Severity profiles in patients diagnosed of benign prostatic hyperplasia in Spain

B. Miñana a, *, A. Rodríguez-Antolín b, M. Prieto c, E. Pedrosa c

a Servicio de Urología, Hospital Morales Meseguer, Murcia, Cátedra de Urología de la Universidad Católica San Antonio de Murcia (UCAM), Murcia, Spain
b Servicio de Urología, Hospital Doce de Octubre, Madrid, Spain
c Departamento Médico Astellas Pharma, Madrid, Spain

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KEYWORDS
Prostatic hyperplasia; Prostatism; Prevalence; Severity; Disease progression

Abstract
Objectives: To analyze the severity profiles and progression criteria in patients diagnosed of benign prostatic hyperplasia (BPH) in urology clinics in Spain.


Results: A total of 1.115 patients were evaluated. Mean age was 65.7 years. Mean time from the onset of symptoms to diagnostic was 18.8 months. Mean IPSS score was 17.2. 63 patients (5.7%) had mild symptoms; 670 (60.1%) had moderate symptoms with a mean IPSS score of 14.6 and 382 (34.3%) had severe symptoms with a mean IPSS score of 23.7. Mean PSA was 2.6 ng/ml and ultrasound measured prostatic volume was 49.2 cc. A total of 713 (63.9%) patients met progression criteria (PSA > 1.5 ng/ml and volume > 30 cc). Symptons severity was directly correlated with age, prostatic volume, PSA, presence of progression criteria and time from the onset of symptoms and inversely correlated with urine flow rate (p < 0.001). Progression criteria were directly correlated with age, symptoms severity and inversely with urine flow rate (p < 0.01).

Conclusions: More than 90% of patients diagnosed of BPH in urology clinics in Spain had moderate to severe symptoms. Two-thirds met progression criteria that correlate with age and severity of symptoms.

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Perfiles de severidad en pacientes diagnosticados de hiperplasia benigna prostática en España

Resumen
Objetivos: Analizar los perfiles de severidad y presencia de criterios de progresión en pacientes diagnosticados por primera vez de hiperplasia benigna prostática (HBP) en consultas de Urología.
Material y métodos: Estudio observacional, transversal, multicéntrico español, realizado entre mayo y noviembre de 2008, en el que participaron 392 urólogos, que recogieron la información de 3 nuevos pacientes consecutivos con diagnóstico clínico de HBP.
Resultados: Se reclutaron un total de 1.115 pacientes. La edad media fue de 65,7 años. El tiempo promedio desde el inicio de los síntomas hasta la consulta fue de 18,8 meses. La media de puntuación IPSS fue de 17,2. Sesenta y tres pacientes (5,7%) presentaron síntomas leves; 670 (60,1%) síntomas moderados con un IPSS medio de 14,6 y 382 (34,3%) síntomas severos con un IPSS medio de 23,7. El PSA promedio fue de 2,6 ng/ml y el volumen prostático ecográfico de 49,2 cc. Setecientos trece pacientes (63,9%) presentaron criterios de progresión (PSA > 1,5 ng/ml y volumen > 30 cc). Se observó una correlación directa de la severidad de los síntomas con la edad, volumen prostático, PSA, criterios de progresión y tiempo de evolución e inversa con el flujo urinario (p < 0,01). La presencia de criterios de progresión se correlacionó directamente con la edad y severidad de los síntomas, e inversamente con el flujo urinario (p < 0,01).
Conclusiones: Más del 90% de los pacientes diagnosticados de HBP en las consultas de Urología presentan síntomas moderados o severos. Dos tercios tienen criterios de progresión que se correlacionan con la edad y severidad de los síntomas.

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Introduction

Benign prostatic hyperplasia (BPH) is a highly prevalent disease in men over 50 years of age. This disease may significantly affect the quality of life and is one of the main reasons for urological consultation.

The lower urinary tract symptoms (LUTS), both drainage and storage, are its major manifestation. Although the former tend to be more prevalent and to have higher prognostic value, the latter interfere more with daily activities and, therefore, seem to affect life quality.1

In a significant proportion of patients BPH behaves as a progressive disease in which the symptoms may progress to acute urinary retention (AUR) and the need for surgery. Longitudinal population studies and placebo groups of clinical trials have provided data to establish its progressive nature.2,3 Among the factors associated with progression, those considered as having higher predictive value are age, severity of symptoms, urinary flow impairment, prostate volume and PSA (2). Prostate volume increased above 30 cc together with a PSA ≥ 1.5 ng/ml that has been correlated with risk of AUR and need for surgical intervention.4

The goal of drug therapy is to improve LUTS trying to minimize the risk of progression. Watchful waiting, treatment with an alpha-blocker (AB), a 5α-reductase inhibitor (ARI 5) or a combination of both allow the discrimination of different patient profiles and give the highest probability of symptom control modifying its natural history.

