



How to Make the Diagnosis of Benign Prostatic Disease

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Abstract

We have a number of clinical points which we can use to assess whether or not a man with symptoms suffers from benign prostatic enlargement and/or bladder outlet obstruction due to benign prostatic hyperplasia. These clinical points are lower urinary tract symptoms, digital rectal examination, ultrasound of the prostate and bladder (measuring prostate volume and bladder wall thickness), flow rates, residual urine, and pressure–flow studies. The diagnosis of symptomatic BPE and the decision of whether or not specific treatment is advisable will be based on the combination of several of these examinations, of which some are more important than others.

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1. Introduction

A valid definition of what used to be called *prostatism* is no longer available. Although this condition is diagnosed clinically every day, we have difficulties in finding a definition which fulfils clinical, pathological, and pathophysiologic requirements. Certainly, it is no longer synonymous with *benign prostatic hyperplasia* (BPH).

Although the clinical condition essentially is due to BPH, prostatism is a histologic diagnosis, and purists argue that it should only be used when such a diagnosis has been obtained. Although the pathologists diagnose BPH, what is it clinically? Abrams has introduced the definitions of *benign prostatic enlargement* (BPE), *benign prostatic obstruction* (BPO), *bladder outlet obstruction* (BOO), and *lower urinary tract symptoms* (LUTS) to specify the different components of prostatism [1].

BPE is enlargement of the prostate due to BPH in the absence of prostate cancer. BOO is an

obstruction of the bladder outlet without a specified cause, and BPO is obstruction of the bladder outlet due to benign prostatic growth (in the absence of prostate cancer). BPO is usually but not necessarily associated with BPE, but small prostates also may cause outflow obstruction. LUTS are symptoms of altered bladder function which often but not always disturb the patient and lead to consultation with a physician. All of these conditions, BPE, BPO, and LUTS, are frequently associated with BPH.

There are many things we do not know about BPH, including its precise aetiology [2,3]. What we do know is that, like prostate cancer, BPH occurs only in men and dogs and it requires functioning testes [4]. As in prostate cancer, most men with functioning testes will develop this condition if they live long enough, and it is true that many men with BPH will not become symptomatic.

Histologic BPH develops in the transition zone and/or in the periurethral preprostatic sphincter [5]; thus, it is not a generalised disease of the prostate

but rather it is a highly localised condition. Nodular enlargement and growth may lead to overall BPE, LUTS, BOO, changes of bladder function, and acute or chronic retention. In severe cases, bladder dysfunction due to prostatic enlargement can cause changes in renal function.

All of the secondary effects of BPE predominantly affect the bladder. Obstruction of urine outflow is defined by urodynamic measurements, but the term implies that the bladder generates increased voiding pressure to generate urine flow. Consequently, the bladder will first compensate for outflow obstruction by increased detrusor muscle action. With persistent outflow obstruction, detrusor hypertrophy will develop, which can be seen sonographically as thickening of the bladder wall. With time, and often with progressive obstruction, the bladder will eventually fail to compensate fully the outflow obstruction, and bladder emptying will become incomplete (residual urine) and urine flow will decrease (flow rate) [6]. Additionally, the bladder will show morphologic signs of decompensation (trabeculation and the development of pseudodiverticula). Residual urine can lead to further complications of the condition, with the formation of bladder stones and recurrent urinary tract infections (UTIs) [7]. All of the pathophysiologic changes of bladder function due to BPO usually occur in the period of life when changes associated with ageing also affect the bladder [8].

Thus, we have a number of clinical points which we can use to assess whether or not a man with symptoms suffers from BPE and/or BOO due to BPH. These clinical points are LUTS, digital rectal examination (DRE), ultrasound of the prostate and bladder (measuring prostate volume and bladder wall thickness [BWT]), flow rates, residual urine, and pressure-flow studies. The diagnosis of symptomatic BPE and the decision of whether or not specific treatment is advisable will be based on the combination of several of these examinations, of which some are more important than others.

2. Symptoms

The term LUTS is defined by a specific set of symptoms that are common in men with prostatic problems but are not specific either for a prostatic cause or for the male sex [9,10]. The definition of LUTS was originally based on symptom scores specifically designed to quantify the typical symptoms of a man with prostatism. These scores were the Boyarski score; the Madsen-Iversen score; and the American Urological Association (AUA)

symptom score, which later became the International Prostate Symptom Score (IPSS) [11]. Other scores of less clinical importance are the Danish Prostate Symptom Score (DAN-PSS) and the International Continence Society (ICS)-male questionnaire. The IPSS is the most widely used score and has been adopted as a recommended investigation by all national and international guidelines for the assessment of men investigated for benign prostatic disease.

