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Benign prostatic hyperplasia–A literature review of three recent advances

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Abstract
Benign prostatic hyperplasia (BPH) is a common ailment in men demonstrated by about 50% of men by the age of 60 years and about 90% as the age reaches 85 years. Etiopathogenesis is still not fully clear and there is a wide variety of invasive, less invasive and medical treatment modalities. Traditional understanding links BHP with testosterone but in last few years, a theory linking it to varicocele has been propounded which marks a departure from all traditional theories. Besides, two novel and effective treatment modalities have been introduced in the form of Prostatic artery embolization and Urolift. This article reviews these recent advances in BPH under the light of current literature.

Keywords: benign prostatic hyperplasia, prostatic artery embolization, urolift, testosterone, quality of life

Introduction

Benign prostatic hyperplasia (BPH), also known as benign prostatic hypertrophy, is considered a normal component of the aging process in men demonstrated by about 50% of men by the age of 60 years and about 90% as the age reaches 85 years. BPH involves the hyperplasia of stromal and epithelial elements of the prostate arising in the periurethral and transition zones of the gland. This may result in restriction of the flow of urine from the bladder (Figure 1) and a range of Lower Urinary Tract Symptoms (LUTS) in about 15- 25% of cases, negatively impacting the Quality of life (QOL). BPH is believed to be linked to the androgen testosterone though, there is no clear experimentally proven cause and effect relationship' with the serum testosterone levels. The circulating testosterone is metabolized into dihydrotestosterone (DHT) in the prostate gland by type-II 5-alpha-reductase and that acts by binding to the androgen receptors of the prostrate cells. However, it is also established that the level of serum testosterone in men decreases with age and hence some other factors must also be playing role in the development of BHP which might include the metabolic syndrome, genetic polymorphism, inflammatory cytokines, hyperinsulinemia, norepinephrine, angiotensin II, and insulin-like growth factors (IGFs) [1].

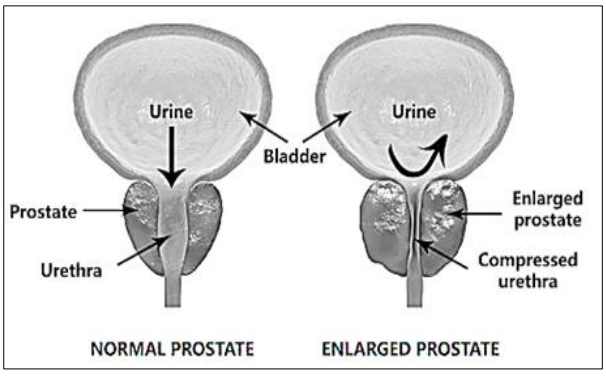

Fig 1: Normal Prostrate and Benign Prostatic Hyperplasia (BPH)

Therapeutic options for (BPH) include the following [2-4]

1. **Watchful Waiting:** For patients with mild to moderate LUTS that don't disturb the life.
2. **Medications:** For patients with bothersome, moderate-to-severe LUTS. These include alpha-adrenoceptor blockers (Abs), 5alpha-reductase inhibitors (5ARIs), phytotherapeutics, antimuscarinics (AMs), beta3-adrenoceptor agonists and phosphodiesterase type 5 inhibitors (PDE5Is) are available, alone or in combination.
3. **Interventional therapy:** For patients with moderate-to-severe LUTS and those who have developed complications of BPH. The therapies include Transurethral Resection of the Prostate (TURP), Transurethral Laser Surgery, Photoselective Vaporization of the Prostate (PVP), Holmium Laser Ablation of the Prostate (HoLAP) and Holmium Laser Enucleation of the Prostate (HoLEP).

New advances in the understanding of the etiopathogeneses and management of BPH regularly come in the literature and in the article, we briefly review the literature related to three such recent advances that appear to have significant impact.

Methods

The articles in English language, dealing with the IBC were reviewed in PubMed, ResearchGate, HINARI, Google Scholar and Web of Science after search on the keywords: Benign prostatic hyperplasia (BPH), Varicocele, Prostatic artery embolization (PAE) and Prostatic urethral lift (PUL). Time limits were set from January 2008 to June 2021.

