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Intravesical Prostatic Propulsion as Predictor of Treatment Response with Alpha Blocker Medications in Patients with Benign Prostate Hyperplasia

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A B S T R A C T

Introduction: Benign prostate hyperplasia (BPH) can develop into Benign Prostate Enlargement (BPE) then can cause Benign Prostatic Obstruction and manifested as lower urinary tract symptoms (LUTS). Pharmacotherapy, mainly alpha blocker, is the initial treatment of choice for patients with moderate-severe LUTS based on International Prostate Symptom Score (IPSS). Intravesical prostatic protrusion (IPP) measurement on ultrasonography is simple and non-invasive parameter of the prostate and can be used to predict response to alpha blocker medications.

Method: A systematic search of English literature was conducted using the PubMed, ProQuest, and ScienceDirect databases. Articles published between 2012 and May 2025 were selected based on a set of preestablished inclusion criteria. These articles were analysed according to the PRISMA-2020 guideline.

Result: Nine articles including 1672 patients met the eligibility criteria. The included studies reported the correlation between IPP compared to others parameter and treatment outcome with alpha blocker after follow up. In addition, some studies also explore the relationship between IPP, uroflowmetry, and several US parameter of the prostate.

Conclusion: This systematic review showed that IPP can predict response to alpha blocker medications in patients with BPH. Higher degree of IPP related to poorer response to alpha blocker. It had stronger correlation than prostate volume to predict treatment response.

Keywords: intravesical prostatic protrusion, ultrasound, benign prostate hyperplasia, alpha blocker

1. INTRODUCTION

Benign prostate hyperplasia (BPH) is histological diagnosis of increased tissue proliferation within prostatic transition zone, including epithelial, stromal, and glandular tissue. This hyperplasia is considered normal part of aging male and thought to occur due to various risk factors, but the main risk factor is dihydrotestosterone (DHT), active metabolite of testosterone. DHT exerts physiological effect on development of prostate gland as well as hyperplasia of the prostate. BPH incidence is increasing by age, starting at age 40-45 about 45% and 80% by age 70 [1].

BPH itself doesn't always symptomatic nor require treatment. BPH which develop into Benign Prostate Enlargement (BPE) then can cause Benign Prostatic Obstruction and manifested as lower urinary tract symptoms (LUTS) is the target of therapy. LUTS resulting from BPE are due to 2 component mechanisms: 1. Static component due to bladder outlet obstruction (BOO) of the enlarged prostate; and 2. dynamic components due to increased smooth muscle tone and resistance in the enlarged prostate [2]. These LUTS can be manifested inf the form of obstructive symptom (weak stream, intermittency, hesitancy, incomplete voiding, and urinary retention) or irritative symptom (urgency, frequency, and nocturia) which can lead to several complication, such as acute urine retention, recurrent urinary tract infection, haematuria, urinary stone, and kidney failure [3].

Main objective of the treatment is symptomatic improvement of LUTS and preventing progression of complication of BPH. Several pharmacotherapy classes used in LUTS/BPH treatment including alpha blocker, 5-alpha reductase inhibitor (5-ARI), phosphodiesterase-5 inhibitor (PDE5), and anticholinergic which can be chosen as single or combination therapy. Pharmacotherapy, mainly alpha blocker, is the initial treatment of choice for patients with moderate-severe LUTS based on International Prostate Symptom Score (IPSS). It can alleviate symptoms rapidly by reducing smooth muscle tone in the prostate, bladder neck, and urethra, thus reducing BOO [4].

Ultrasonography (USG) is a simple and non-invasive choice in evaluating BPE. Several USG parameters can help in deciding treatment for BPE, such as prostate volume (PV), post void residual urine (PVR), and intravesical prostatic protrusion (IPP). This evaluation needs a careful radiologist examination. IPP is the result of morphological change in hypertrophied prostate causing protrusion into the bladder. Multiple studies showed that the

presence of IPP had positive correlation with PV, prostate specific antigen (PSA), negative correlation with therapeutic respond to alpha blocker [5 6 7]. However only few studies have evaluated the effect of IPP degree and treatment response to alpha blocker, therefore this systematic review aimed to evaluate the role of IPP in predicting the success of alpha blocker therapy in patients with BPE.

2. METHODS

2.1. Protocol

This study was conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting the findings.