The IPSS consists of seven items that ask about specific urinary and voiding symptoms over the previous 4 wk. Scores range from 0-35 in severity (0-5 for each symptom). The specific symptoms can be divided into *storage* symptoms (urgency, frequency, nocturia, and urge incontinence) and *voiding* symptoms (poor stream, hesitancy, feeling of incomplete emptying). Although this separation may be useful for clinical studies, it is not often useful in clinical practice. Furthermore, individual voiding and storage symptoms do not correlate well with urodynamic findings [12-14].

One of the leading symptoms concerning impact on the quality of life (QoL) of affected men is nocturia [15]. The IPSS contains only a single question on QoL. Since the effects on QoL are often quite different, *bother* scores such as the AUA bother score can be used to assess the bother caused by each symptom [16]. Bother scores are useful in clinical trials but clinically are not very relevant [17].

Traditionally, patients are classified into having none or mild, moderate, or severe LUTS based on the IPSS (0-7, 8-21, and 21-35 points, respectively). The IPSS has been validated for many languages and has been shown to be reliable and consistent [18]. The score decreases after BPE treatment, be it medical or surgical [19-21]. The IPSS is a useful clinical instrument for diagnosis and treatment monitoring of BPE.

3. Urinalysis

Basic urinalysis should always be done. Acute or chronic UTI may cause LUTS and, therefore, must be excluded. Patients with BPO and significant residual also may have UTI, which must be treated regardless of other treatments that may later be required for BPE.

4. Digital rectal examination

DRE does not provide much additional information for the diagnosis of BPE, other than to exclude other

conditions which can also cause LUTS. DRE is needed to exclude palpable prostate cancer and acute prostatitis. A positive DRE will necessitate biopsy to exclude prostate cancer, and a DRE with a painful prostate also will require further investigations. Other than that, a benign DRE in patients with LUTS will give a palpable estimate of the extent of prostatic enlargement (prostate size) but no information on the severity of BPO.

5. Ultrasound of the prostate and bladder

Suprapubic ultrasonographic assessment of both the prostate and the bladder are useful in the man with LUTS, as it gives valuable information about the two organs which together cause the symptom complex of LUTS and BPO. For the prostate, ultrasound is useful to measure prostatic size (needed for possible treatment decisions) and to assess whether prostatic enlargement is uniform or predominantly intravesical [22,23]. Additionally, information about the presence and the extent of intraprostatic calcifications is often useful with regard to coexisting chronic inflammation, which is very common when BPH is diagnosed histologically. Prostate size, however, does not correlate at all with the extent of BPO, either urodynamically or concerning LUTS [24].

Transrectal ultrasound is not routinely helpful in BPE. It provides better and more accurate measurement of prostate volume, and it allows for the separate volume determination of the transition zone. This data can be of interest for clinical trials but not for routine patient care.

For the bladder, ultrasound is used to measure residual volume and to assess BWT. The presence of bladder stones also will become apparent, and, occasionally, bladder tumours can be seen (which can also cause LUTS).

Although many guidelines do not routinely recommend ultrasound as an investigation in men with LUTS, ultrasound provides extremely useful information. Recommendations to use or not to use ultrasound in different national guidelines have a lot to do with whether ultrasound is done primarily by urologists or requires a referral to a radiologist.

6. Flow rates

The measurement of urinary flow rates is a urodynamic investigation. It assesses the combination of detrusor force and outflow opening and, thus, gives an indirect indication of these aspects of

bladder function. Flow rates must be interpreted together with the voided volume. Low volumes give inaccurate flow-rate measurements [25,26]. The most important parameter in men with LUTS is the maximum flow rate (Q_{\max}); additional information is gained by looking at the voiding time and the flow pattern. It is mandatory to have more than one flow-rate measurement, as they can be variable (depending on voided volume, diurnal variation). The voided volume should be >150 ml [27].

For patients with decreased flow rates who are suspected of BPO, urodynamic studies have shown that BOO was present in 88% of those with a $Q_{\max} <10$ ml/s, in 57% of those with a Q_{\max} of 10–14 ml/s, and in only 33% of those with a $Q_{\max} >15$ ml/s [28]. Thus, a decreased flow rate implies a high likelihood of BOO due to BPO. Following this study by Abrams et al [28], a Q_{\max} cut-off of 15 ml/s has been widely accepted as signifying BPO requiring treatment.

7. Postvoid residual urine volume

The persistent presence of postvoid residual (PVR) urine volume implies weakness of detrusor contraction relative to bladder outflow. In men with BPE, it usually signifies that due to BOO the detrusor muscle is no longer able to compensate by generating an increased voiding pressure high enough to allow for complete bladder emptying. Residual urine, however, can also be due to detrusor dysfunction rather than to BOO.

