

# Staging of Benign Prostate Hyperplasia is Helpful in Patients with Lower Urinary Tract Symptoms Suggestive of Benign Prostate Hyperplasia

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## Abstract

**Introduction:** We prospectively evaluated the staging of benign prostate hyperplasia (BPH) to decide transurethral resection of prostate (TURP) therapeutic modality and the final outcomes in patients with lower urinary tract symptoms (LUTS) suggestive of BPH. **Materials and Methods:** Male patients above 50 years old presented with LUTS suggestive of BPH were included in this study. The initial assessment included the International Prostatic Symptoms Score (IPSS) and the Quality of Life (QOL) index, digital rectal examination (DRE). Transabdominal ultrasound was done to measure the prostate volume, intravesical prostatic protrusion (IPP) and the post void residual (PVR) urine. BPH was classified according to the degree of IPP using grades 1 to 3. The staging of BPH was performed according to the presence or absence of bothersome symptoms (QOL $\geq$ 3) and significant obstruction (PVR>100ml). Patients with stage I BPH with no bothersome symptoms and no significant obstruction were generally observed. Those with stage II BPH, bothersome symptoms but no significant obstruction, received pharmacotherapy in the first instance, and were offered TURP if symptoms persisted or worsened. Patients with significant obstruction, persistent PVR >100ml, irrespective of symptoms would be classified as stage III, and were advised to undergo TURP as an option. Lastly, those with stage IV (complications of BPH) were strongly recommended to undergo TURP. **Results:** A total of 408 patients were recruited in this study and after a mean follow-up of 30 months (range, 6 to 84), 96 (24%) eventually had TURP. Sixteen(13%), 50(21%), 28(64%) and 2(100%) patients who underwent TURP were initially diagnosed as stage I, II, III and IV, respectively. Eighty-seven (91%) of the 96 patients significantly improved to stage I BPH post TURP. **Conclusions:** These results showed that the staging of BPH can assist in the tailoring of treatment for patients with LUTS suggestive of BPH, with good outcome in 91% post TURP.

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**Key words:** Intravesical prostatic protrusion, Post void residual urine, Quality of life, Symptoms score

## Introduction

Benign prostate hyperplasia (BPH), one of the most common diseases of ageing men, affects the quality of life by interfering with normal daily activities and sleep patterns.<sup>1</sup> The current treatment options for patients with lower urinary tract symptoms (LUTS) suggestive of BPH mainly depend on the severity of the symptoms of BPH. Watchful waiting is the preferred management strategy for patients with mild symptoms. It is also an appropriate option for ageing men with moderate to severe symptoms who have not yet developed complications of BPH. Medical treatment is recommended for patients with mild-

moderate symptoms, and minimally invasive therapies or surgery for patients who failed medication or conservative management and who have moderate-severe symptoms, and/or complications of BPH which require surgery.<sup>1-3</sup> However, the clinical evaluation of patients with LUTS suggestive of BPH, as recommended by the International Consultation on BPH, reported a controversial correlation of symptoms International Prostatic Symptoms Score (IPSS) with urodynamic evidence of bladder outlet obstruction (BOO).<sup>4-7</sup> The severity of symptoms does not correspond to the severity of the disease as measured by the degree of BOO. There is also no strong correlation between the IPSS and quality of life (QOL).<sup>7</sup> Therefore, the traditional

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wisdom of routine therapeutic strategy for patients with LUTS suggestive of BPH needs to be relooked.

With better understanding of the natural history of BPH, and the availability of urodynamics and ultrasound, the assessment of patients with LUTS suggestive of BPH has undergone rapid changes in recent years. Since 1995, bedside ultrasound has been routinely used for classifying grading and staging of patients with LUTS suggestive of BPH at our institution.<sup>8-12</sup> We prospectively evaluated the results of our transurethral resection of prostate (TURP) and the feasibility of this therapeutic strategy using the staging system.

**Materials and Methods**

*Patients' Eligibility*

Between July 1997 and December 2003, 408 consecutive male patients above 50 years of age, presenting with LUTS suggestive of BPH in the urology clinic, were prospectively recruited in this study. Patients with a known history of previous lower urinary tract surgery, prostatic cancer, neurological disease such as cerebral vascular accidents and Parkinsonism were excluded. A total of 96 patients had TURP done eventually.

