Etiology, Pathogenesis, And Management Options Of Infra-Vesical Obstruction Due To Benign Prostatic Hyperplasia, Urinary Bladder Stone, Or Both: Review Article

Ahmed Mahmoud Hassan[a], Mostafa Abdel Razik[a], Omar Mohammed Elsoghier[a], Ahmad Abdeen Ahmad[a*], Atef Fathi Ali[a], Gamal A. Alsagheer[a]

[a]Urology Department, Faculty of Medicine, South Valley University, Qena, Egypt.

Abstract

Urinary bladder stones may be a primary stone formed in the urinary bladder or migrating calculus from the upper urinary tract. Bladder stones become more symptomatic when associated with infra-vesical obstruction. The most common cause of infra-vesical obstruction in elderly men is benign prostatic hyperplasia. Benign prostatic hyperplasia can be identified clinically by a complex of symptoms. These symptoms, known as lower urinary tract symptoms, range from incomplete emptying, weak stream, nocturia, and increased urinary frequency, and can potentially progress to urinary urge incontinence and urinary retention. About 35% of elderly men above fifty years will seek medical advice and have medical treatment for infra-vesical obstruction. About 24% of patients with mild to moderate LUTS will undergo surgical management for BPH. The strong association between infra-vesical obstruction due to benign prostatic hyperplasia and urinary bladder stones has led to the dogma that any BPH associated with bladder stones should be managed surgically. This study aims to review the etiology, pathogenesis, and management options of infra-vesical obstruction caused by BPH, urinary bladder stones, or both. We have searched literature in the American National Center for Biotechnology Information (NCBI), PubMed, Google scholar, Egyptian bank of knowledge, and science direct.

Keywords: Bladder stones, cystolitholapaxy, benign prostatic hyperplasia, transurethral resection of the prostate.

DOI: 10.21608/svuijm.2021.66062.1107

*Correspondence: drabdenn@gmail.com

Received: 6 March,2021.
Revised: 20 March,2021.
Accepted: 25 March,2021
Cite this article as: Ahmed Mahmoud Hassan, Mostafa Abdel Razik, Omar Mohammed Elsoghier, Ahmad Abdeen Ahmad, Atef Fathi Ali, Gamal A. Alsagheer (2022). Etiology, Pathogenesis, And Management Options Of Infra-Vesical Obstruction Due To Benign Prostatic Hyperplasia, Urinary Bladder Stone, Or Both: Review Article. *SVU-International Journal of Medical Sciences*. Vol.5, Issue 2, pp: 401-409 .

1. Benign prostatic hyperplasia & LUTS

Benign prostatic hyperplasia (BPH) defines non-malignant growth of the prostate gland related most commonly to the aging process**(Foo, 2017).**

Bladder outlet obstruction (BOO) refers to the presence of a pressure gradient at the level of the bladder neck & prostatic urethra. Benign prostatic hyperplasia is not the only cause for BOO, other causes may include bladder neck sclerosis, urethral stricture, or other conditions which may cause significant urinary tract obstruction while not being associated with histologic BPH **(Arun Kumar, 2012)**.

Urinary symptoms in many older males may not be due to prostate enlargement. So that, the terminology "lower urinary tract symptoms is independent of benign prostatic hyperplasia" has been used and is meeting widespread acceptance **(Füllhase et al., 2013)**.

1.1.Diagnostic evaluation

- **Medical history**

Should be assessed carefully to identify possible causes and associated comorbidities which may include medical and neurological diseases. Lifestyle habits and medication must be stressfully reviewed. A self-completed validated symptom questionnaire should be obtained to assess the severity of LUTS**(De Nunzio et al., 2017)**.

- **Physical examination and digital-rectal examination**

Prostate shape, symmetry, nodularity, and firmness should be assessed so that BPH could be distinguished from prostatic carcinoma**(Roehrborn et al., 1997)**.

- **Urine analysis**

Urinalysis (dipstick or sediment) can identify urinary tract infections (UTI), micro-haematuria, and diabetes mellitus**(Abrams et al., 2009)**.