The present study seeks to quantify the prevalence of the different profiles of severity and the progression criteria in Urology consultations in Spain.

Material and methods

An observational cross-sectional multicenter study conducted between May and November 2008. 392 urologists, on a weighted representation of the different regions of Spain according to the number of inhabitants, participated.

The ethics committee of the Morales Meseguer Hospital in Murcia following Spanish law approved the study.

Every urologist included 3 consecutive patients newly diagnosed with BPH, according to his usual practice. Patients accepted inclusion signing an informed consent. Patients with known or suspected urinary tract infection, neurogenic bladder dysfunction, previous history of prostate or bladder cancer and those cases with absolute surgical indication were excluded from the study.

Three types of variables were collected: sociodemographic, clinical and patient-centered. The sociodemographic included age and place of residence (metropolitan, urban, semi-urban or rural, defined by the number of inhabitants). The clinics included: family history of HBP, time from onset of symptoms, prostate volume by digital rectal examination and PSA.

According to usual practice in Spain, ultrasound measurement of prostate volume and urinary flow rate by uroflowmetry in the initial evaluation were performed in all cases.1 This practice is considered optional by most clinical practice guidelines (CPG). Finally, patient-centered variables included: quantification of the intensity of symptoms by self-administered IPSS and impact on life quality through IPSS question 8.

The severity of symptoms was established in relation to the value of the IPSS: mild (0–7), moderate (8–19) and severe (20–35). The score of IPSS question 8, covering the
range from 0 (delighted) to 6 (very bad), measured the impact on life quality.

In order to quantify the prostate volume measured by digital rectal examination and to correlate it with the ultrasound measurement, four qualitative groups were defined according to standard practice: volume I (≤ 30 cc); volume II (31–50 cc); volume III (51–75 cc) and volume IV (> 75 cc), depending on subjective criteria of the urologist.

A prostate volume ≥ 30 cc (volume by touch degrees II–IV) and a PSA ≥ 1.5 ng/ml were considered as risk of progression.

**Statistical analysis**

Descriptive analysis of sociodemographic, clinical and patient-centered variables determining mean, standard deviation (SD) and confidence interval 95% (95% CI). Comparison between groups was performed using the chi-square test or Kruskal Wallis, and Tukey test was used for multiple comparisons.

The agreement between the assessment of prostate volume by digital rectal examination and external ultrasound was performed by analysis of variance and the degree of agreement was measured by the weighted kappa statistic with CI 95%.

Data analysis was performed using SPSS 15.0 for Windows. We considered statistical significance level of 0.05.

**Results**

A total of 1115 patients were enrolled. The mean age (SD) was 63.7 (7.9) years, 5% were from an urban or metropolitan environment and 45.6% reported a family history of HBP.

**Clinical severity**

The mean (SD) IPSS score was 17.2 (5.9). Sixty-three patients (5.7%) presented mild symptoms with an average score of 5.3 (1.7); 670 (60.1%) had moderate symptoms, with an average score of 14.6 (3.1); finally, 382 (34.3%) showed severe symptoms with an average score of 23.7 (2.9) (Fig. 1). The severity was directly correlated with age, time to consultation, prostate volume, PSA and presence of progression criteria and inversely with urinary flow (p < 0.01) (Table 1).

The median time from symptom onset to consultation was 18.8 (22.0) months.

**Progression of benign prostatic hyperplasia**

Prostate volume was >30cc in 82.2% of cases and PSA >1.5 ng/ml in 71.9%. A total of 713 (63.9%) patients showed progression criteria (95% CI: 61.1–66.7%). These criteria were more common in older patients (p < 0.01) and with greater severity, and less common in patients with higher Q<sub>max</sub> (p < 0.01) (Fig. 2).

**Quality of life associated with benign prostatic hyperplasia**

Overall, 42.7% reported being ‘’mostly dissatisfied’’ with their clinical situation. The quality of life score increased with the severity of symptoms (p < 0.01). 50% of patients with mild symptoms reported being ‘’mostly satisfied.’’ 39% of those with moderate symptoms declared being ‘’mostly dissatisfied’’ and 34.1% were ‘’equally satisfied than

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Mean values (standard deviation) of the clinical variables and patient-centered according to severity.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild (IPSS ≤ 8)</td>
</tr>
<tr>
<td>N</td>
<td>63</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62.2 (7.5)</td>
</tr>
<tr>
<td>Months of evolution</td>
<td>13.4 (33.1)</td>
</tr>
<tr>
<td>Ultrasound prostate volume (cc)</td>
<td>41.7 (26.9)</td>
</tr>
<tr>
<td>Q&lt;sub&gt;max&lt;/sub&gt; (ml/sc)</td>
<td>14.4 (4.1)</td>
</tr>
<tr>
<td>Volume &gt; 30 cc</td>
<td>60.3%</td>
</tr>
<tr>
<td>PSA &gt; 1.5 ng/ml</td>
<td>58.7%</td>
</tr>
<tr>
<td>Progression criteria&lt;sup&gt;a&lt;/sup&gt;</td>
<td>46%</td>
</tr>
<tr>
<td>IPSS</td>
<td>5.2 (1.7)</td>
</tr>
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<sup>a</sup> PSA > 1.5 ng/ml and volume > 30cc.
Severity profiles in patients diagnosed of benign prostatic hyperplasia

Table 2  Average patient characteristics in this study and other international studies.