BPH and Varicocele

Gat *et al*.in 2008 proposed a novel and provoking theory on the origin of BPH. In a study involving 28 BPH patients, varicocele was detected in all the patients (100%) and it was suggested the

malfunction of the valves in the internal spermatic vein (ISV) leads to varicocele and elevation of the hydrostatic pressure as compared to the pressure in the prostatic venous system and this pressure difference results in retrograde flow of blood. This retrograde blood flows through interconnected vessels, the most prominent being the deferential vein. It was also detected that the free testosterone (FT) levels were far higher (about 100-fold) in the ISV as compared to that in the systemic veins [5]. On the basis of these findings, they concluded that the prostate due to exposure

1. To high venous pressure undergoes hypertrophy and
2. To higher free testosterone concentrations undergoes hyperplasia.

Varicocele was treated and this was followed by elimination of the back-pressure and the retrograde blood flow leading to rapid reduction of the prostrate volume and regression of urinary symptoms in all the enrolled BPH patients [6].

In 2018, Gat and Goren [7] showed that sclerotherapy of the both ISV exhibited significant reduction in the volume of prostate volume as well as the urinary symptoms at about 24 months of follow-up in 81.5% of the enrolled BPH patients and the study led to the conclusion that by effectively managing the varicocele, significant decrease of prostate volume and regression of prostatic symptoms can be expected though a very large sized prostate at presentation might act as a limitation. The procedure was otherwise found to be safe and only a few minor self-limiting side effects were encountered.

Goren and Gat in 2018 presented a study that dealt with the level of prevalence of varicocele in the patients presenting with BPH. A total of 901 patients were enrolled and three diagnostic methods were used for detection of varicocele including: physical examination, colour flow Doppler ultrasound and contact liquid crystal thermography. Bilateral varicocele was revealed in all the enrolled patients of BPH (100%) by at least one of three diagnostic methods [8].

Strunk *et al* implemented the treatment strategy proposed by Gat *et al*. in clinical practice and to report the results of their study in 2015 [9]. They enrolled 30 patients with BPH and embolised bilateral ISV in each of them. Subjective evaluation by registration of responses to International Prostate Symptom Score [IPSS] and Quality of Life score [QOL] questionnaires and objective evaluation by determination of prostate volume, peripheral testosterone levels and prostate-specific antigen (PSA) were undertaken before the procedure and at 6 months follow-up after the procedure. IPSS and QoL scores were significantly decreased 6 months after the intervention leading to patients' satisfaction but the objective changes in prostatic volumes, PSA and peripheral total testosterone levels were not significant statistically. The study concluded that the interventional occlusion of the ISV in patients with BPH is a feasible outpatient procedure with a low complication rate with satisfactory intermediate results [9].

Prostatic artery embolization (PAE)

Prostatic artery embolization (PAE) is an outpatient, minimally invasive procedure for BPH performed by interventional radiologists and involves the release of microscopic, polyvinyl chloride beads into the prostatic arteries thereby blocking off the blood flow. This technique was first reported in 2008 and since then, multiple series have been published, projecting it as an attractive, safe and effective alternative for BPH management with no significant complications in form of urinary incontinence, retrograde ejaculation and erectile dysfunction [10].

However, PAE is a technically demanding procedure as, the procedure is usually performed in older patients with atherosclerosis and comorbidities and since the prostatic vascular anatomy is described to be complex and variable [10].

PAE is primarily believed to act by

1. Shrinkage of the enlarged prostate gland as a result of PAE-induced ischemic infarction &
2. Potential effects to decrease the tone of prostatic smooth muscle by reducing the number and density of α1-adrenergic receptors in the prostate stroma.

Sun *et al*. in 2016 reviewed the likely mechanisms behind PAE, and mentioned the following [11]:

1. apoptosis induced and enhanced by:
a. ischemia in the embolized prostate
b. blockage of androgens circulation to the embolized prostate,
2. secondary denervation following PAE, &
3. Potential effect of nitric oxide pathway immediately after embolization.

