prostatic occlusion of the urethra, and estimated prostate size [23]. It can confirm causes of outflow obstruction and eliminate intravesical abnormalities. It is recommended as an optional diagnostic test in these guidelines; however, it should be performed if patients are to receive surgical treatment.

Recommended Guidelines for the Diagnosis of BPH

1. Among all the different urinary symptom score systems currently available, the use of the I-PSS is recommended because of its world-wide distribution and use.
2. In patients undergoing investigation for LUTS, the minimal requirement is to assess the upper urinary tract function by a creatinine measurement and or an ultrasonographic examination.
3. There is consensus that if imaging of the upper urinary tract is performed, ultrasonography is the method of choice.
4. Imaging of the upper urinary tract is recommended in patients with LUTS and a:
   a. History of or a current urinary tract infection
   b. History of urolithiasis
Hyperplasia

EAU Guidelines on Benign Prostatic Hyperplasia

Measurements of postvoid residual urine volume and peak flow rate. There are several types of treatment commonly used for BPH: surveillance, medical, surgical and non-surgical.

1. Watchful Waiting (WW)

The WW treatment option is recommended for patients with a symptom score of less than 7, i.e., mild symptoms that do not interfere with daily life activities. A multifactorial approach, combining the presence of symptoms, their bothersomeness and their influence on daily life, as well as cost-effectiveness, should be taken into account before deciding on the WW treatment option.

2. Medical Treatment

5α-Reductase Inhibitors. Finasteride was the first 5α-reductase inhibitor used for the treatment of BPH. Several clinical trials have demonstrated that finasteride can reduce the size of the prostate gland by 20–30%, improve symptom scores by approximately 15%, and cause moderate improvements in urinary flow rates [24–26]. While the maximum effects of finasteride are seen after 6 months, long-term benefits have been reported for up to 6 years [27]. Side effects are minimal and are related to sexual function. Finasteride is more effective in men with enlarged prostate (>40 ml) and should be considered an acceptable treatment option [28]. No additional patient benefits have been seen when finasteride is combined with α1-blockers [29, 30]. Although finasteride lowers serum PSA levels, it does not mask the early detection of prostate cancer [31, 32].

α-Blockers. The use of the α1-blockers, alfuzosin, doxazosin, indoramin, prazosin, and terazosin and the α1A-blocker tamsulosin for the symptomatic relief of BPH has increased in the past 10 years. These drugs relax the smooth muscle of the prostate gland and bladder neck to improve urine flow and to reduce bladder outlet obstruction. Reductions of 20–50% in symptom scores and improvements of 20–30% in urinary flow rates have been reported [33]. Improvements are seen within 48 h and maintained for up to 42 months. While they all have similar efficacy and side effect profiles, they differ in their pharmacokinetic properties and cost. The most commonly reported side effects are headaches, dizziness, postural hypotension, asthenia, drowsiness, nasal congestion, and retrograde ejaculation. Patients with specific indications for surgery such as urinary retention, recurrent urinary tract infections, chronic renal impairment, and recurrent prostatic bleeding should not be considered for α-blocker therapy. Patients on antihypertensive therapy and those with postural hypotension should be carefully monitored when receiving α-blocker therapy.

Phytotherapy. The treatment of BPH with phytotherapeutic agents has gained popularity in recent years [34].
While their mode of action is unclear, encouraging results using *Serenoa repens* have been reported in clinical trials [35]. The efficacy of phytotherapeutic agents has to be demonstrated before their introduction into clinical practice.

(3) Surgical Treatment

**Surgery.** The best long-term solution for patients with BPH is probably surgery which removes the enlarged part of the prostate and usually relieves the obstruction and incomplete emptying caused by BPH. Transurethral resection of the prostate (TURP), TUIP, and open prostatectomy are the three surgical treatment options for BPH. Surgery is recommended for patients with bothersome BPH symptoms refractory to medical treatment. Refractory urinary retention, recurrent urinary tract infection, recurrent haematuria, renal insufficiency, and bladder stones are the complications of BPH which require surgery [36, 37]. TUIP is recommended for patients with a small prostate gland, no median lobe, and a low risk of associated prostate cancer (normal DRE and serum PSA levels) [38]. TURP is the most frequently performed surgical procedure and is recommended for moderately enlarged prostate glands, provided it can be completed within 60 min [39]. Open prostatectomy is recommended for severely enlarged prostate glands [40]. Urinary tract infections should be treated before surgery. The number of patients experiencing complications and morbidity due to surgical interventions has decreased during the past decade.

**Laser.** The use of laser surgery to treat BPH has been rapidly developed within the past decade. Clinical studies using side-firing Nd:YAG and ILC lasers have demonstrated equivalent improvements in symptom scores and urinary flow when compared with TURP. However, the long-term effects of laser surgery are unknown and eagerly awaited. Holmium laser resection of the prostate (normal DRE and serum PSA levels) [38]. TURP is the most frequently performed surgical procedure and is recommended for moderately enlarged prostate glands, provided it can be completed within 60 min [39]. Open prostatectomy is recommended for severely enlarged prostate glands [40]. Urinary tract infections should be treated before surgery. The number of patients experiencing complications and morbidity due to surgical interventions has decreased during the past decade.