- **Prostate-specific antigen (PSA)**

A free/total PSA cutoff of 0.18 significantly enhanced the ability to differentiate between a cancerous prostate and non-cancerous one as compared with the use of total PSA alone. A study reported that a percentage of free PSA cutoff of 25% would lead to the detection of 95% of prostatic carcinoma**(Meyer et al., 1997)**.

- **Imaging**

Intravenous urography and computerized tomography scan are not indicated for patients with BPH unless they also have concomitant hematuria, urinary tract infection, renal insufficiency, or history of urinary stones, or previous surgery**(Stravodimos et al., 2009)**.

- **Urethrocystoscopy**

The anatomy of the prostate, the presence of an intravesical enlarged median lobe, the anatomy of the bladder neck and mucosa might be a determinant of the surgical approach**(El**

Din et al., 1996).

- **Urodynamics**

Are the best tests to determine whether a patient has bladder neck obstruction or not. Appropriate nomograms have been established for normal values of pressure-flow parameters, and it is widely accepted that the best marker of obstruction is the pressure within the bladder formed by the tone of the detrusor muscle at the moment of the peak urinary flow rate(**Abrams, 1994**).

1.2 Management of Benign prostatic hyperplasia with LUTS

1.2.1 Conservative treatment

1.2.1.1.Watchful waiting (WW)

The progression of symptoms in patients having mild to moderate symptoms as well as the development of significant complications is very slow. Watchful waiting and reassurance is a good strategy(**Millán-Rodríguez et al., 1999**).

1.2.1.2.Pharmacological treatment

- **α1-Adrenoceptor antagonists (α1-blockers)**

The most commonly used drugs for the management of LUTS associated with BPH. Prostatic smooth muscle tone is mediated by α1-adrenergic receptors. An increase in the tone leads to outlet obstruction, and so, a reduction in the urinary flow rate and worsening of LUTS. Accordingly, a blockage of those receptors leads to improvement of the urinary flow rates and LUTS(**Schwinn, 2001**).

- **5α-reductase inhibitors**

Serum testosterone, found in the prostate gland acini, is converted by the 5α-reductase isoenzyme to DHT. DHT acts by binding the androgen receptor found in the epithelial cell, inducing changes in the deoxyribonucleic acid, leading to some metabolic effects as protein synthesis and secretion and growth of the prostate(Andriole et al., 2004).

Finasteride, a type 2 5α-reductase inhibitor, and dutasteride, which inhibit both type 1 and type 2 α-reductase enzymes, represent the paradigm for androgen suppression. The principal side effects are loss of libido and ED, but these are seen at the initiation of therapy and decline over time with treatment(**Roehrborn et al., 2004**).

- **Combined α1-blockers&5α-reductase inhibitors**

This combination therapy has a rapid clinical effect within hours or days. Studies revealed that the α1-blocker was superior to finasteride in symptom improvement, whereas combination therapy of both agents is superior to α1-blocker monotherapy(**Kirby et al., 2003**).

1.2.2. Surgical treatment

1.2.2.1.Transurethral resection of the prostate(TURP) and transurethral incision of the prostate

Transurethral resection of the prostate (TURP) acts by removing tissues from the transitional zone of the prostate gland. It is the gold standard for the management of BPH. Bipolar resection presented an advancement in TURP to resects a larger adenoma with a lower complication rate especially the TUR syndrome. Transurethral incision of the prostate described by Orandiis a technique at which

incision of the bladder outlet is done without tissue removal **(Orandi, 1987)**. This may replace TURP in some cases, with prostate sizes < 30 mL and no middle lobe enlargement. TURP causes significant mean Qmax improvement with a significant reduction in IPSS score, QoL score, and PVR**(Autorino et al., 2009)**.

1.2.2.2.Open prostatectomy

The oldest surgical option for management of BPO associated with moderate-to-severe LUTS. It is suitable for enlarged prostates (> 80-100 mL).

