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Diagnosis of lower urinary tract symptoms resulting from benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is by far the most prevalent condition affecting the prostate, accounting for over 80% of clinical presentations for prostate disease. It is currently estimated to afflict more than 2 million men in the UK. Patients in whom BPH is suspected or who simply require reassurance that they do not have a prostate disorder should undergo a basic evaluation including clinical examination and some simple tests. The recommendations set out in this article are in line with the guidelines set out by the British Association of Urological Surgeons, the 2006 European Association of Urology Guidelines and the 2010 National Institute for Health and Clinical Excellence guidelines on the management of lower urinary tract symptoms (LUTS) in men.

The GP curriculum and benign prostatic hyperplasia

Curriculum statement 10.2: Men's health outlines the role of the GP in dealing with benign prostatic hyperplasia. Specifically, it is expected that GPs should:

- Be able to manage the primary contact of men who present with a genitourinary problem
- Have knowledge of prostatism and benign prostatic hypertrophy, including the principles of primary care treatment
- Be able to describe the indications for and role of the prostate-specific antigen (PSA) blood test and evaluate the arguments for and against a national PSA screening programme
- Be able to perform a digital rectal examination
- Have knowledge of secondary care investigations, including prostate biopsy
- Be able to explain the indications for urgent referral to specialist services, including for suspected prostate cancer

History and symptom assessment

BPH is characterized by a spectrum of obstructive and irritative symptoms known collectively as LUTS. These include a reduced urinary flow and a sensation of incomplete bladder emptying, together with frequency and urgency of urination (Box 1).

Box 1. Symptoms of BPH

- Urinary frequency
- Nocturia
- Urgency
- Poor flow
- Incomplete bladder emptying

It should be remembered, however, that these symptoms are not specific to BPH; they may also occur in patients with prostate cancer, prostatitis or other disorders, such as carcinoma in situ of the bladder (Box 2). Poor urinary flow and the sensation of incomplete bladder emptying are the two symptoms that correlate most closely with the

Box 2. Differential diagnosis of BPH

- Bladder neck obstruction
- Urethral stricture
- Carcinoma in situ of the bladder
- Parkinson's disease
- Cauda equina lesions
- Nocturnal polyuria
- Diabetes mellitus

eventual need for prostate surgery. Dribbling after micturition is usually due to pooling of urine in the bulbar urethra rather than obstruction.

The history should focus on the urinary tract and general health issues, as well as overall fitness. Conditions that may cause similar urinary symptoms should be excluded, including Parkinson's disease, stroke, polyuria from diabetes or congestive heart failure, history of urethral strictures or treatment with medications such as anticholinergic or antidepressant drugs.

LUTS have been shown to constitute an independent risk factor for sexual dysfunction in older men (Rosen *et al*., 2003). Since sexual dysfunction is associated with impaired quality of life and is readily treatable, men presenting with BPH should be specifically asked about the presence or absence of this problem.

Prostate symptom scores and frequency voiding charts

The frequency of symptoms can be assessed quantitatively by means of the International Prostate Symptom Score (IPSS) or American Urological Association (AUA) Symptom Score Index (Barry *et al.*, 1992). These symptom scores are identical and consist of seven questions relating to the severity of symptoms. The maximum possible score is 35; scores of 0–8 are generally regarded as mild, 9–19 as moderate and 20 or above as severe. A further four questions evaluate the 'bothersomeness' of the symptoms. This is known as the BPH Impact Index (BII) and carries a maximum score of 13. The IPSS and AUA scores are used to measure symptom severity only and are not diagnostic tests to determine whether symptoms are due to BPH (Barry *et al*., 1992). Frequency voiding charts, filled in by the patient himself, may also be helpful in gauging symptoms, for example, the number of times an afflicted individual needs to get out of bed during the night to pass urine.

The physical examination

A digital rectal examination (DRE) should form the cornerstone of the physical examination of patients with BPH. DRE provides useful information about the size, consistency and anatomical limits of the prostate and can be performed with the patient in the left lateral position. The normal prostate should have a soft consistency, like the tip of the nose. A so-called nodule of prostate cancer has a hard consistency like a knuckle of the hand. A normal 30-g prostate is roughly the same size as a walnut. Studies suggest that DRE provides a reasonably accurate estimation of volume in prostates of 50 cm^3 or less. However, the volume of larger glands tends to be underestimated by this technique.

In addition to DRE, the abdomen should be examined to see if there is a palpable bladder caused by chronic urinary retention. The physical examination should also include a focused neurological examination, together with some specific enquiries, to exclude disorders of the nervous system (such as a cauda equina lesion or Parkinson's disease) as the underlying cause of the patient's symptoms.

Urinalysis

Ideally, urinalysis—either by dipstick or by microscopic examination of sediment—should be performed in all men presenting with LUTS. Such investigations help to distinguish BPH from urinary tract infection or bladder cancer, which may produce symptoms similar to those of BPH. If the dipstick result is positive for blood, urine microscopy and culture should be performed and further imaging and evaluation of the renal tract considered. Urine cytology should be requested in those with severely irritative symptoms to exclude a diagnosis of carcinoma in situ of the bladder. If urine cytology is positive for malignant cells, an urgent referral to a urology department should be made, as an intravenous urogram or computed tomography scan with contrast and lower tract endoscopy and biopsy are mandatory.

