

Chapter 56

What is benign prostatic hyperplasia and how is it treated?

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Prostate anatomy

The prostate, a male reproductive gland, originates from the endodermal urogenital sinus. It has an ovoidal shape; in adults, it measures 4x3x2 cm approximately, and weights around 20 gr. It's located anterior to the rectum, above the urogenital diaphragm, posterior to the symphysis pubis, and below the base of the bladder (Chapter 20). It surrounds the urethra, which travels through the gland from the bladder neck to prostate's apex. Based on the antomo-histological characteristics, it can be divided into three zones, the peripheral zone, as the largest (70% of the gland), the central zone (20%), which is surrounded by the peripheral zone, the transitional zone (10%), where the benign prostatic hyperplasia (BPH) most commonly develops and lastly, the anterior fibromuscular stroma. Close to prostate apex, the ejaculatory ducts (which travel across the gland) are located. The ducts are the result of the fusion of seminal vesicles and vas deferens, and they empty the transported semen into the urethra at the level of seminal colliculus (verumontanum).

Prostate physiology

The gland physically participates on urinary bladder output and urethral lumen control. By closing the urethra, it controls seminal fluid transmission and impedes semen from entering the bladder during ejaculation. During urination, the central zone muscles prevent urinary influx into ejaculatory system by closing the prostatic ducts. As an exocrine gland, it secretes 20-30% of seminal fluid volume (as alkaline fluid). The components of this fluid are PSA, prostatic acid phosphatase, citric acid, zinc, spermine, and prostatic inhibin. These secretions liquefy semen and enhance sperm viability by stimulating sperm motility and reducing urethral acidity. PSA, an

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androgen-regulated serine protease, it's used to help in the early diagnosis of prostate cancer (PCa), and to assess progression and treatment outcomes on patients with the diagnosis. Finally, 5 α -reductase type 2 convert testosterone to dihydrotestosterone in the prostate.

Prostate physiopathology

The prostate is susceptible to various benign and malignant diseases. The 3 most common conditions affecting the prostate are prostatitis, benign prostatic hyperplasia, and prostate cancer. Prostatitis is an infectious or non-infectious inflammation of the gland, which may present either acutely or chronically, and its main symptom besides low urinary tract symptoms (LUTS) is pelvic pain. PCa was the fifth cause of cancer leading death in USA in 2020. The most common clinical presentation is asymptomatic prostate-specific antigen (PSA) elevation. Treatment depends on the disease stage ranging from active surveillance, surgical or non-surgical treatments or combination of both. Of note, PSA elevation may also be related to BPH and prostatitis, as well as recent manipulation.

What is BPH?

BPH is a non-malignant prostatic glandular enlargement (Fig. 1). There is no global accepted epidemiological definition of BPH. However, disease prevalence increases with age and affects approximately 50% of men over 50 years and up to 80% by the age of 80. Histologically, it's an increase in epithelial and, mainly, stromal cell numbers (hyperplasia). This increase in cell numbers, is secondary to proliferation of both, epithelial and stromal cells, the imbalance between cell renewal and death (impaired cellular apoptosis), or a combination of both. Some suspected contributing factors are aging, family history, hormonal, and growth factors, as well as inflammatory factors. The pathophysiology is complex, hyperplastic prostatic tissue increase urethral resistance, causing outflow obstruction with subsequent compensatory alteration in the urinary bladder function, which is reflected clinically as LUTS.

Symptoms and diagnosis

Despite not all men with BPH present symptoms, of all the conditions leading men to develop LUTS, it's the most frequent, and the one most studied so far. The symptoms and its severity can vary

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widely among patients and non-prostatic causes must be excluded. LUTS attributed to BPH include storage and/or voiding symptoms (Table 1). Some patients can develop recurrent UTI's, bladder stones, impaired kidney function, hematuria, and urinary retention. The diagnosis is done clinically and can be supported with further exams. Evaluating a patient with LUTS mandates initially, a full medical history, assessment of symptom severity with a validated questionnaire, physical examination including a digital rectal exam (DRE), and urine analysis (to rule out any other LUTS cause). Serum creatinine, PSA, urine cytology, post-void residual urine volume (PVR), flow rate (Qmax), urodynamics, obstructive sleep apnea assessment, and ultrasonography are supplementary optional tests suggested in selected cases. The International Prostate Symptom Score (IPSS) is a questionnaire that quantifies symptom severity and frequency using 7 questions; the classification ranges from mild (0-7) to moderate (8-19) or severe (20-35) and includes a final question regarding Quality of life (QoL). DRE provides an approximation of prostate size, and mainly, it's done to detect nodules that may indicate PCa. Prostate size doesn't correlate with symptom severity. PSA is recommended for those patients in whom its measurement may change the management of their voiding symptom or those with 10-year life expectancy in whom the presence of PCa would divert the management; PSA can provide size estimate and prediction of progression risk. PVR and Qmax are suggested for men considering surgical therapy.