<table>
<thead>
<tr>
<th></th>
<th>Present study</th>
<th>PLESS\textsuperscript{14}</th>
<th>MTOPS\textsuperscript{15}</th>
<th>CombAT\textsuperscript{16}</th>
</tr>
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<tbody>
<tr>
<td>( N )</td>
<td>1.115</td>
<td>3.040</td>
<td>3.047</td>
<td>4.844</td>
</tr>
<tr>
<td>Age (years)</td>
<td>65</td>
<td>64</td>
<td>62</td>
<td>66</td>
</tr>
<tr>
<td>IPSS</td>
<td>18.7</td>
<td>15</td>
<td>16.8</td>
<td>16.4</td>
</tr>
<tr>
<td>Ultrasound prostate volume (cc)</td>
<td>49.2</td>
<td>55</td>
<td>36.3</td>
<td>55</td>
</tr>
<tr>
<td>PSA (ng/ml)</td>
<td>2.62</td>
<td>2.8</td>
<td>2.3</td>
<td>4</td>
</tr>
<tr>
<td>( Q_{\text{max}} ) (ml/s)</td>
<td>11.3</td>
<td>11</td>
<td>10.5</td>
<td>10.4</td>
</tr>
</tbody>
</table>

Figure 2  Distribution of clinical severity in patients with newly diagnosed BPH in specialty care consultations in Spain.

dissatisfied”. More than half (55.3%) patients with severe symptoms were “mostly dissatisfied”.

Discussion

About 35% of men over 50 years have moderate or severe symptoms related to BPH, reaching 45% in the 70s.\textsuperscript{6,7} A study on men aged more than 40 years was carried out in Spain, in which BPH was defined as the coexistence of IPSS > 7, prostate volume > 30 cc and urinary flow less than 15 ml/s obtained a prevalence of 11.8%, reaching 30% among men older than 70 years.\textsuperscript{8}

The progressive nature of BPH involves a worsening of symptoms that would explain the correlation of clinical severity with age, PSA and prostate volume, that we have observed, previously verified by Vela-Navarrete et al.\textsuperscript{9} However, we had no data on the prevalence of progression criteria in patients consulting for the first time.

CPGs establish therapeutic selection criteria based on patient profiles where the use of a 5-ARI is reserved for those patients with progression criteria defined by a volume ≥ 30 cc and PSA ≥ 1.5 ng/ml.\textsuperscript{10-13} Although CPGs allow surveillance in patients with moderate symptoms or onset surgery in patients with severe symptoms (AUA), most of those with moderate or severe symptoms will be considered susceptible to drug treatment.

As observed in the present study, more than 90% of patients attending urological consultations would be candidates for drug therapy. This could be related to the delay in the application of care, as well as to a possible selection bias once passed through the prior filter of primary care, where the practice is quite heterogeneous.\textsuperscript{14} However, on a European observational study on management profiles of BPH in primary care, Fourcade et al. detected IPPS of 16, similar to the IPPS of 17 of the present study, in the Spanish subgroup during specialized consultations.\textsuperscript{15} These data, together with the observed average evolution time of 18 months, suggest both a delayed consultation by patients as an early referral from primary care. It would explain that the scientific societies in our country have agreed guidelines for management and referral from primary care to specialized care, that were not in force at the time of this study.\textsuperscript{16}

The average patient characteristics in Spain are equivalent to those observed in other international studies, suggesting that the sample is truly representative\textsuperscript{17-19} (Table 2).

The present study establishes that 64% of patients have progression criteria when they come to consultation. This would mean that 1/3 of them will be candidates for an exclusive treatment with AB since they do not show prostatic growth. The remaining 2/3 would be candidates for treatment with AB, 5 ARI or a combination of both.

The presence of criteria for progression was more likely in patients with higher clinical severity. 75% of those presenting severe symptoms had progression criteria and would be eligible for combined treatment in the beginning. The determinant of the treatment is not the presence itself of progression criteria, due to the fact that they are observed in 46% of those with mild symptoms, but the severity of symptoms, which affects the quality of life.

Conclusions

The majority of patients attending urology consultations occur with moderate or severe symptoms that can be treated. Two-thirds have progression criteria at diagnosis, which augurs a progressive evolution of the disease that should be taken into account when selecting therapy.

Funding

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Conflict of interests

Dr. Emilio Pedrosa and Dr. Marta Prieto belong to the medical department of Astellas. The remaining authors declare no conflicts of interest.
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