2.2. Literature Search Strategy

Systematic search of English literature was conducted in PubMed, Proquest, ScienceDirect, and Google Scholar. The search terms used were: ((Intravesical prostatic protrusion) OR (Intravesical prostate protrusion) OR (IPP)) AND ((alpha blocker) OR (α-blocker))). Duplicates were removed in each database. Included studies were published up to May 2025.

2.3. Process of Data Collection

Authors reviewed selected studies gathered from all databases, disagreements resolved through discussion. The process of studies selection conducted in multiple stages as depicted in Figure 1. Flow diagram was developed following the PRISMA 2020 guideline.

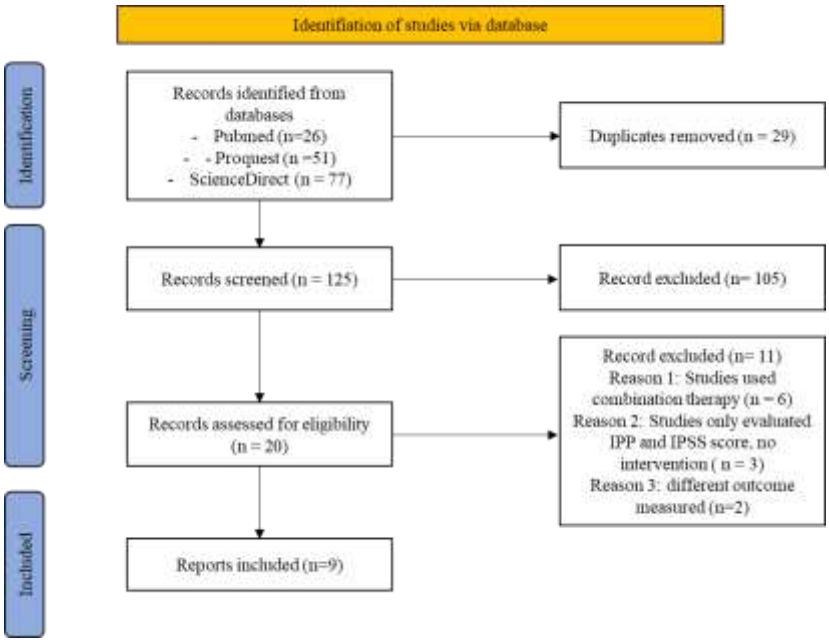

Figure 1. Diagram showing PRISMA flow for this systemic review

2.4. Data Extraction

The following data were extracted from each article: year of publication, study design, sample size, population characteristics, USG technique (transabdominal or transrectal) to evaluate IPP, degree of IPP, type and dose of alpha blocker used for treatment, duration of follow up, and outcome.

2.5. Outcome

The primary outcome evaluated was effectiveness of alpha blocker in alleviating LUTS based on degree of IPP. Effectiveness of alpha blocker measured by improvement of IPSS, ultrasonographic parameter improvement, and uroflowmetric measurement.

2.6. Analysis of The Quality of Included Studies

All the selected studies were examined to identify any risk of bias. Authors independently analysed all the selected studies, and any disagreements were resolved through consensus. Quality of studies were assessed by Newcastle Ottawa Scale (NOS) as all studies included were done in nonrandomized

setting. Total NOS score of 0-4, 5-7, 8-9 were classified as low-, moderate-, and high-quality studies [8]. The result of quality of studies assessment showed in Table 1.

Table 1. Quality assessment of Included Studies

Authors	Domain 1 (Selection)	Domain 2 (Comparability)	Domain 3 (Outcome)	Conclusion
Kalkanli et al [9]	4	1	3	8
Topazio et al [10]	4	2	3	9
Matsukawa et al [11]	4	2	3	9
Park et al [12]	4	1	2	7
Cumpanas et al [13]	4	2	2	8
Ahmed [14]	4	2	3	9
Radwan et al [15]	4	2	2	8
Zaghloul et al [16]	4	2	2	8
Kuei et al [17]	4	1	1	6

3. RESULTS

3.1. Study selection and characteristics

The literature search provided 154 studies: 26 in Pubmed, 51 in ProQuest, and 77 in ScienceDirect. After removing duplicates, 125 studies included in screening. Next, 20 studies with full text available were reviewed, and finally 9 studies were included in this systematic review. Among these studies, eight studies were prospective observational studies and one studies is retrospective observational study. Total sample comprised 1672 males. The characteristics of included studies in this review provided in Table 2.