Kamalov *et al*. [12] in 2020 presented the data of 1,015 cases managed with superselective version of PAE, termed as 'PErFecTED' technique where in there is 'Proximal vessel Embolization First and Then Distal Embolization'. At 24 months of follow-up, both the IPSS and QOL scores were about three times better. However, stress was laid upon further improvement in the technique due to the risk of postembolization syndrome.

Li *et al*. [13] in 2015 presented the results therapy of PAE with combined polyvinyl alcohol particles 50 μm and 100 μm in size, in 24 patients with severe LUTS due to large BPH (≥80 cm) and refractory to medical treatment. Bilateral PAE was performed in 19 (86%) patients and unilateral in 3 (14%) patients Clinical success rate was found to be 92% as determined with use of IPSS, QOL, peak urinary flow rate, postvoid residual volume (PVR), , PSA levels , and prostatic volume (measured by magnetic resonance imaging) at one , three , six, and every six-months thereafter.

Tapping *et al*. [14] assessed the effectiveness of PAE in the control of haematuria BPH with normal upper urinary tract. They enrolled 12 consecutive patients with haematuria in their prospective study. Bilateral PAE was carried out with particles (200-500 μm) and follow-up was undertaken at 3, 12 and 18 months following the procedure. All cases of haematuria had resolved by the 3-month follow-up (100%).and in all, there was a reduction in LUTS and significant improvements in QOL indices, IPSS and IIEF. There was no associated sexual dysfunction.

Ray *et al*. [15] conducted the UK Register of Prostate Embolization (UK-ROPE) study to compare the outcomes of PEA with TURP by conducting as recruiting 305 patients across 17 urological/interventional radiology centres of UK. 216 of the participants underwent PAE and 89 underwent TURP. The results of that major study proved that PAE to provide significant improvement in urinary symptoms and QOL safely with decreased hospital stay and earlier return to normal life. IPSS

score improvement was though better with TURP.
Carnevale *et al*. [16] compared the outcomes of TURP to PAE and superselective PAE (PErFecTED -PAE) and concluded that both TURP and PAE are safe and effective management options for BPH. When it comes to urinary symptoms, TURP, PAE and PErFecTED-PAE yield similar degree of relief, but if assessed by urodynamic studies, TURP is a better option. However, PAE has significantly lesser adverse outcomes and quicker return to normal activities of life after the procedure. A recent meta-analysis of randomized controlled trials by Xiang *et al*. [17] also yielded similar results.

Uro Lift
The Prostatic urethral lift (PUL). Procedure, more commonly known as UroLift is a recently introduced, non-invasive, cost-effective and innovative tool of addressing BPH. The UroLift System is a straightforward procedure, conducted under mild sedation and local anaesthesia, and involved implantation of tiny implants through the urethra to lift and hold the enlarged prostate tissue out of the way so it no longer blocks the urethra (Figure 2). The procedure is non-ablative and involves no cutting, heating or removal of prostate tissue and hence there are no sexual side effects (such as erectile dysfunction, retrograde ejaculation) [18]. Improvements in functional outcomes including IPSS & QOL are significant and return to work is within a few days [19]. Adverse effects are usually mild to moderate, and are transient in nature including hematuria and dysuria. However, UroLift would not be appropriate option if the patients have unfavourable anatomy, e.g., very large prostate or a large "middle lobe '[20-21].

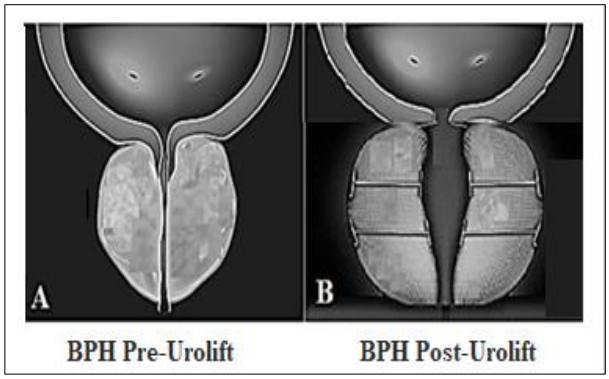

Fig 2: (A) Benign hyperplasia of prostrate with compressed urethra. (B) Prostrate after application of UroLift appliances, with patent urethra.