*Evaluations*

Initial evaluation consisted of the IPSS, which was used to assess the severity of LUTS, and QOL score which assessed how much the symptoms bothered the patients. The medical history of patients was recorded and physical examination was done. Digital rectal examination (DRE) was performed to exclude prostatic malignancy, and neurological examinations were employed to exclude neurogenic bladder dysfunction. The patients were then assessed by bedside transabdominal ultrasonography (TAUS) with 3.5 MHz probe.<sup>12</sup> Prostatic volume was measured by TAUS in the transverse plane. It had been shown in our earlier study that the TAUS measurement of prostatic volume correlated well with the transrectal measurement when bladder volume was less than 400 ml.<sup>11</sup> The bladder had to have a capacity of 150 to 250 ml before the extent of IPP was measured. The degree of intravesical prostatic protrusion (IPP) was graded by measuring the perpendicular distance from intravesical protruding prostatic tip down to the bladder circumference at the prostate base in the midsagittal plane.<sup>12</sup> The degree of IPP was classified as follows: Grade 1: 5 mm or less; Grade 2: more than 5 to 10 mm; Grade 3: more than 10 mm.<sup>9-12</sup> After the TAUS assessment, uroflowmetry was performed to assess uroflow ( $Q_{max}$ ) and then PVR was measured by TAUS. Serum prostate specific antigen (PSA) was also investigated.

Based on the above evaluations, the staging of BPH was classified as follows: stage I, patients with no bothersome symptoms ( $QOL < 3$ ) and no significant BOO (persistent

$PVR < 100ml$ ); stage II, patients with bothersome symptoms ( $QOL \geq 3$ ) but no significant BOO; stage III, patients with significant BOO as defined by a persistent PVR of more than 100 ml and generally a  $Q_{max}$  of less than 10 ml/s, irrespective of bothersome symptoms; stage IV, patients with various complications resulting from BPH, such as bladder stones, recurrent urinary tract infections (UTI), recurrent gross haematuria and retention of urine.<sup>8,9</sup> The distribution of the grade and stage, and the combination of both, are shown in Figures 1, 2, and 3, respectively.

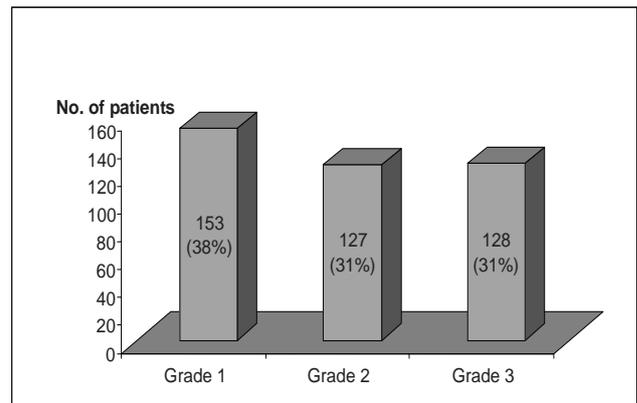


Fig. 1. Grading of LUTS patients suggestive of BPH between 1997 and 2003 (n = 408).

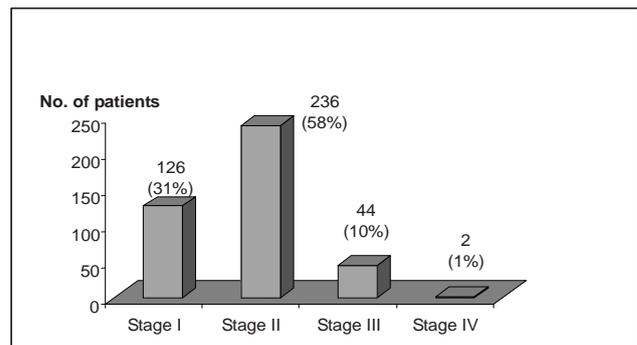


Fig. 2. Staging of LUTS patients suggestive of BPH between 1997 and 2003 (n = 408).