Table 2. Characteristics of Included Studies

Author	Publication Year	Country	Study Design	Participant	Age (years)	Alpha blocker given	Follow-up time
Kalkanli et al [9]	2016	Turkey	Prospective Observational	49	59.6 ± 6.4	Tamsulosin	1 month and 3 months
Topazio et al [10]	2018	Italy	Prospective Observational	130	50-57	Tamsulosin 0.4 mg/d	3 months
Matsukawa et al [11]	2017	Japan	Prospective Observational	103	69.2 ± 8.2	Silodosin 8 mg/d	6 months
Park et al [12]	2012	South Korea	Retrospective Observational	134	65.01± 7.38	Tamsulosin 0.2 mg/d	3 months
Cumpanas et al [13]	2013	Romania	Prospective Observational	183	60-74	Tamsulosin 0.4 mg/d	3 months
Ahmed [14]	2016	Egypt	Prospective Observational	166	65.62 ± 9.14	Tamsulosin 0.4 mg/d	6 months
Radwan et al [15]	2021	Egypt	Prospective Observational	750	50-66	Tamsulosin 0.4 mg/d	6 months
Zaghloul et al [16]	2018	Egypt	Prospective Observational	45	-	Tamsulosin 0.4 md/d	3 months
Kuei et al [17]	2015	Taiwan	Prospective Observational	112	65.5 ± 10.9	Tamsulosin 0.2 mg	6 months

3.2. Settings, treatment of choice, and format

All samples were gathered by consecutive sampling and done in single centre study. Most of studies used tamsulosin as their specific alpha blocker treatment, but dosing varies from 0.2-0.4 mg/d. Silodosin were used only in one study[11]. Follow up period varied from 3-6 months. Based on ultrasonographic examination of the prostate, 6 studies applied transrectal approach[10,12,14–17], 2 studies[11,13] applied transabdominal approach, while 1 study[9] using both approach and compared them.

3.3 Quality Assessment of The Study

The results of the NOS assessment of eligible studies presented as in Table 2. Overall quality of study belongs to high quality study with 77.8% (7) of the studies, only 22.2% (2) studies belong to moderate quality.

3.4. Outcome

Overall studies showed the potency of IPP in predicting treatment response with alpha blocker in BPE patients presenting with LUTS as showed in table 3. IPSS was used in 8 studies to define treatment response based on symptomatic improvement, while only 1 study [17] used Global Response Assessment (GRA) questionnaire. Correlation coefficient was showed in 2 studies which is consistently negative between IPP and IPSS (-0.410 and -0.56) [9,11]. ROC analysis were performed in 4 studies, 2 studies defined 8.2 mm was the best cut-off measurement of IPP with AUC were 0.866 and 0.836 with PPV 73.3%, 72.4% and NPV 98.18%, 95.0% [15,16]. Another study used different cut-off measurement of IPP, one used 12.9 mm with AUC was 0.876 with PPV 78.2% and NPV 90.5% [14]. The other one used 11 mm as cut off and resulted 78% in sensitivity and 92% in specificity [11].

Pre-defined grading of IPP into grade I (<5 mm), grade II (5-10 mm) and grade III (>10 mm) implemented in analysis of 3 studies. The odd ratio to obtain a treatment success, defined as post treatment IPSS score reduction > 3 points was 59 (CI 95% 11.8–296) and 8.1 (CI 95% 1.7–38) in grade I and grade II compared to grade III. Improvement of uroflowmetry parameters also better in low grade IPP (Grade I vs Grade II with p= 0.016 and Grade I vs Grade III with p= 0.005) [10]. Another study showed only IPP significantly related to whether both IPSS and Qmax were improved (IPSS, p=0.044; Qmax, $p < 0.001$). In-grade analysis showed medication improved total IPSS and subscores ($p < 0.001$), QoL ($p < 0.001$), Qmax ($p < 0.001$), and PVR (p=0.030) in grade I. In grade II, it improved total IPSS (p=0.01), irritative subscore ($p < 0.001$), and obstructive subscore (p=0.03). In grade III, only total IPSS (p=0.01) and irritative score ($p < 0.001$) were significantly improved [12]. Only one study used GRA to evaluate outcome of treatment, it showed that grade I had better improved outcome compared to grade II and III (36.8% vs 74.3%; p 0.001) [17].