Prostate-specific antigen

Although prostate-specific antigen (PSA) determination is an optional test, it should be seriously considered for all men with a life expectancy of 10 years or more, for whom identification of prostate cancer would influence treatment decisions. Measurement of PSA increases the likelihood of detecting prostate cancer over and above DRE alone and is therefore most relevant in this group of men, who are most likely to benefit.

As PSA tends to rise progressively with age, some clinicians adopt age-adjusted PSA cut-off points. According to Oesterling (1995), a man who is under 50 years should have a PSA below 2–5 ng/ml, whereas in a man over 70 years a PSA of up to 6.5 ng/ml may be considered normal. A risk-based assessment, which factors in the family history and findings of DRE, has been recommended by Roobol (2010) and may be the best approach.

Overall, if PSA levels are above the upper limit of normal (i.e. 4.0 ng/ml), the likelihood of prostate cancer is about 20–25%. If PSA is considerably elevated (more than 10 ng/ml), the likelihood of cancer rises to over 50%. Generally, a higher PSA confers a greater probability of prostatic malignancy being present (Catalona *et al*., 1991). However, in reality it is often not possible to distinguish men with localized prostate cancer from those with BPH on the basis of a single PSA measurement without recourse to a transrectal ultrasound-guided prostatic biopsy, and patients should be informed of this uncertainty.

It has also become apparent that, in the absence of prostate cancer, measurement of serum PSA values can provide

a useful indication of overall prostate volume (Roerhborn *et al*., 1999). This can predict those patients most likely to suffer BPH progression and, in turn, facilitate the selection of agents for medical therapy of BPH. Not surprisingly, men with enlarged prostates and high PSA values (arbitrarily set as volume more than 30 cm^3 and PSA value more than 1.4 ng/ml) appear to benefit most from 5-alpha-reductase inhibitors (such as finasteride or dutasteride), which act primarily by reducing the prostate volume. It should be borne in mind that these drugs can lower PSA levels by around 50% although finasteride may actually improve the detection of prostate cancer, probably by reducing the degree of benign enlargement of the gland (Thompson, 2007).

The screening debate

One of the most hotly contested issues in medicine at present is screening for prostate cancer (Qureshi, 2011). Those advocating population screening point out that early detection by PSA testing, in combination with DRE, identifies cancers that are confined to the gland and therefore potentially curable in 70–80% of cases. Critics, however, maintain that some of the cancers diagnosed would never have become clinically manifest within the patient's natural lifespan. As yet, no screening-related reduction in prostate cancer–specific mortality has been definitively demonstrated, and the debate is likely to continue until the final results of ongoing randomized studies of screening in Europe and the USA are available (Brawer *et al*., 1992). A recent report has reported a 21% reduction in deaths from prostate cancer in the screened arm, but at the cost of over-diagnosing low risk, clinically insignificant cancers (for which the incidence was almost 50%) (Schroeder *et al.*, 2012).

Uroflowmetry

Electronic measurement of urine flow rates is an extremely useful noninvasive test in most patients with BPH. It is helpful in identifying patients whose peak flow rate is not diminished and thus are very unlikely to benefit from surgery. Such patients are more likely to be suffering from an overactive bladder than from BPH.

Uroflowmetry measures a number of parameters of obstruction, of which the most important is the peak flow rate. A peak flow rate below 15 ml/second (with a voided volume of at least 150 ml) suggests obstruction, although in older men (70–80 years of age), values of 10–15 ml/second may be normal. The presence of a markedly reduced peak flow rate (less than 10 ml/second) usually indicates some degree of obstruction; this is most often caused by BPH, but uroflowmetry cannot distinguish between obstruction and impaired bladder contractility as the cause of a low flow rate (Chancellor *et al.*, 1991). In general, those men with severe impairment of urine flow (less than 10 ml/second) more often suffer disease progression and eventually require medical or surgical intervention.

Measurement of residual urine

Measurement of post-void residual (PVR) urine is also a useful optional test in the evaluation of BPH, as it can identify patients who are likely to respond less well to active surveillance (watchful waiting) or medical therapy. A normal, unobstructed bladder is completely empty at the end of micturition. In general, PVR values above 200–300 ml usually indicate a higher likelihood of the need for invasive therapy and also a higher risk of acute urinary retention (Bruskewich *et al.*, 1982). The test cannot, however, be used to confirm or exclude BPH. It may be useful as a safety measure in monitoring the progress of patients who opt for active surveillance.

It is almost always best to measure PVR non-invasively by transabdominal ultrasound; less commonly, urethral catheterization is used. However, there is considerable void-to-void variation, and thus treatment decisions should not be based on a single measurement alone. Those patients with a consistently high PVR (more than 300 ml) should usually be referred for further evaluation and consideration for eventual transurethral surgery (see Box 3 for the normal findings of investigations used in the evaluation of BPH).