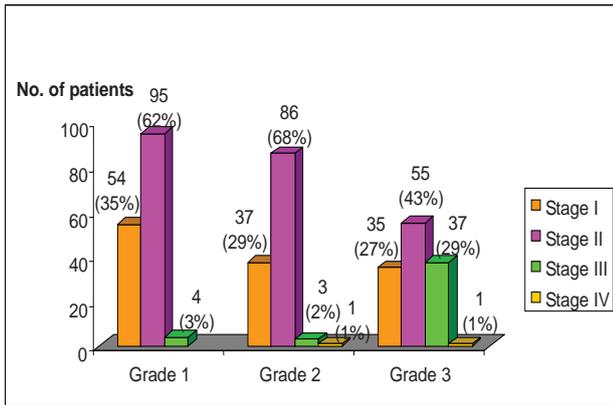
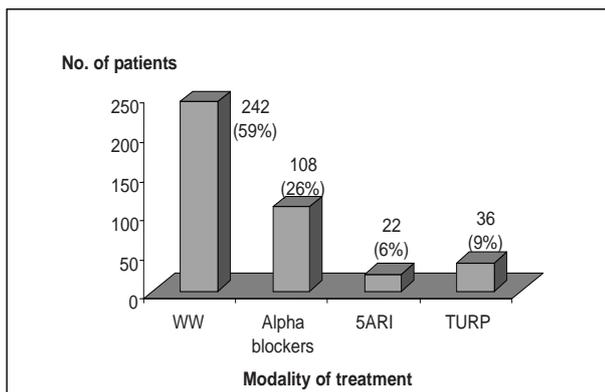


Fig. 3. Correlation of grading and staging (n = 408).

**Treatment and Follow-up**

With the above grading and staging of BPH, BPH treatment was guided as follows: for stage I, generally watchful waiting was recommended; for stage II, medical treatment was given first; patients would be offered TURP if there was no improvement with pharmacotherapy; for stage III, TURP was advised as an option; for stage IV, TURP was strongly recommended. All treatment options had to take into account the patients’ age and comorbidity. The initial treatment modalities of the cohort of patients are shown in Figure 4. Patients who had TURP were followed-up for at least 6 months postoperatively.

Assessment during follow-up consisted of IPSS score, QOL index, uroflowmetry and PVR evaluation.



WW: Watching Waiting; 5ARI: 5 alpha reductase inhibitors; TURP: transurethral resection of prostate

Fig.4. Initial treatment of LUTS patients suggestive of BPH between 1997 and 2003 (n = 408).

**Statistical Analysis**

The data were expressed as mean ± standard deviation (SD), and analysed using the SPSS 10.0 software. The T student's t test and chi-square test were used when appropriate.

**Results**

With a mean follow-up of 30 months (range, 6 to 84), 96 (24%) of 408 patients with symptomatic BPH included in this prospective study eventually had TURP. The patients’ mean age was 65 years (range, 50 to 90), mean serum PSA±SD was 6.60±6.435 ng/ml, mean prostate size 49.32±40.169 ml, mean IPSS 13.91±7.530, mean QOL 3.33±1.265, mean Q<sub>max</sub> 9.01±4.991 ml/sec and mean PVR 91.31±118.349 ml (Table 1). Post TURP, mean IPSS, QOL and PVR decreased to 4.57±4.140 (P <0.01), 1.44±1.188 (P <0.01) and 10.48±3.997 (P <0.01), respectively while postoperatively mean Q<sub>max</sub> increased to 18.56±7.112 (P <0.01).

Table 1. Change of QOL, Q<sub>max</sub>, IPSS and PVR of 96 Patients with Clinical BPH Pre- and Post-treatment

Items	Initial (mean±SD)	Current (mean±SD)	t	P
QOL	3.33±1.265	1.44±1.188	6.255	<0.001
Q <sub>max</sub>	9.01±4.991	18.56±7.112	-12.890	<0.001
IPSS	13.91±7.530	4.57±4.140	11.149	<0.001
PVR	91.31±118.349	10.48±3.997	11.504	<0.001

