

## Review

# Evaluation of the Accuracy of the Use of Intravesical Prostatic Protrusion Degree as the Predictor of Benign Prostatic Hyperplasia Management

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## ABSTRACT

Managing symptoms of benign prostatic hyperplasia (BPH) is important but preventing the progression of the disease is also necessary. Medical therapy is commonly used to treat BPH as initial therapy. However, not every medical therapy is effective for treating BPH. Intravesical prostatic protrusion (IPP), a manifestation of BPH is used to evaluate BPH progression thus helping clinicians in choosing the effective treatment option. Patients with higher IPP degrees may experience more severe bladder outlet obstruction (BOO). They may not respond well to medical therapies, suggesting that IPP measurement can guide treatment decisions for BPH patients. This study evaluates the accuracy of using IPP degree as a predictor of BPH management by reviewing relevant literature. A comprehensive approach was undertaken, including the selection and filtering of articles from reputable databases and scholarly repositories using specific keywords related to the study's objectives. By measuring IPP degrees, the severity of clinical BPH can be categorized, allowing clinicians to choose effective treatment options and predict treatment outcomes.

**Keywords:** Benign Prostatic Hyperplasia, Bladder Outlet Obstruction, Intravesical Prostatic Protrusion, Management, Transabdominal Ultrasound.

Benign prostatic hyperplasia (BPH) impacts more than 50% of men by the age of 60, leading to substantial healthcare costs for managing lower urinary tract symptoms (LUTS) and urinary obstruction.<sup>1</sup> The management of BPH presents a significant challenge in urological practice. However, there is no universally accepted or definitive practical standard for determining the extent and seriousness of obstruction, aside from pressure-flow studies.<sup>2</sup>

The histopathology term "BPH" is commonly used to describe benign prostatic enlargement (BPE) in daily practice.<sup>3</sup> BPH is characterized by its impact on specific zones of the prostate, primarily the transitional and periurethral regions. Unlike diffuse hyperplasia affecting all zones uniformly, BPH manifests as nodular adenomatous hyperplasia, leading to distinct nodules or often multiple nodules clustered together to form adenomata. Clinical BPH is abnormal anatomy of the prostate named prostate adenoma/adenomata (PA) leads to benign

prostatic obstruction (BPO) that may damage the bladder and kidney. PA can be classified based on intravesical prostatic protrusion (IPP) and prostate volume (PV). It's been shown that the site impacts more obstruction than the size of adenoma.<sup>4</sup> An overgrowth of median lobe into the bladder called IPP causes more obstruction due to distortion of the bladder outlet than adenoma forming the lateral lobes which would need to grow much bigger before causing compression then obstruction.<sup>2,4</sup>

This study explores optimizing BPH treatment by considering IPP grades' influence on outcomes. It proposes a novel IPP grading system to personalize care, predicting treatment effectiveness based on IPP grades. Studies indicate that IPP severity correlates with treatment response, impacting medical and surgical options. Using IPP as a predictive parameter can enhance treatment efficacy. Innovative imaging and biomarkers may further refine IPP assessment for better treatment outcomes. Integrating IPP measurement into BPH management can guide tailored approaches, improving care quality.

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## METHODS

The literature review methodology employed in this study was comprehensive and systematic, aiming to gather a diverse range of articles from reputable academic sources. The search process involved scouring reputable databases and scholarly repositories, including Google Scholar, using a combination of keywords related to the study's objectives. The selected journals spanned various publication years, providing a comprehensive overview of research conducted in this field. This extensive search yielded 586 journals, reflecting the depth and breadth of the literature review. Following the initial search, duplicate articles were meticulously removed to ensure the integrity of the dataset, resulting in a refined selection of 200 articles. Subsequently, articles were screened based on stringent inclusion criteria, which encompassed studies elucidating IPP's pathophysiology, clinical manifestations, measurement techniques, evaluation, and management in the context of BPH. Articles not meeting these criteria were excluded from the final analysis. Through this process, an additional 160 articles were excluded, primarily due to lack of relevance to the study objectives or insufficient methodological rigor. This meticulous process culminated in a final set of 32 journals published within the last 10 years selected for detailed analysis and review.