Cumpanas et al. also used pre-defined grading of IPP but into 2 grades, grade I (≤10 mm) and grade II (>10 mm). This study than made a cross-tabulation analysis comparing grades and patient's response based on IPSS and Qmax improvement. Statistically significant differences were noted for IPSS -35% responders (78% grade I vs 58% grade II), -3 points IPSS responders (82% vs 64%, P <0.01). While Qmax +25% responders (82% vs 58%), and Qmax +1.6 mL/s responders (85% vs 62%, P <0.01) also significantly different between 2 grades [13].

While the other studies use either transrectal or transabdominal technique on ultrasonography examination of the prostate, one study used both technique and compared them. The result was transabdominal and transrectal measurement of IPP didn't show any significant difference [9].

Table 3. Summary of Findings of Included Studies

Author	Method	USG technique	Result
Kalkanli et al	Baseline evaluation of IPSS, uroflowmetry, prostate specific antigen (PSA) Treatment outcome measurements were carried out on 1st and 3rd month after initiation of an alpha-receptor specific blocker by IPSS and uroflowmetric measurement of Qmax.	Transrectal and transabdominal	- IPP negatively correlated with baseline Qmax values (p = 0.001, r = -0.485) and positively correlated with PSA (p = 0.013, r =0.353) and PV (p = 0.003, r =0.420). - Measurements of 1st month IPSS = 6.88 ± 4.84, Qmax = 15.51 ± 4.68 ml/s (test p=0.000) and 3rd month IPSS = 5.24 ± 3.15, Qmax = 15.70 ±4.73 ml/s (p=0.003) showed significant improvement compared to baseline (IPSS = 17.29 ± 5.58, Qmax = 12.77 ±3,94 ml/s - The only parameter to have a significant correlation with the change in IPSS was IPP for 1st month (r = -0.410, p = 0.004) & 3rd month (r= -0.293 p=0.046) TR measurements. - Transabdominal and transrectal measurement of prostate parameters were similar (p=0,001).

Topazio et al	Ultrasound was performed to measure IPP and prostatic volume. IPP then graded as Grade 1 (< 5 mm), Grade 2 (5 - 10 mm) and Grade 3 (> 10 mm). Treatment success, defined as post-treatment IPSS score reduction > 3 points after follow up.	Transrectal	- Treatment success obtained in 82%, 38,5% and 7,1% of patients respectively. - The odd ratio to obtain a treatment success was of 59 (CI 95% 11.8–296) and 8.1 (CI 95% 1.7–38) in group A and group B in comparison to group C. - Positive improvement of uroflow parameters after treatment in patients with a low grade IPP to patients with a higher grade IPP (p value = 0.016 Group A vs Group B; p value = 0.005 Group A vs Group C).
Matsukawa et al	IPSS, IPSS-QOL, and Overactive Bladder Symptom Score (OABSS) were assessed at baseline and 1 year after the start of treatment. Qmax, PVR, Pdet Qmax and BOOI were evaluated as parameters of voiding function. Patients divided into two groups based on the grade of improvement in subjective symptoms; patients with an IPSS improvement of ≥50% were classified as IPSS-GR and those with improvement <25% were classified as IPSS-PR and into two groups based on the grade of improvement in BOO; patents with BOOI improvement of ≥50% were classified as BOOI-GR and those with improvement <25% were classified as BOOI-PR. Analysis done by comparing the backgrounds of the two groups and evaluated pretreatment factors related to therapeutic effects improving the IPSS and BOOI.	Transabdominal	- 39 patients (37.9%) were IPSS PR while 36 patients (35.0%) were BOOI-PR. - PV, Qmax, and IPP were independent predictors of ineffective treatment. - Multiple linear regression analysis showed that IPP was the only significant factor for predicting improvement of IPSS ($r = -0.56$, $P < 0.001$) and BOO ($r = -0.59$, $P < 0.001$). - Based on improvement of IPSS, ROC analysis identified 11 mm as the optimal cut-off value for IPP; this value yielded a sensitivity of 78% and a specificity of 92%. - Regarding the improvement of BOOI, ROC analysis also calculated 11 mm as the best cut-off value for IPP (sensitivity of 89% and a specificity of 94%).
Park et al	Patients divided into 3 groups according to the extent of IPP: group A ≤ 5 mm, group B 5-10 mm, and group C > 10 mm. The IPSS/QoL, Qmax, and PVR before and after tamsulosin 0.2 mg administration were compared.	Transrectal	- Mean IPPs were 0.90±1.39 mm (group A, n=90), 6.92±1.10 mm (group B, n=24), and 16.60±4.06 mm (group C, n=20). - PV, prostatic urethral length (PUL), prostatic adenoma urethral length (PAUL), PSA, Qmax, and PVR showed significant correlations with IPP ($p < 0.05$). - Comparison of parameters before and after 3 months showed that medication improved total IPSS and subscores ($p < 0.001$), QoL ($p < 0.001$), Qmax ($p < 0.001$), and PVR ($p=0.030$) in group A. In group B, it improved total IPSS ($p=0.01$), irritative subscore ($p < 0.001$), and obstructive subscore ($p=0.03$). In group C, only total IPSS ($p=0.01$) and irritative score ($p < 0.001$) were significantly improved. - Multiple linear regression analysis showed only IPP was statistically significantly related to whether both