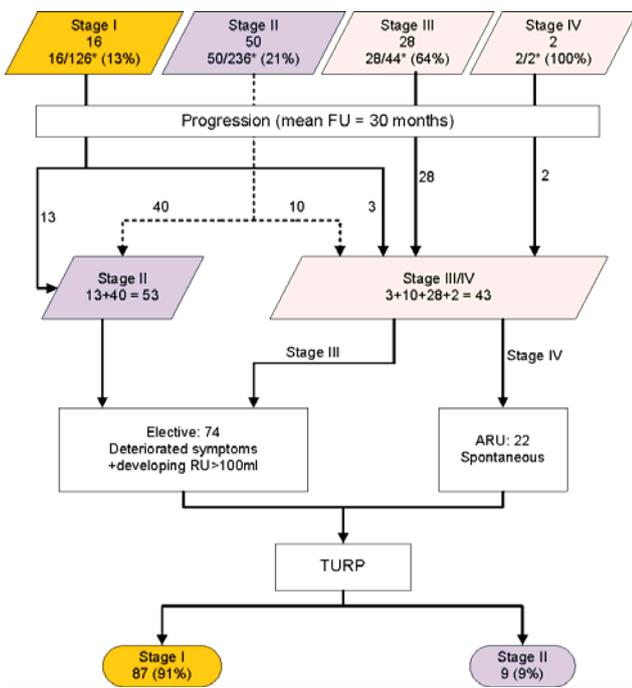
Of 96 (24%) patients who underwent TURP, 16, 50, 28 and 2 patients were initially in stage I, II, III and IV, respectively. This translated into 13% (16/126), 21% (50/236), 64% (28/44) and 100% (2/2) of each stage of all patients included in this study. A significant trend was observed, patient with high grade BPH progressed and eventually required TURP. Out of the 96 patients, 88 (92%) were in grade 2 and grade 3. Comparing the 74 patients who had no Acute Retention of Urine (ARU) and 22 patients who experienced ARU, there was no significant difference (Table 2, x<sup>2</sup>=0.372, P = 0.830).

During watchful waiting, out of the 16 patients initially at stage I, 13 cases eventually deteriorated to stage II and the other 3 with grade 3 IPP, to stage III/IV, and TURP was done. Fifty patients initially at stage II received medical treatment. Subsequently, 10 patients progressed to stage III/IV, and the other 40 patients who had no improvement or had deterioration in symptoms required TURP.

Table 2. Distribution of Grade between 22 Patients with ARU and 74 Patients without ARU

Grade	ARU (%)	Non ARU (%)	$\chi^2$	<i>P</i>
1	2 (9.1)	6 (8.1)	0.372	0.83
2	5 (22.7)	21 (28.4)		
3	15 (68.2)	47 (63.5)		
Total	22 (23.2)	74 (76.8)		

After TURP, a total of 87 (91 %) patients improved significantly, being down-staged to stage I. Two patients with pre-TURP stage III were down-staged to stage II. Seven cases of pre-TURP stage II remained in status quo (Fig. 5).



\*number of the original stage among the 408 BPH patients

Fig. 5. Summary of results showing the deterioration from their initial stage, and subsequent improvement of patients after TURP (n = 96).

**Discussion**

TURP is associated with low re-operation rates and therefore remains the gold standard in BPH therapy.<sup>13,14</sup> However, with the relatively recent introduction of pharmacological and other surgical treatment modalities, the performance of TURP appears to be in decline.<sup>15</sup> The current treatment options mainly depend on the severity of the symptoms of BPH.<sup>1-3</sup> However, IPSS has its limitations, as it has been shown to have poor correlation with obstruction.<sup>4-9</sup> If IPSS is used as a guide for further management of BPH, as many as 51% of patients with obstruction and mild IPSS (0 to 7) would be undertreated. On the other hand, 37%

to 43% of patients with severe symptoms (IPSS >21) may be overtreated as they have no obstruction.<sup>7,9</sup>

Obstruction is more important than symptoms in the assessment of BPH.<sup>8</sup> Obstruction would be significant if the functions of the bladder are affected. Post void residual urine (PVR) can be considered as a measure of emptying function of the bladder. Persistent PVR of more than 100 ml had been shown to predict retention of urine. In a study of pool analysis of 11 control studies with alfuzosin, 6 out of 7 patients who developed ARU had PVR of more than 100 ml at initial evaluation.<sup>16</sup> Thus in our staging system, the emphasis is placed on persistent PVR of more than 100 ml, generally with a flow rate of less than 10 ml/s. That would be classified as stage III, irrespective of symptoms. Stage III together with a high grade IPP should trigger a more active management as the functions of the bladder is affected.