(4) Non-Surgical Treatment

**Transrectal High Intensity Focused Ultrasound (HIFU).** Transrectal HIFU is the only technique that provides non-invasive tissue ablation. Clinical data are only available for one device Sonablate® [41]. Transrectal HIFU is well tolerated, but requires general anaesthesia or heavy intravenous sedation. Urinary symptom improvement in the range of 50–60% and mean Qmax increases of 40–50% have been shown. Long-term efficacy is limited, with a treatment failure rate of approximately 10%/year. Clinical data from randomized trials are limited, and transrectal HIFU should be considered an investigational therapy.

**Transurethral Needle Ablation (TUNA®).** TUNA is a simple and safe technique that delivers low-level radiofrequency energy to the prostate gland. It can be performed under local anaesthesia in a significant number of patients. It results in an improvement of urinary symptoms in the range of 50–60% and mean Qmax increases of 50–70%. Clinical efficacy has been proven in randomized, controlled trials, although there is limited evidence of long-term efficacy.

**Transurethral Microwave Thermotherapy (TUMT).** TUMT uses computer-regulated microwaves to deliver heat through a catheter to selected portions of the prostate gland and to destroy excess prostate tissue. A cooling system protects the urinary tract during the procedure. The morbidity is relatively low, and TUMT can be performed without anaesthetic; patients in poor health are particularly good candidates for thermotherapy. These guidelines recommend low-energy TUMT for patients with smaller prostates and lower grades of bladder outlet obstruction. It has an excellent subjective response and minimal morbidity. High-energy TUMT is recommended for patients with larger prostates and higher grades of bladder outlet obstruction. It has excellent subjective and objective responses, but has a higher morbidity than low-energy TUMT [42]. New TUMT procedures aim at reducing morbidity and treatment time with sustained objective results and durability [43]. A recent report of a shorter treatment has demonstrated similar results as seen with 1-hour high-energy TUMT protocols [44].

**Recommended Guidelines for the Treatment of BPH**

(1) The WW policy should be recommended to patients with mild symptoms that have minimal or no impact on their quality of life.

(2) Finasteride is an acceptable treatment option for patients with bothersome LUTS and an enlarged prostate (>40 ml). It can be used when there is no absolute indication for surgical treatment.

(3) Alphablocker therapy is a treatment option for patients with bothersome LUTS, irrespective of prostate volume, who do not have an absolute indication for surgical treatment.

(4) Surgical management (TURP, TUIP, or open prostatectomy) is recommended as first-line treatment for patients with (an absolute indication for the treatment of) LUTS.

(5) Significant postoperative morbidity, disappointing long-term data, and high costs have resulted in a substantial decline in the clinical use of side-fire and ILC. It is not recommended as a first-line surgical treatment for patients with LUTS. It may have a role in the treatment of high-risk patient subgroups.
Holmium laser resection of the prostate is a promising new technique with outcomes in the same range as those of TURP.

Transrectal HIFU therapy is currently not recommended as a therapeutic option for elderly patients with LUTS and is considered an investigational therapy.

Due to a significant treatment failure rate, TUNA is not recommended as a first-line therapy for patients with LUTS.

TUMT should be reserved for patients who prefer to avoid surgery or who no longer respond favourably to medication.

### Follow-Up

All patients who receive treatment for BPH need follow-up. Follow-up schedules depend on the type of treatment administered and are presented in tables 2 and 3. Patients who subsequently develop chronic retention will require evaluation of their upper urinary tract by serum creatinine measurement and/or renal ultrasound. They may also be candidates for urodynamic assessment and surgical treatment.

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**Watchful Waiting**

Patients on the WW treatment option should be followed up at 6 months and then annually, provided that there is no deterioration of symptoms or the development of absolute indications for surgical treatment.

**Medical Treatment**

1. **5α-Reductase Inhibitors.** Patients should be reviewed at 12 weeks and 6 months to determine their response to 5α-reductase inhibitors. Thereafter, these patients should be followed up annually, provided that there is no deterioration of symptoms or the development of absolute indications for surgical treatment.

2. **5α-Blockers.** After the first 6 weeks of therapy with α-blockers, the patients should be reviewed to determine their response. If these patients gain symptomatic relief without any troublesome side effects, treatment with α-blockers may be continued. Patients should be followed up at 6 months and then annually, provided that there is no deterioration of symptoms or the development of absolute indications for surgical treatment.

**Surgical Treatment**

Patients who received surgical treatment should be seen within 6 weeks to discuss histological findings and to iden-
tify early postoperative morbidity. Long-term follow-up should be scheduled at 3 months to determine the final outcome. Any patients who fail surgical treatment should have urodynamic studies with pressure-flow analysis.

Alternative Therapies
Long-term follow-up is recommended for patients who receive alternative therapies (HIFU, TUNA, and TUMT). For minimally invasive therapies follow-up is recommended at 6 weeks, at 3 and 6 months, and then annually.

References