			IPSS and Qmax were improved (IPSS, p=0.044; Qmax, p＜0.001)
Cumpanas et al	patients with divided in 2 groups according to IPP: group A ≤10 mm; group B >10 mm. IPSS changed -35% and -3 points; and maximum urinary flow (Qmax) assessed by uroflowmetry (+1.6 mL/s and +25%) response criteria were defined. Patients' responses from the 2 groups were compared.	Transabdominal	- Qmax increased, with 2.74 mL/s (25%) in group A (P <0.01) and 1.59 mL/s (19%) in group B (P 0.07). - IPSS decreased, with 39.9% (P < 0.01) and 29.7% (P 0.08). - Statistically significant differences were noted for IPSS -35% responders (78% group A vs 58% group B, P <0.01), -3 points IPSS responders (82% vs 64%) - Qmax +25% responders (82% vs 58%), and Qmax +1.6 mL/s responders (85% vs 62%, P <.01).
Ahmed	The treatment outcomes determined by comparing pre-treatment and 6-month follow-up values of IPSS, QoL score and Qmax. According to the overall treatment efficacy, patients were divided into effective and ineffective treatment groups.	Transrectal	- Logistic regression analysis revealed that, the baseline IPSS storage subscore (p=0.010), Qmax (p=0.019), Bladder Wall Thickness (p=0.042), ultrasound estimated bladder weight (p=0.045) and IPP (p=0.022) were the factors associated with ineffective treatment. - The AUCs were 0.939 (95% CI= 0.890-0.988; p<0.001; cut-off value 9.3mm) for BWT, 0.897 (95% CI=0.839-0.954; p<0.001; cut-off value 34.5g) for UEBW and 0.876 (95% CI=0.809-0.942; p<0.001; cut-off value 12.9mm) for IPP. - The positive predictive value (PPV) and negative predictive value (NPV) were 83.6% and 92.4%; 78.2% and 85.6%; 80.3% and 90.5% for BWT, UEBW and IPP.
Radwan et al	Treatment outcomes were measured by comparing pre- and 6-month post treatment follow-up values of IPSS, QoL scores, and Qmax. According to the overall treatment efficacy, patients were divided into effective and ineffective treatment groups.	Transrectal	- From the measured prostate and bladder sonographic parameters, IPP was only significant parameter. The AUC for IPP was 0.866 with cut off alue 8.2 mm; providing PPV and NPV were 73.3% and 98.18%.
Zaghloul et al	Response to treatment on the basis of IPSS, QoL score and Qmax was evaluated. The impacts of baseline parameters on treatment outcome were statistically analyzed.	Transrectal	- BWT, UEBW, and IPP were ultrasonography parameter as independent predictor of treatment failure. - The AUC of BWT, UEBW and IPP were 0.870, 0.908 and 0.836 at cut-off values of 9mm, 36g and 8.2mm. PPV were 75.0% and 97.6%; 72.4%, while NPV were 96.0%; 67.5% and 95.0% for BWT, UEBW and IPP.
Kuei et al	IPP ≤5 mm was classified as Grade I, 5–10 mm as Grade II, and >10 mm as Grade III. Patients rated their symptoms after treatment compared with their symptoms at baseline using a validated Global Response Assessment (GRA) questionnaire, a 7-point scale ranging from markedly worse (−3) to markedly	Transrectal	- Sixty-nine patients (61.6%) reported an improved outcome (GRA ≥ 1), whereas 43 (38.4%) patients reported no improvement - Patients with significant IPP (Grade II and Grade III) had significantly lower rates of improved outcome than those without significant IPP (36.8% vs 74.3%; p 0.001).