It is emphasized that for accurate assessment of PVR, the reading must be persistent, and the patient is asked to repeat urination if the initial PVR is more than 100 ml.

In this study, 408 patients with clinical BPH were included. According to our staging system for BPH, 126, 236, 44 and 2 patients were initially diagnosed with stage I, II, III, IV, respectively (Fig. 2). One hundred and fifty-three, 127 and 128 cases were in grade 1, 2, 3, respectively (Fig. 1). The combination of both grade and stage is shown in Figure 3. It is important to note that the majority of low grade 1 and 2 patients are in stage I and II category, while for stage III patients, the majority are grade 3. Subsequently modalities of treatment for each patient were done according to our therapeutic strategy. The majority of patients (59%) could be watched, 32% were on pharmacotherapy (Fig. 4). On subsequent follow up with a mean of 30 months, a total of 96 patients (24%) had TURP because of no improvement or deterioration in symptoms, or the development of persistent residual urine (stage III) or acute retention (stage IV) (Fig. 5).

Patients showed significant improvement (*P* <0.01) in IPSS, QOL, PVR and  $Q_{max}$ , post TURP (Table 1). Using the staging system, 87 patients (91%) were down staged to stage I with no significant obstruction and no bothersome symptoms. Seven patients with initial stage II remained in stage II, and the other 2 with pre-TURP stage III were down-staged to stage II. The 9 patients, who remained in stage II with bothersome symptoms could possibly have elements of “ageing” bladder, with improvement in uroflow and no significant PVR postoperatively. Thus, using the staging system gives a clearer picture in real life of how many of our patients actually improved after surgery, instead of the average improvement of the various parameters as shown in Table 1.

We further investigated the distribution of BPH grade between 22 patients who experienced ARU and 74 patients without ARU. No significant difference of grade was found. The 22 patients developed ARU spontaneously and of these patients, 68% had grade 3 IPP while 23% and 9% had grade 2 and grade 1 IPP, respectively. The 74 non-ARU patients (elective) who underwent TURP, 64% were grade 3 IPP, while 28% and 8% were grade 2 and grade 1, respectively. This suggested that the grading of BPH not only correlated to the staging of BPH, but also to the deterioration of this disease subsequently requiring TURP. These results also showed that the higher the grade, the higher the stage and that we selected patients for TURP according to staging and not by grade. If we had not done so, the selection would have been biased and more patients for elective TURP would have higher grade in the distribution.

TURP would be an option of treatment for patients with high stage and high grade BPH. For patients with significant obstruction, it has been shown by Flanigan et al<sup>17</sup> that the earlier the obstruction is removed, the better would be the outcome. Grading with IPP helps to predict the progression of the disease<sup>18</sup> and staging helps to classify the severity for clinician to take appropriate actions. For patients with low stage but high grade BPH, a close follow-up would be advised.

Staging for management of benign prostatic enlargement (BPE) can potentially help to avoid undertreatment or overtreatment, and hence would contribute to increase cost-effectiveness. The majority of patients with grade 1, stage I BPE can be placed under watchful waiting while only patients with high stage BPE need to be treated more aggressively.

This staging system is also feasible to objectively assess the efficacy of TURP according to the percentage of patients who actually improved. This is a better indicator of improvement in real life, compared to the average improvement in IPSS, QOL, PVR or flow rate.

As compared to assessing the severity of BPH using IPSS only, this staging and grading system incorporated the 3 fundamental aspects of BPH, that is the gland itself, graded according to IPP, the symptoms (IPSS and QOL) and obstruction (PVR and  $Q_{max}$ ). Thus, it has the advantage of being a complete assessment for BPH and it can be further used as a relatively objective standard for assessment of outcome after BPH treatment.

## Conclusions

The staging of BPH using non-invasive parameters is feasible to select patients with LUTS suggestive of BPH for TURP with good outcome of 91%.

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