Simple open prostatectomy should be considered when the enlarged prostate weighs more than 75 g. If sizable bladder diverticula is found, prostatectomy and diverticulectomy should be performed in the same setting. If the diverticulectomy is not performed, persistent urinary tract infection may occur. Large urinary bladder calculi that could not be easily removed transurethral may be removed during the open procedure(**Ferretti and Phillips, 2015**).

1.2.2.3.Holmium laser enucleation and holmium laser resection of the prostate

Holmium laser is absorbed by tissues causing tissue necrosis and coagulation with good hemostasis. HoLEP techniques have more symptomatic improvement than TURP with fewer reoperation rates, fewer peri and postoperative complications, and fewer periods of hospital stay**(El Tayeb et al., 2016)**.

2. Urinary bladder stones and bladder outlet obstruction

2.2. Prevalence, etiology, and risk factors

Bladder stones represent about 5% of stones that affect the urinary tract. they are common in males, with a male: female ratio of about 4:1 **(Halstead, 2016)**.

They can be classified into primary and secondary. Primary bladder stones are those which are not associated with urinary tract pathology, mostly found in children with attacks of diarrhea and metabolic abnormalities associated with poor hydration and nourishment**(Douenias et al., 1991)**.

Secondary bladder stones are associated with urinary tract abnormalities, including bladder outlet obstruction, chronic infection, foreign bodies, bladder diverticula, and neurogenic bladder**(Douenias et al., 1991)**.

2.3. Etiopathogenesis of Bladder Calculi associated with BOO

Poor bladder emptying and resultant urinary stasis may be considered the main causes of bladder stone formation. So, to prevent the formation of new calculi and allow the elimination of stone fragments, BPH and bladder stones are usually treated simultaneously. Historically, suprapubic prostatectomy and cystolithotomy were combined as an ideal procedure for the elimination both pathologies. Patients with histological BPH have an eight times higher incidence of bladder stones as compared with those without BPH. Local factors are more important than systemic factors in the formation of bladder stones**(Otnes, 1983)**.

2.4. Presentation

Increased urinary frequency, haematuria, dysuria, and suprapubic pain which is initiated

or increased by movement and exercise. However, patients may only complain of recurrent urinary tract infections.

2.5. Diagnostic evaluation

2.5.1. Diagnostic investigations for bladder stones

Plain X-ray of kidney ureter bladder (KUB) can provide information regarding radio-opacity of the stones which are of benefit in both treatment and follow-up. Ultrasound (US) is a sensitive tool for diagnosing bladder stones. Computer tomography (CT) is the most sensitive for detecting bladder stones(**Salinawati et al., 2015**).

2.5.2. Diagnosing the cause of bladder stones

The primary cause of the urinary bladder stone including outlet obstruction should be identified before starting treatment. This could be achieved through physical examination and rectal examination; uroflowmetry and post-void residual urine assessment; urine dipstick; good metabolic assessment including serum (creatinine, ionized calcium, uric acid, blood cell count, sodium, potassium); stone analysis using X-ray diffraction or infrared spectroscopy(**O'Connor et al., 2002**).

2.6. Disease Management

2.6.1. Conservative treatment

If there is no concomitant bladder outlet obstruction, migratory stones less than one centimeter are expected to pass spontaneously. Primary and secondary bladder stones usually need active management(**Tzelves et al., 2002**).

2.6.2. Medical management of bladder stones

Chemolitholysis could be performed for bladder stones. urinary alkalinization can be achieved using oral alkaline agents like citrate or sodium bicarbonate to dissolve stones formed of uric acid(**Lopezet al, 1987**).

2.6.3. Bladder stone interventions

2.6.3.1.Suprapubic cystolithotomy

Open suprapubic cystolithotomy is more effective than any other procedure for stone removal, but with longer catheterization periods and longer hospital stay(**Donaldson et al., 2019**).

2.6.3.2. Transurethral Cystolitholapaxy and Lithotripsy

The transurethral approach for the elimination of bladder stones is preferred as it allows the use of a natural urethral opening for access. A lithotrite may be used but with a high incidence of mucosal trauma and bladder perforation. It is not suitable for the fragmentation of large calculi more than 2.5 cm. A high rate of stone recurrence was observed post lithotrite usage(**Singh and Kaur, 2011**).