Storage:

Frequency
Nocturia
Urgency
Incontinence

Voiding:

Slow stream
Splitting or spraying
Intermittent stream
Hesitancy
Straining

Post-micturition:

Feeling of incomplete emptying
Postmicturition dribble

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Table 1. Classification of lower urinary tract symptoms (LUTS)

Unless clinically indicated, it is not recommended to perform in the initial evaluation urethro-cystoscopy, urodynamics, upper or lower urinary tract imaging or prostatic biopsy.

Treatments

Symptom severity and impact on QoL, will determine whether treatment is necessary or not. Treatment should be offered to patients with moderate and severe symptoms and for those with severe bother regardless of the symptom severity.

For patients with mild and/or minimally bothersome symptoms, lifestyle changes are suggested, including fluid restriction (particularly in the evening), avoidance and monitoring of certain drugs, timed voiding avoidance or treatment of constipation and pelvic floor exercises.

Alpha blockers, and/or 5-alpha-reductase inhibitors (5ARIs) are the mainstay of medical treatment options; however, antimuscarinics, beta-3 agonists and PDE5 inhibitors (PDE5-I) can also improve LUTS.

Surgery is indicated in men with refractory or recurrent urinary retention, recurrent urinary infections, bladder stones, recurrent

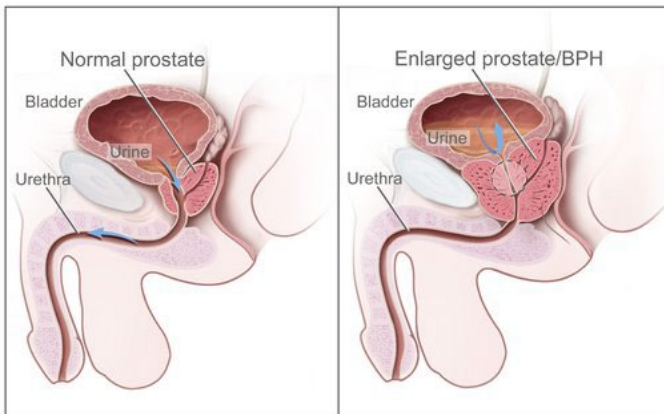


Figure 1. Two-panel drawing shows normal male reproductive and urinary anatomy and benign prostatic hyperplasia (BPH). Panel on the left shows the normal prostate and flow of urine from the bladder through the urethra. Panel on the right shows an enlarged prostate pressing on the bladder and urethra, blocking the flow of urine.

Source: National Cancer Institute.

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hematuria, renal insufficiency secondary to BPH, LUTS refractory to other therapies, according to patient preference.

Oral medication

Alpha-blockers are an excellent first-line options and offer dynamic relaxation of the prostatic urethra to improve urine flow. The choice of which agent to prescribe is based on patient comorbidities, age, and possible side effects. These medications don't alter BPH natural progression. The most common side effects are dizziness and retrograde ejaculation.

5-ARIs shrink the prostate volume approximately 20-30 %, altering natural BPH history, and decreasing the risk of acute urinary retention. These medications are recommended when the prostate volume is >30cc and/or PSA > 1.5 ng/dL. Side effects predominantly sexual in nature (e.g., erectile dysfunction, and decreased libido). Gynecomastia is an uncommon side effect.

Alpha-blockers and 5-ARIs used in a combined fashion have shown superiority in improving IPSS and peak urinary flow (Qmax) compared to monotherapy.

Antimuscarinic and beta-3 agonist notably improve storage symptoms. Precautions regarding urinary retention should be taken, especially in elderly patients and those with PVR >200cc or with significant BOO.

For patients with LUTS and erectile dysfunction (ED), Tadalafil (a PDE5-I) taken on a daily dose of 5mg has proved to improve both.

Transurethral resection of the prostate (TURP)

Using either monopolar or bipolar energy, TURP is the surgical procedure of reference in patients with 30-80 cc prostates. Complications are most common in larger prostate volumes (>60 cc) and include extravasation, bleeding, infection, persistent or recurrent retention, need for repeat surgery, incontinence, bladder neck contracture, ED, and TUR syndrome. Morbidity is decreased with bipolar TURP, especially when it comes to bleeding and TUR syndrome.