Urolift device is manufactured by Neotract and as per the evidence report [22] published in 2016 on the basis of available evidences, Urolift as an effective device that markedly improves IPSS score. On comparison with TURP and HoLEP , Urolift does not yield better clinical outcomes in terms of improvements in IPSS, QOL and maximum urinary flow rate but Urolift does appears to excel in terms of fewer and milder complication profile. Roehrborn *et al*. [23] in 2017 published results of the prospective, multi-center, randomized, blinded sham control trial of UroLift in men with bothersome LUTS due to BPH The study concluded that UroLift offers rapid improvement in symptoms, QOL and flow rate. IPSS improvement after UroLift was 88% greater than that of sham at 3 months and return to preoperative physical activity was within 8.6 days. The improvement in indices was durable through 5 years and were achievable with minimal use of a postoperative urinary catheter, and preservation of both erectile and ejaculatory function. Symptom improvement was commensurate with patient satisfaction.
In a recently published study by Page *et al*. [24], the real-world outcomes of prostatic urethral lift (UroLift) procedures conducted in 80 hospitals across England between 2017 and 2020 in 2942 patients were determined retrospectively. 85.3% of procedures were conducted as day-case surgery and in-hospital complication rate was 3.4%. 93% of men were catheter-free at 30 days. 12.0% has required visit to accident and emergency unit within 30 days. and another 12% required re-treatment at 2 years. This real-world analysis of UroLift shows that the procedure can be conducted safely in a day-case setting with minimal morbidity.

Conclusion
Benign prostatic hyperplasia (BPH) is a very common disorder in aging males and in last few years, a radical shift in the understanding of the etiopathogenesis had occurred by linking varicocele to the development of BPH. Newer and less invasive modalities of treatment including Prostatic artery embolization and Urolift are very promising and it is hoped that in coming years, patients of BHP would get more relief.

Source of images
Self-created on Paint application

Conflicts of interest
None

Source of funding
None

References
1. Schauer I, Madersbacher S. Medical treatment of lower urinary tract symptoms/benign prostatic hyperplasia: anything new in 2015. Curr Opin Urol,2015:25(1):6-11.
2. Agrawal M, Kumar M, Pandey S, Aggarwal A, Sankhwar S. Changing profiles of patients undergoing transurethral resection of the prostate over a decade: A single-center experience. Urol Ann,2019:11(3):270-5.
3. Dimitropoulos K, Gravas S. New therapeutic strategies for the treatment of male lower urinary tract symptoms. Res Rep Urol,2016:8:51-9.
4. De Nunzio C, Presicce F, Tubaro A. Combination therapies for improved management of lower urinary tract symptoms/benign prostatic hyperplasia. Drugs Today (Barc),2016:52(9):501-17.
5. Gat Y, Joshua S, Vuk-Pavlović S, Goren M. Paying the price for standing tall: Fluid mechanics of prostate pathology. Prostate,2020:80(15):1297-1303.
6. Gat Y, Gornish M, Heiblum M, Joshua S. Reversal of benign prostate hyperplasia by selective occlusion of impaired venous drainage in the male reproductive system: novel mechanism, new treatment. Andrologia,2008:40:273-81.
7. Gat Y, Goren M. Benign Prostatic Hyperplasia: Long-term follow-up of prostate volume reduction after sclerotherapy of the internal spermatic veins. Andrologia,2018:50(2):10.1111