Figure 1: Flowchart showing the detailed procedure of the method

## IPP MEASUREMENT

An overgrowth of median lobe into the bladder along the path of least resistance that becomes manifestation of BPH which can produce bladder outlet obstruction and related storage and voiding symptoms is called IPP.<sup>2</sup> It has been confirmed to be a better predictor of bladder outlet obstruction (BOO) than prostate specific antigen (PSA) or prostate volume (PV).<sup>5</sup> There are some modalities to measure IPP including ultrasound, magnetic resonance imaging, computed tomography scan and flexible cystoscope, but it can't be well identified by traditional digital rectal examination (DRE) and bimanual palpation of bladder.<sup>2</sup> Ultrasound measurement of intravesical prostatic protrusion (IPP) provides superior diagnostic value in bladder outlet obstruction (BOO) compared to total prostate volume (TPV) and numerous other non-invasive assessments.<sup>6</sup> Ultrasound, both transabdominal (TAUS) and transrectal (TRUS) are cheap, readily available, accurate, and free of ionizing radiation becoming the most preferable modality in measuring IPP.<sup>7</sup>

Intravesical prostatic protrusion (IPP) study originated from the Singapore General Hospital by Prof. Foo and his colleagues in the 21<sup>st</sup> century. They prefer to use TAUS that is faster and more comfortable to the patients. The use of TAUS is more beneficial due to its lower invasiveness and greater accessibility, including availability at patients' bedsides and in remote hospitals, in contrast to TRUS.<sup>7</sup> However, TAUS measurement of prostatic volume shows less variation and relates well with the TRUS measurement.<sup>8</sup>

An appropriate filled bladder is essential when imaging prostate by TAUS as it acts as an acoustic window and affects IPP measurement. IPP is ideally measured at bladder volume 100-200 ml, empty or very full bladder (>400 ml) is not recommended for the examination.<sup>8</sup> IPP is measured in the sagittal view from the tip of the intravesical protrusion to the circumference of the bladder at the bladder neck, according to this, IPP is measured in millimeters then divided into 3 grades, Grade I (<5mm) considered as low grade; grade II or medium grade(5-10mm); Grade III or high grade (>10mm).<sup>9</sup>

## IPP AND SEVERITY OF BPH

Measuring the size of the prostate can not determine the severity of BPH symptoms.<sup>3</sup> It may depend on the site and shape of prostate.<sup>4</sup> Median lobe arises from periurethral zone at the bladder neck may trigger a ball-valve type obstruction which may cause more obstruction than compression which is caused by lateral lobe enlargement sited deep in the transitional zone.<sup>4,10,11</sup> As distortion produced by IPP causes more obstruction than compression by large lateral lobes in the prostate, the study suggests that prostate shape due to IPP is more important than prostate volume (PV).<sup>4</sup>

Measuring IPP to consider its correlation to BOO incident was first done by The Singapore group. Singapore group also compared IPP, prostate volume and prostate specific antigen (PSA) to predict BOO.<sup>8</sup> Although they relate well each other, IPP has better value than PV and PSA.<sup>5,8</sup> The grade of IPP is correlated to the clinical progression of BPH and urodynamic evidence of BOO.<sup>12</sup> The study shows further evidence that IPP influences BOO independently.<sup>13</sup> IPP has provided a positive value of 72 % for BOO.<sup>2</sup> The greater IPP relates to more obstruction and the disease will progress.<sup>4</sup>

The severity of the disease is important in deciding which therapy should be given to patients for cost-effective treatment. The severity of clinical BPH can be established based on obstruction and symptoms. It can be then categorized based on the degree of obstruction which is measured by two main functions of the bladder, namely emptying, indicated by persistent post-void residual urine (PVRU) > 100 ml and storage maximum voided volume (MVV) < 100 ml and bothersome symptoms or patient's quality of life (QoL  $\geq$  3). They are: stage I with no significant obstruction and symptoms to stage IV with complication of BPH. The grade of IPP correlates to the severity of clinical BPH, the lower the grade of IPP the lower the severity of clinical BPH. The study has confirmed that patients with low grade PA are associated with low stage of the disease, vice versa.<sup>4</sup>

## IPP AND BPH TREATMENT OPTIONS

Improving symptoms, quality of life and decreasing the progression of the disease are the

aims of treatment in patients with benign prostate enlargement.<sup>14</sup> There are some choices for BPH management including watchful waiting/lifestyle modifications, medical therapy and surgery. The following drugs  $\alpha$ -blocker/5  $\alpha$ -reductase as single therapy or combination are commonly used as medical therapy for BPH. Transurethral resection of the prostate (TURP) has been the best surgical procedure standard for more than 50 years. For patients with larger prostate volume (80-100 ml), open prostatectomy with variation enucleation techniques becomes the surgical standard which is increasingly forced back nowadays.<sup>15</sup> Patient preferences, risk of the surgery and some personal factors must be considered in surgical approach.