Box 3. Normal values of investigations used for the evaluation of BPH

- IPSS: Less than 10
- PSA: Less than 4.0 ng/ml
- Maximum flow rate: More than 15 ml/second
- PVR: Nil
- Prostate volume: Less than 30 ccs

Pressure/flow measurements

Pressure/flow measurements (or urodynamics) involve introducing a small catheter, either urethrally or suprapubically, to measure pressure within the bladder. This can be used to distinguish outflow obstruction from impaired detrusor contractility. The method is invasive, and inevitably causes some degree of discomfort to the patient; it is not indicated as a routine test in BPH. The current consensus is that this investigation should be confined primarily to those patients with equivocal findings in whom invasive therapy is being considered as, in the absence of demonstrable obstruction, surgery is not usually appropriate. If urodynamic assessment is recommended, patients should be informed of the pros and cons of the investigation.

Transrectal ultrasonography and further investigations

Transrectal ultrasonography (TRUS) (Fig. 1) is a test performed in secondary care. It is indicated when DRE findings and/or PSA values suggest the possibility of prostate cancer; it also serves to guide the automatic prostate biopsy needle. In addition, it can be used to determine prostate volume, which, as already noted, may provide prognostic information and facilitate treatment decisions. A large prostate is an established risk factor for the development of acute urinary retention (Roerhborn *et al*., 1999). TRUS should not, however, be regarded as a standard investigation for all patients with bladder outflow obstruction due to BPH.

Transrectal biopsy is not indicated as an investigation for BPH but is sometimes employed, under local anaesthesia

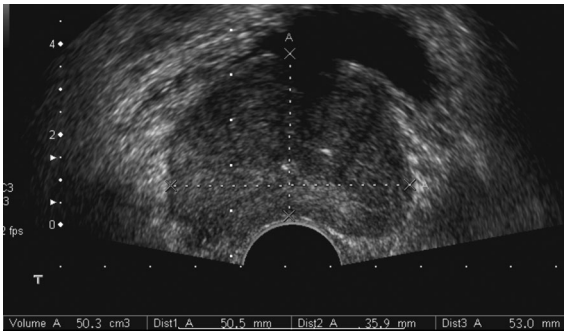

Figure 1. A transrectal ultrasound of the prostate showing BPH.

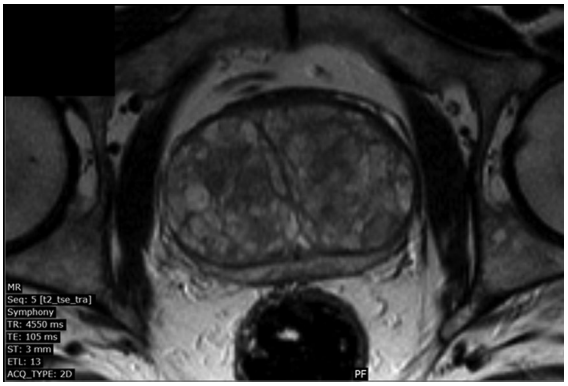

Figure 2. A magnetic resonance image of the prostate showing BPH.

and antibiotic cover to confirm or exclude a diagnosis of prostate cancer. Magnetic resonance imaging (Fig. 2) is not used routinely in the evaluation of BPH but can be useful in differentiating BPH from prostate cancer.

Summary of guidelines for diagnosis of BPH

Patients presenting with LUTS, or who are simply seeking reassurance, should be evaluated using the following criteria:

- A detailed history and assessment of symptoms
- A physical examination, including a DRE
- Dipstick urinalysis (and urine microscopy/culture if positive)

In addition, PSA determination should be considered in men with a life expectancy of at least 10 years (McConnell *et al.*, 1994). In some instances it may be necessary to refer patients to a urologist (Box 4 lists situations in which this is appropriate).

Box 4. Indications for referral to a urologist

- A markedly elevated symptom score, a high BPH impact index or very reduced flow rate
- Bothersome LUTS not responding to medical therapy
- A history of heamaturia, urinary retention or recurrent urinary tract infections
- Abnormalities detected by DRE or a palpable bladder
- PSA above 4.0 ng/ml
- PSA above age-adjusted values, especially in association with a family history of prostate cancer

Conclusion

The diagnosis of uncomplicated BPH can now be made in primary care and medical treatment safely initiated. More complicated cases, such as those presenting with haematuria or an elevated PSA, will need to be referred to a urologist (Kirby and Gilling, 2011). Good teamwork between clinicians in primary and secondary care will be required to ensure that each and every patient receives good quality evaluation and treatment.

Key points

- BPH symptoms can be quantified with the IPSS
- Physical examination should involve a DRE
- PSA measurement helps to estimate the risk of prostate cancer and provides a surrogate indication of prostate volume
- Uroflowmetry helps estimate the severity of obstruction
- PVR volume (with some variability) reveals voiding efficiency
- Urodynamics may be helpful in selected cases

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