Photoselective Vaporization of the prostate (PVP)

Potassium-titanyl-phosphate (KTP) or Greenlight laser, is the most used energy to perform PVP. Functional outcomes are similar to TURP with regard to IPSS reduction and Qmax improvement, and PVP is a treatment of choice for patients actively taking anticoagulant or anti platelet medications due to decreased risk of bleeding. Retreatment

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rates are low on <80 cc prostates. The main drawbacks are transient post-operative dysuria, higher re-intervention rates for larger prostates, and lack of pathological specimen.

Open Simple Prostatectomy (OSP)

OSP is effective for patients with >80 cc prostates and is the treatment of choice for large glands when LEP is not available. Indications also include concurrent bladder procedure (e.g., diverticulectomy or cystolithotomy), and hip disease precluding the dorsal lithotomy position. OSP is the most invasive surgery for BPH, and requires a longer hospitalization stay and catheterization. Post-operative complications also include transient urinary incontinence (8-10%), and the transfusion rates are higher than with any other technique.

Laser Enucleation of the Prostate (LEP)

LEP mimics an open prostatectomy, but performed in a minimally invasive fashion, using an energy (such as laser), to enucleate the adenoma trans-urethrally. A variety of sources may be used, including holmium, thulium, and KTP lasers (HoLEP, ThuLEP, and GreenLEP respectively), as well as bipolar energy (BipoLEP). Enucleation is a size-independent technique which removes more tissue than any other technique. After HoLEP, all subjective (IPSS and QoL) and objective (PVR and Qmax) parameters improve immediately, and the PSA decreases by 75%. Reoperation rates are <1.5% at 18 years. Complications are the same as with TURP, without the risk of TUR syndrome, and with reduced risk of bleeding, and shorter catheterization times. Transient urinary incontinence is the most common early post-operative event and has a 4.3% chance of being permanent. ThuLEP have shown similar enucleated weight, operative time, hospital stay and catheterization time, with no significant differences in PSA, Qmax, PVR, IPSS and QoL.

Minimally Invasive Surgery Techniques (MIST)

These technologies were developed to limit surgical morbidity, decrease anesthesia risks, as well as post-operative recovery period.

Prostatic urethral lift (Urolift™)

It's an option for patients who desire preservation of erectile and ejaculatory function and who have a prostate volume between 30-80 cc. Having a median lobe is no longer considered as a contra-indication, as the middle lobe can be tacked to the side. The procedure is performed under cystoscopic guidance and can be

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done under local anesthesia. The delivery device (a disposable cartridge with nonabsorbable monofilament suture tabbed implants) is placed through the urethra, then the implants are placed compressing the lateral lobes, creating an open prostatic urethra. Subjective parameters improvement has been shown by cohort studies, meanwhile, Qmax and PVR have only small improvement. Side effects are dysuria, hematuria, discomfort, and recurrence.

Prostatic Artery Embolisation (PAE)

PAE, performed by interventional radiologists, is a procedure during which, the prostatic arteries are blocked with particles, causing ischemia of intraprostatic vessels and consequently progressive shrinkage of the prostate. Indications include patients not suitable for surgery or anesthesia, men who want to preserve ejaculation, >65 cc prostate, and recurrent hematuria. The failure rate is 19% and 15% of the patients require a TURP within the first year after PAE. Complications include dysuria, hematuria, hematospermia, urinary retention non-target embolization and recurrent treatment.

Water Vapor Therapy (Rezum™)

This system transforms sterile water into vapor steam (thermal energy), which disrupts the cell membranes of the prostatic transition zone causing cell necrosis, and subsequent tissue ablation. This therapy is recommended for men with prostates <80 cc who are interested in preserving ejaculatory function. The procedure is usually performed as day surgery, using local anesthesia and/or sedation. Presence of median lobe obstruction is not an exclusion criteria. 5-year data have shown that IPSS, Qmax, QoL, and PVR improve significantly after Rezum™, and sexual function is not affected.

Aquablation

It consists of image-guided robot-assisted waterjet ablation. Guided by transrectal ultrasound, hydrodissection is performed using high-pressure saline, ablating the prostatic parenchyma, but sparing its capsule and vessels. Despite demonstrable efficacy in >150 cc prostates, in outcomes are comparable to TURP in <80cc prostates. Sexual function is preserved in almost 100% of the cases, and retreatment rate at 5 years is low.

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Summary

BPH is a frequent condition that can lead to male LUTS. Men presenting with urinary symptoms should be fully evaluated to assess the severity of these symptoms and the impact on their QoL. Once evaluation is complete, therapeutic shared decision-making is guided by, symptom severity, patient age, comorbidities, expectations, and potential treatment side effects to select the best treatment.

Suggested reading

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