Perforation of the bladder is a common complication for cystolitholapaxy due to punching of the bladder wall with the stone punch.Further complications are bleeding, infection, and urethral injury. Conversion to an open approach is necessary if the stone burden was shown to be underestimated(**Nseyo et al., 1987**).

The use of the holmium laser, electrohydraulic lithotripter, and lithoclast

technology has been reported in modern studies, with high success rates in both adults and children. However, electrohydraulic energy is associated with a higher incidence of complications, including mucosal injury and hematuria, in addition, multiple fragmentation probes are required.

Holmium laser lithotripsy has become the technique of choice, owing to its ability to fragment large stones. Most patients undergoing laser lithotripsy will be free of stones in one procedure with no significant complications.

2.6.3.3.**Percutaneous cystolithotripsy**

This approach is suitable in patients with large bladder stones with less urethral manipulation and subsequently low incidence of urethral stricture. Contraindications for this approach include the presence of bladder tumor, previous history of pelvic irradiation, active urinary tract infection. It can be performed in combination with transurethral resection of the prostate. It is obtained by placing an Amplatz sheath suprapubically**(Okekeet al, 2004)**.

2.6.3.4.**Extracorporeal shock wave lithotripsy**

The least invasive intervention with lower stone-free rates than any other procedure **(Bhatia and Biyani, 1994)**.

2.6.3.5.Laparoscopic cystolithotomy.

3. Treatment for bladder stones secondary to bladder outlet obstruction

Urinary bladder stones in elderly men over forty years result mostly from BOO associated with BPH, which needs attention for management of BPH in addition to stones. The presence of a urinary bladder stone was consideredpreviously as an absolute indication for surgical treatment for BPH. Recent reports considered the need for prostate surgery due to the presence of bladder stones as an old dogma that could be modified.

One study reported a high complication rate when TURP was combined with cystolitholapaxy. It was found that combined treatment should not be performed without due regards. With the advancement in stone fragmentation techniques like ultrasonic power, Electrohydraulic lithotripsy, the safety of combined procedures had increased. The safety and efficacy of combined TURP with pneumatic lithotripsy were later confirmed by a more recent series of studies **(Sinik et al., 1998; Chtourou et al., 2001)**.

A study compared 64 patients undergoing transurethral cystolithotripsy. They have been divided into two groups of 32 patients. The first group underwent transurethral resection of the prostate (TURP), the other was given medical treatment for BPO (α-blocker with or without 5-alpha reductase inhibitor). No men on medication had had a stone recurrence, but 34% needed TURP **(Philippou et al., 2011)**.

Another study of 23 men undergoing cystolithotripsy starting medical treatment for bladder outlet obstruction found an incidence of 22% for complications related to BOO. 17% of patients has had recurrent stones**(O'Connor et al., 2002)**.

Conclusion

1- Benign prostatic hyperplasia (BPH) defines non-malignant growth of the prostate gland mostly after the age of forty due to aging process.

2- Urinary bladder stones may be a primary stone formed in the urinary bladder or migrating one from the upper urinary tract. They become more symptomatic when associated with infra-vesical obstruction.

3- There are multiple management options for BPH, bladder stones or both. One of the best options is combined transurethral resection of the prostate and cystolitholapaxy.