8. Goren M, Gat Y. Varicocele is the root cause of BPH: Destruction of the valves in the spermatic veins produces elevated pressure which diverts undiluted testosterone directly from the testes to the prostate. Andrologia,2018:50(5):e12992.
9. Strunk H, Meier M, Schild HH, Rauch M. Treatment of benign prostatic hyperplasia by occlusion of the impaired urogenital venous system - first experience. Rofo,2015:187(3):180-6.
10. Carnevale FC, de Assis AM, Moreira AM. Prostatic Artery Embolization: Equipment, Procedure Steps, and Overcoming Technical Challenges. Tech Vasc Interv Radiol,2020:23(3):100691.
11. Sun F, Crisóstomo V, Báez-Díaz C, Sánchez FM. Prostatic Artery Embolization (PAE) for Symptomatic Benign Prostatic Hyperplasia (BPH): Part 2, Insights into the Technical Rationale. Cardiovasc Intervent Radiol,2016:39(2):161-9.
12. Kamalov A, Kapranov S, Neymark A, Kurbatov D, Neymark B, Karpov V *et al*. Prostatic Artery Embolization for Benign Prostatic Hyperplasia Treatment: A Russian Multicenter Study in More Than 1,000 Treated Patients. Am J Mens Health,2020:14(3):1557988320923910.
13. Li Q, Duan F, Wang MQ, Zhang GD, Yuan K. Prostatic Arterial Embolization with Small Sized Particles for the Treatment of Lower Urinary Tract Symptoms Due to Large Benign Prostatic Hyperplasia: Preliminary Results. Chin Med J (Engl),2015:128(15):2072-7.
14. Tapping CR, Macdonald A, Hadi M, *et al*. Prostatic Artery Embolization (PAE) for Benign Prostatic Hyperplasia (BPH) with Haematuria in the Absence of an Upper Urinary Tract Pathology. Cardiovasc Intervent Radiol,2018:41(8):1160-4.
15. Ray AF, Powell J, Speakman MJ, Longford NT, DasGupta R, Bryan T *et al*. Efficacy and safety of prostate artery embolization for benign prostatic hyperplasia: an observational study and propensity-matched comparison with transurethral resection of the prostate (the UK-ROPE study). BJU Int,2018:122(2):270-82.
16. Carnevale FC, Iscaife A, Yoshinaga EM, Moreira AM, Antunes AA, Srougi M. Transurethral Resection of the Prostate (TURP) Versus Original and PErFecTED Prostate Artery Embolization (PAE) Due to Benign Prostatic Hyperplasia (BPH): Preliminary Results of a Single Center, Prospective, Urodynamic-Controlled Analysis. Cardiovasc Intervent Radiol,2016:39(1):44-52.
17. Xiang P, Guan D, Du Z, *et al*. Efficacy and safety of prostatic artery embolization for benign prostatic hyperplasia: a systematic review and meta-analysis of randomized controlled trials. Eur Radiol,2021:31(7):4929-46.
18. Perera M, Roberts MJ, Doi SA, Bolton D. Prostatic urethral lift improves urinary symptoms and flow while preserving sexual function for men with benign prostatic hyperplasia: a systematic review and meta-analysis. Eur Urol,2015:67(4):704-13.
19. Garcia C, Chin P, Rashid P, Woo HH. Prostatic urethral lift: A minimally invasive treatment for benign prostatic hyperplasia. Prostate Int,2015:3(1):1-5.
20. McNicholas TA. Benign prostatic hyperplasia and new treatment options - a critical appraisal of the UroLift system. Med Devices (Auckl),2016:9:115-23.
21. McNicholas TA, Woo HH, Chin PT *et al*. Minimally invasive prostatic urethral lift: surgical technique and multinational experience. Eur Urol,2013:64(2):292-9.
22. Ray A, Morgan H, Wilkes A, Carter K, Carolan-Rees G. The Urolift System for the Treatment of Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia: A NICE Medical Technology Guidance. Applied Health Economics and Health Policy,2016:14(5):515-26.
23. Roehrborn CG, Rukstalis DB, Barkin J, Gange SN, Shore ND, Giddens JL, *et al*. Three year results of the prostatic urethral L.I.F.T. study. Can J Urol,2015:22(3):7772-82.
24. Page T, Veeratterapillay R, Keltie K, Burn J, Sims A. Prostatic urethral lift (UroLift): a real-world analysis of outcomes using hospital episodes statistics. BMC Urol,2021:21(1):55.