Grading IPP immediately can assist physicians in predicting the effectiveness of medical treatment and serve as a predictive factor for acute urinary retention in patients with BPH.<sup>2,16</sup> The study validated that IPP can be a potential parameter and helps in predicting obstruction, the severity of BPH and response rate to medical therapy, thus helping clinicians in considering which best treatment to serve patients with BPH for more cost-effective management.<sup>17</sup>

Although there is only a few data on the correlation between IPP and treatment outcome of medical therapy, it has been reported that there is correlation between intravesical prostatic protrusion (IPP) and the BOO index. These studies highlight that moderate to severe degree of IPP significantly affects BOO and influences the effectiveness of alpha receptor inhibitors in managing lower urinary tract symptoms (LUTS) in patients with benign prostatic hyperplasia (BPH)<sup>18</sup>. These patients may not respond with medical treatment either  $\alpha$ -blocker/5  $\alpha$ -reductase<sup>12,19,20</sup> mono-therapy<sup>21</sup> or combination therapy,<sup>22-24</sup> comparing to the patients with mild degree of IPP which the odd ratio of success of medical therapy is 59 times higher than the patients with a high grade IPP.<sup>13,22</sup>

Patients with IPP show less improvement of storage symptoms after 12 weeks of medical treatment.<sup>19</sup> The study from Park *et.al* stated that men with IPP grade 3 ( $\geq$ 10mm) had poor response with alpha adrenoreceptor antagonists (tamsulosin) among patients with LUTS due to benign prostatic obstruction, prostatic volume <40 ml, and PSA <1.5

ng/ml.<sup>25,26</sup> Moreover, the study from Kalkanli *et al.* showed that the higher the grade of IPP the lower the response to alpha adrenoreceptor antagonists therapy and thus may benefit from early surgical therapy.<sup>17,21</sup> The study also revealed that alpha receptor-specific management is not beneficial to patients with higher IPP degrees.<sup>17</sup> Patients with significant IPP measuring 10 mm or more at the initial evaluation are twenty times more likely to require prostate surgery on follow-up, indicating a higher risk of surgeries related to BPH in this group.<sup>27</sup>

Benign prostatic obstruction (BPO) identification is necessary to determine the severity of the disease thus helping clinicians in treating the patients and measuring the outcome of the treatment.<sup>28</sup> Medical therapy is the most commonly used as an initial treatment in patients with BPO that helps in relieving symptoms and progression of the disease.<sup>9</sup> However, patients with more severe symptoms and larger prostate volumes have a higher risk of medical treatment failure.<sup>1</sup> Patients with significant IPP during their initial assessment encounter an elevated risk of BPH-related surgeries.<sup>29</sup> Therefore, it would be better to identify patients before the treatment whether they will or not respond to medical treatment.<sup>28</sup>

As  $\alpha$ -receptors are mostly present inferior to the bladder neck (distal to the area of the protrusion),<sup>2</sup> it may not be effective for treating IPP with alpha-adrenoreceptor antagonists, due to its configuration that protrudes into the bladder above the bladder neck.<sup>30</sup> Due to low proportion of stromal component in the prostate with higher grade IPP in BPH patients, the combination therapy of tamsulosin and dutasterid has insufficient efficacy<sup>23</sup> and only reduces total prostate volume and transitional zone volume.<sup>21,22,24</sup> Thus, surgery including open prostatectomy and TURP are more effective for patients with significant IPP but small volume of prostate (<30 ml).<sup>31</sup>

Clinical BPH definition is essential that the disease may progress and produce complications and cause harm to the patients. As obstruction is more important than symptoms, it is necessary to give it more focus in deciding on the treatment for the patient.<sup>32</sup> This can be done by considering the severity of clinical BPH. After assessing PVRU and MVV and bothersome symptoms QoL ( $QoL \geq 3$ ),

significant obstruction (with PVRU >100ML or MVV <100ML) can be confirmed, and the severity of clinical BPH can then be graded from stage I to stage IV.<sup>4</sup>

Patients with no significant obstruction and troublesome symptoms could be generally watched and counseled and considered as stage I. Medical therapy can be initiated to patients with no significant obstruction but have some bothersome symptoms and this is considered stage II. The patients with significant obstruction and bothersome symptoms considered as stage III, generally need more aggressive therapy including 5- $\alpha$  reductase inhibitors and surgical intervention may be offered. Stage IV, in which patients have complications of clinical BPH such as retention of urine, bladder stones, and recurrent bleeding urinary tract infection would generally need surgical therapy.<sup>32</sup> Grade of IPP correlates to the severity of clinical BPH, the lower the grade of IPP the lower the severity of clinical BPH. The study validated that patients with low-grade IPP are associated with low-stage disease, and vice versa.<sup>4</sup> Hence, IPP measurement can help clinicians in considering the right management and predicting treatment outcomes thus avoiding unuseful prescriptions in managing BPH patients.

## CONCLUSION

IPP, a manifestation of BPH can be a potential parameter in diagnosing clinical BPH. Its presence is important as it predicts the outcome of BPH management. By measuring IPP, the severity of clinical BPH can be categorized then the right management can be considered.

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