References

- **Abram P (1994)**. In support of pressure-flow studiesfor evaluating men with lower urinary tract symptoms. Urology, 44(2): 153-155.
- **Abrams P, Chapple C, Khoury S, Roehrborn C, de la Rosette J; International Scientific Committee (2009)**. Evaluation and treatment of lower urinary tract symptoms in older men. The Journal of Urology, 181(4): 1779-1787.
- **Andriole G, Bruchovsky N, Chung LW, Matsumoto AM, Rittmaster R, Roehrborn C, et al. (2004)**. Dihydrotestosterone and the prostate: the scientific rationale for 5α-reductase inhibitors in the treatment of benign prostatic hyperplasia. The Journal of Urology, 172(4 Part 1): 1399-1403.
- **Akman T, Binbay M, Tekinarslan E, Tepeler A, Akcay M, Ozgor F, et al.(2013)**. Effects of bipolar and monopolar transurethral resection of the prostate on urinary and erectile function: A prospective randomized comparative study. BJU Int.111(1):129–36.
- **Arun Kumar K (2012).** Role of Transition Zone Index in Assessing Bladder Outflow Obstruction due to Benign Prostatic Hyperplasia (Doctoral dissertation, Madras Medical College, Chennai).
- **Autorino R, Damiano R, Di Lorenzo G, Quarto G, Perdonà S, D'Armiento M, et al. (2009).** Four-year outcome of a prospective randomised trial comparing bipolar plasmakinetic and monopolar transurethral resection of the prostate. European urology, 55(4): 922-931.
- **Bhatia V, Biyani CS(1994)**. A comparative study of cystolithotripsy and extracorporeal shock wave therapy for bladder stones. International Urology and Nephrology, 26(1): 27–31.
- **Chtourou M, Ben Younes A, Binous MY, Attyaoui F, Horchani A (2001).** Combination of ballistic lithotripsy and transurethral prostatectomy in bladder stones with benign prostatic hyperplasia: report of 120 cases. Journal of endourology, 15(8): 851-853.
- **De Nunzio C, Roehrborn CG, Andersson KE, McVary KT (2017).** Erectile dysfunction and lower urinary tract symptoms. European urology focus, 3(4-5), 352-363.
- **Donaldson JF, Ruhayel Y, Skolarikos A, MacLennan S, Yuan Y, Shepherd R, Thomas K, et al. (2019).** Treatment of bladder stones in adults and children: a systematic review and meta-analysis on behalf of the European association of urology urolithiasis guideline panel. European urology, 76(3): 352-367.
- **Douenias R, Rich M, Badlani G, Mazor D, Smith A (1991).** Predisposing factors in bladder calculi: review of 100 cases. Urology, 37(3): 240-243.

- **El Din KE, de Wildt MJ, Rosier PF, Wijkstra H, Debruyne FM, de la Rosette JJ (1996).** The correlation between urodynamic and cystoscopic findings in elderly men with voiding complaints. The Journal of urology, 155(3): 1018-1022.
- **El Tayeb MM, Jacob JM, Bhojani N, Bammerlin E, Lingeman JE (2016).** Holmium laser enucleation of the prostate in patients requiring anticoagulation. Journal of endourology, 30(7): 805-809.
- **Ferretti M, Phillips J (2015).** Prostatectomy for benign prostate disease: open, laparoscopic and robotic techniques, The Canadian Journal of Urology TM : International Supplement.
- **Foo KT (2017)**. Pathophysiology of clinical benign prostatic hyperplasia. Asian Journal of Urology. Editorial Office of Asian Journal of Urology: pp. 152–157.
- **Froehner M, Hakenberg OW, Koch R, Schmidt U, Meye A, Wirth MP (2006).** Comparison of the clinical value of complexed PSA and total PSA in the discrimination between benign prostatic hyperplasia and prostate cancer. Urologia internationalis, 76(1): 27-30.
- **Füllhase C, Chapple C, Cornu JN, De Nunzio C, Gratzke C, Kaplan SA, et al. (2013).** Systematic review of combination drug therapy for non-neurogenic male lower urinary tract symptoms. European urology, 64(2): 228-243.
- **Gilling PJ, Cass CB, Malcolm AR, Fraundorfer MR(1995).** Combination holmium and Nd: YAG laser ablation of the prostate: initial clinical experience. Journal of endourology, 9(2): 151-153.
- **Halstead SB (2016).** Epidemiology of bladder stone of children: precipitating events. Urolithiasis, 44(2): 101-108.
- **Jung K, Meyer A, Lein M, Rudolph B, Schnorr D, Loening SA (1998).** Ratio of free-to-total prostate specific antigen in serum cannot distinguish patients with prostate cancer from those with chronic inflammation of the prostate. The Journal of urology, 159(5): 1595-1598.
- **Kirby RS, Roehrborn C, Boyle P, Bartsch G, Jardin A, Cary MM, et al. (2003).** Efficacy and tolerability of doxazosin and finasteride, alone or in combination, in treatment of symptomatic benign prostatic hyperplasia: the Prospective European Doxazosin and Combination Therapy (PREDICT) trial. Urology, 61(1): 119-126.
- **Lopez JR, Jenkins CE, Millares M (1987).** Irrigating solutions in bladder stone dissolution. Drug intelligence & clinical pharmacy, 21(11): 872-874.
- **Millán-Rodríguez F, Chéchile-Toniolo G, Palou-Redorta J, Ponce de Leon X, Salvador-Bayarri J(1999).** Re: 5-Year Outcome of Surgical Resection and Watchful Waiting for Men With Moderately Symptomatic Benign Prostatic Hyperplasia: A Department of Veterans Affairs Cooperative Study. The Journal of urology, 161(2): 614-614.
- **Nseyo UO, Rivard DJ, Garlick WB, Bennett AH(1987).** Management of bladder stones: should transurethral prostatic resection be performed in combination with cystolitholapaxy?. Urology, 29(3): 265-267.
- **O'Connor RC, Laven BA, Bales GT, Gerber GS (2002)**.Nonsurgical management of benign prostatic hyperplasia in men with bladder calculi. Urology, 60(2): 288–291.
- **Okeke Z, Shabsigh A, Gupta M (2004).** Use of Amplatz sheath in male urethra during cystolitholapaxy of large bladder calculi. Urology, 64(5): 1026-1027.
- **Orandi A** (1987). Transurethral incision of prostate compared with transurethral