	improved (+3). Patients with a GRA score ≥ 1 at 4 weeks after the treatment were considered as having improved outcome and were maintained on their current medication. Patients with a GRA score <1 were then either administered combined therapy or switched to another medication at the discretion of the investigator.		- patients with prostatic calcification also had significantly lower rates of improved outcome than those without (47.9% vs 71.9%; p = 0.017) - Multivariate logistic regression analyses showed that both IPP (p = 0.019) and prostatic calcification (p = 0.024) are predictors of unfavorable medical treatment outcomes (GRA < 1)

4. DISCUSSION

This systematic review showed that IPP was a strong predictor of treatment failure with alpha blocker medications. This also supported by meta-analysis had shown that IPP is a strong predictor of BOO and failure of trial without catheter in patient with acute urinary retention due to BPE [7]. Lim et al. reported that IPP was better predictor of BOO caused by BPH than either PSA or PV. While larger volume of prostate would had greater IPP by US examination in two studies included in this analysis [9,12] this is also true confirmed by 3D model MRI examination of prostate [18]. Conversely, IPP can occur even without significant enlargement of prostate with prostate volume < 40 ml [19]. This could mean that IPP is more sensitive objective indicator to predict treatment of choice for patients with BPH.

Several mechanisms explain the possible relationship between IPP and failure of therapy with alpha blocker medications. IPP is an anatomical property of prostate that arises in present of prostatic overgrowth into the bladder. While enlargement of lateral lobes can compress the prostatic urethra, IPP is developed from prostatic adenoma around periurethral zone which originates from the middle lobe. It then distorts the natural urinary flow in the bladder neck that can act as "ball-valve" obstruction and leads to mechanical obstruction of bladder outlet. The extent of IPP is measured as the vertical distance from the tip of the intravesical protrusion to the circumference of the bladder at the bladder neck. This property can cause BOO independently without significant increase of prostate volume (<40 ml) [20].

Because IPP can increase urethral resistance, it also affects hydraulic pressure that drives micturition. Compression of prostatic urethra and increased variation of cross-sectional area around bladder neck due to IPP can reduce urine flow efficiency [21]. This enlarged bladder neck with a collagen tissue component also can affect the physiological work of internal bladder neck sphincter. Normally during storage phase of the bladder, entry of urine into prostatic urethra is inhibited by bladder neck. However this IPP can loosen the bladder neck and not tightly closed, then prematurely activating micturition reflexes as small amounts of urine can pass into prostatic urethra [22]. Presence of IPP also cause extroversion of prostatic urethral mucous membrane at the bladder neck. This extroversion followed by urethral distension can trigger bladder contraction through urethrovesical stimulating reflex, and in turn responsible for development if storage symptoms and overactive bladder as well as reduced response to obstruction reliever treatments [23].

As α1-adrenoceptors is the main alpha receptors presented in bladder neck, urethra, and prostatic tissue, it is used as the main target of alpha blocker medications in BPE. But its effectivity reduced in greater IPP because α1-adrenoceptors mostly present inferiorly to bladder neck, more distal to the area of protrusion due to IPP configuration that protrudes above the bladder neck. This is also true even when prostate volume < 40 ml but has greater IPP. Even combination therapy of alpha blocker and 5-ARI to reduced prostate size didn't effectively improving symptoms. It did reduce total prostate volume and transitional zone volume, but due to low stromal component proportion in higher grade IPP, this effect also doesn't alleviate symptoms satisfactorily [24]. In this condition, invasive strategy with surgery is more effective for patients with significant IPP but small prostate volume [25].

This study has several limitations. First, all studies included done in observational setting without any control group. Most of included study also done in open label setting. Second, only one study recruited large sample group. Third, there wasn't standardized type of alpha blocker and dosage used in all studies. This could affect different response to treatment. Fourth, different US technique were used in most studies either transabdominal or transrectal and only one study used both technique and compared the result of IPP measurement. This can result in measurement bias of IPP.

5. CONCLUSION

All studies suggest that IPP is a strong predictor of treatment response to alpha blocker in BPE patients presenting with LUTS. Greater degree of IPP related with higher chance of treatment failure.

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