Residual urine can be adequately measured by suprapubic bladder ultrasound or single catheterisation after voiding. Catheter volumes are accurate but are too invasive for daily practice. Ultrasonography has a measurement error which increases with lower intravesical volumes but is accurate enough for daily practice [29]. PVR can also show diurnal variation. It does not correlate with LUTS but does correlate with a certain degree with prostate volume [30].

There is no universally accepted definition of a significant residual urine volume. For clinical practice, PVR <30 ml can be considered insignificant, while residual volumes persistently >50 ml should be regarded as important. Patients with constant PVR >100 ml are traditionally considered to require invasive methods to remove obstruction. Large PVR (>200 – 300 ml) often indicates marked bladder dysfunction and may predispose to unsatisfactory treatment results if invasive BOO treatment is undertaken [31].

An interesting parameter is the *residual fraction*, defined as the proportion of voided volume which

remains as the residual [32]. This parameter has been shown to remain fairly constant in a given patient. Although it is an interesting urodynamic concept, the residual fraction has not consistently been shown to be a clinical parameter that is valuable for diagnosis or treatment decision making.

8. Bladder wall thickness

The increase in BWT due to detrusor hypertrophy can be measured by ultrasound. Because the normal bladder wall is relatively thin, this measurement requires some diligence. Normal values of BWT in men and women have been established [33]. An increase >5 mm in men can be taken as indicating increased BWT which is usually (not always) due to detrusor hypertrophy. It is still not entirely clear whether or not sonographic measurement of BWT must be done with an empty bladder [33]. It has been shown that the measurable BWT decreases as the bladder fills, but it is questionable whether this is clinically relevant. BWT measurement, however, has been shown to have a high predictive value for BOO [34].

9. Pressure-flow studies

An invasive urodynamic investigation gives the best and most accurate information about bladder function in men with BPE and LUTS [35,36]. It requires the continuous measurement of intravesical filling and voiding pressures. Although less invasive methods have been evaluated, reliable pressure-flow studies require the insertion of intravesical and intrarectal catheters and are time consuming as well as unpleasant for the patient [19].

The information gained, however, can be extremely useful. Detrusor instability (a potential cause LUTS) can be seen or excluded, and the detrusor pressure (P_{det}) during voiding is used to define whether or not obstruction is present [37]. Useful nomograms have been established to assess and to grade the degree of obstruction (Schäfer [38], Abrams-Griffins [39]), and many urodynamic machines have incorporated the automated nomographic analysis of the recorded voiding data. A useful numeric value to assess obstruction is the Abrams-Griffin number, calculated as $P_{det}(Q_{max}) - 2 \times Q_{max}$ [40], whereby a value ≥ 40 indicates significant obstruction.

Pressure-flow studies are the most conclusive and definite investigation for the diagnosis of BPO.

They are reproducible, and findings in the same patients are stable for a long time [41]. Because of their invasiveness and cost, however, pressure-flow studies are not routinely done. A clear indication is given in all cases in which the clinical diagnosis of BPO using noninvasive urodynamic tests (flow rate and residual volume) are inconclusive, especially in younger men for whom invasive treatments are considered or in cases of suspected high-pressure high-flow obstruction, and in all cases in which other causes of bladder dysfunction as a cause of LUTS need to be considered [42,43].

10. Guidelines on benign prostatic hyperplasia

Most national and international guidelines agree on the basic assessments required for the clinical diagnosis of benign prostatic disease outlined above; however, there are some differences. The European Association of Urology guidelines now recommend the measurement of serum creatinine as a cost-effective means to distinguish BPH patients with renal impairment from those without. Whether this measurement is really necessary and whether it affects management decisions can be debated. The AUA does not recommend creatinine measurement, although it considers urine cytology to be an option in patients with predominantly irritative symptoms [44]. Regarding the measurement of prostate-specific antigen, the major guidelines recommend it if the diagnosis of prostate cancer would be relevant [31,44,45].

11. Conclusions: Making the clinical diagnosis of benign prostatic obstruction

The standardised assessment and quantification of LUTS with the IPSS, DRE, urinalysis, measurement of flow rate, and measurement of residual urine volume by ultrasound provide indispensable data for the daily assessment of a man with LUTS who is suspected of having BPE which requires treatment. Sonography will define the prostatic volume and will exclude or diagnose other possible bladder conditions. Sonographic measurement of BWT is not universally accepted, although its predictive value for BOO has been reported to be higher than that of flow rate or residual volume [34]. The indication for pressure-flow studies remains restrictive, and such studies should be used for cases in which doubt remains after the aforementioned investigations.

Conflicts of interest

The authors have nothing to disclose.

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