resection of prostate in 132 matching cases. The Journal of urology, 138(4 Part 1): 810-815.

- **Otnes B (1983).** Correlation between causes and composition of urinary stones. Scandinavian journal of urology and nephrology, 17(1): 93-98.
- **Philippou P, Volanis D, Kariotis I, Serafetinidis E, Delakas D (2011).** Prospective comparative study of endoscopic management of bladder lithiasis: is prostate surgery a necessary adjunct?. Urology, 78(1): 43-47.
- **Roehrborn CG, Girman CJ, Rhodes T, Hanson KA, Collins GN, Sech SM,et al. (1997).** Correlation between prostate size estimated by digital rectal examination and measured by transrectal ultrasound. Urology, 49(4): 548-557.
- **Roehrborn CG, Marks LS, Fenter T, Freedman S, Tuttle J, Gittleman M, et al. (2004).** Efficacy and safety of dutasteride in the four-year treatment of men with benign prostatic hyperplasia. Urology, 63(4): 709-715.
- **Salinawati, B., Hing, E. Y., Fam, Zulfiqar, et al. (2015).** Accuracy of ultrasound versus computed tomography urogram in detecting urinary tract calculi. The Medical journal of Malaysia, 70(4): 238-242.
- **Schwinn DA (2001).** The role of 1-adrenergic receptor subtypes in lower urinary tract symptoms. BJU Int, 88(Suppl 2): 27-34.
- **Singh KJ, Kaur J (2011).** Comparison of three different endoscopic techniques in management of bladder calculi. Indian journal of urology: IJU: Journal of the Urological Society of India, 27(1): 10.
- **Sinik Z, Isen K, Biri H, Kupeli B, Sozen S, Deniz N, Bozkirli I(1998).** Combination of pneumatic lithotripsy and transurethral prostatectomy in bladder stones with benign prostatic hyperplasia. Journal of endourology, 12(4): 381-384.
- **Stravodimos KG, Petrolekas A, Kapetanakis T, Vourekas S, Koritsiadis G, Adamakis I,et al. (2009).** TRUS versus transabdominal ultrasound as a predictor of enucleated adenoma weight in patients with BPH. International urology and nephrology, 41(4): 767-771.
- **Tzelves L, Türk C, Skolarikos A (2020)**. European Association of Urology Urolithiasis Guidelines: Where Are We Going?. European Urology Focus.