# CAN PRIMARY CARE PHYSICIANS MANAGE BENIGN PROSTATIC HYPERPLASIA PATIENTS AS UROLOGISTS DO?

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**Disclosure:** We have no conflicts of interest. The declared authors write on behalf of the doctors participating in this study.

## ABSTRACT

Most clinical practice guidelines (CPGs) assume that general practitioners (GPs) can manage non-complicated benign prostatic hyperplasia (BPH)-related lower urinary tract symptoms (LUTS) as urologists do, but this has not been directly compared. Moreover, some studies have demonstrated that the initial management of BPH may vary between the urologist and the primary care physician. We conducted a prospective study to compare the diagnostic and therapeutic decisions of a group of eight GPs with those proposed for an experienced urologist in a set of consecutive, non selected, BPH patients. After some previous meetings in which different guidelines (from the EAU, AUA, and NICE) were reviewed, the GPs and the urologist reached a consensus about defining and managing five different BPH patients' profiles. After completing the diagnostic work-up, the GPs proposed a diagnostic and therapeutic recommendation for each patient. Afterwards, the patients were sent to the urologist, who was blinded to those GP recommendations. An independent central reviewer analysed the agreement between both groups. A total of 117 consecutive patients were diagnosed. In only 31% of the patients the main cause of consultation was LUTS. The urologist confirmed the diagnosis in 81% of cases. With regard to the therapeutic decision, a kappa index of 0.651 was observed which can be considered a good agreement. Nevertheless, GPs tended to use more alpha-blockers and fewer 5-alpha reductase inhibitors even in those patients who had progression criteria. We cannot conclude that GPs can manage BPH patients without assuring enough adherence to the CPG's recommendations, training regarding digital rectal exam, and maybe a periodic re-evaluation by urologists.

Keywords: Benign prostatic hyperplasia, primary care, diagnosis, medical therapy.

## INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most common diseases affecting aging men, and BPH-related lower urinary tract symptoms (LUTS) are some of the most common causes for consultation in urologic clinics.[1] As the population ages the number of affected men is expected to rise substantially, becoming a serious challenge to public health. BPH-related morbidity among aging men accounts for enormous direct and indirect healthcare expenditures. As medical therapy of BPH-related LUTS is considered a life-long strategy, short and long-term cost considerations should play a major role in therapeutic decision-making. Behavioural recommendations, watchful waiting (WW), phytotherapy, alpha-blockers (ABs), muscarinic receptor antagonists, 5-alpha reductase inhibitors (5ARIs), and combination therapy are possible therapeutic options.[2]

**Table 1: Clinical Profiles.**

| Clinical Profile | IPSS | Prostate volume (Ultrasound) | DRE | PSA | Recommended Treatment |
|---|---|---|---|---|---|
| Profile 1 | ≤7 | Any | Any | <4 | Observation |
| Profile 2 | >7 | <30 cc | Volume I, adenomatous | <1.5 | AB |
| Profile 3 | >7 | ≥30 cc | Volume ≥II, adenomatous | <1.5 | AB |
| Profile 4 | >7 and ≤20 | ≥30 cc | Volume ≥II, adenomatous | ≥1.5 | 5ARI |
| Profile 5 | >20 | ≥30 cc | Volume ≥II, adenomatous | ≥1.5 | Combination (AB + 5ARI) |

AB: alpha-blockers; 5ARI: 5-alpha reductase inhibitors; IPSS: international prostate symptom score; DRE: digital rectal exam; PSA: prostate-specific antigen.

Although the biologic mechanisms leading to the development of BPH have not been completely elucidated, BPH has been shown to be a progressive disease.[3] The severity of clinical symptoms, a decreased peak urinary flow, a prostate-specific antigen (PSA) level >1.5 ng/ml, and an increased prostate volume (>35 cc) have been identified as the best predictors of clinical progression.[4]

Theoretically, general practitioners (GPs) would be better positioned to identify men with BPH-related LUTS and those at risk for disease progression, and should consider treatment for those men with mild-to-moderate symptoms without evidence of prostate cancer. In contrast, men with a suspicion of prostate cancer, or with more severe symptoms requiring urgent or emergent treatment (such as surgery), should be seen by a urologist.

Most clinical practice guidelines (CPGs) assume that GPs can manage non-complicated diseases as urologists do, but to our knowledge, this has not been directly compared. Moreover, some studies have demonstrated that the initial management of BPH may vary between the urologist and the primary care physician.[5] This study aims to determine the ability of motivated GPs to diagnose and treat BPH patients compared to experienced urologists.

## MATERIALS AND METHODS

We designed a prospective study to compare the diagnostic and therapeutic decisions of a group of motivated GPs with those proposed for an experienced urologist in a set of consecutive, non selected, BPH patients. The study was carried out in two public health centres (*Ceutí* and *Molina de Segura*) assigned to Morales Meseguer General University Hospital's Health Area in Murcia, Spain. Participation was offered to eight GPs usually working in those health centres and to one experienced urologist (ARH, 53-years-old), a member of the Urology Service of the Morales Meseguer General University Hospital. After three previous consensus meetings conducted by the urologist, held between October and December 2009, in which different guidelines (AUA, NICE, and EAU) were reviewed, the GPs and the urologist reached a consensus about defining and managing different BPH patients' profiles.

The case patient was defined as a man over 50 with LUTS, probably related to BPH by discarding other common causes (neurologic, pharmacologic, etc.), and with a digital rectal exam (DRE) showing changes of adenomatous consistency and/or an increased prostate size. Although there is some controversy regarding the appropriate treatment for a specific patient, five different and mutually exclusive patient profiles were established in order to be able to compare the clinical decisions between the two groups (Table 1). Those with a PSA >4 ng/ml were excluded. CPGs recommend a diagnostic work-up which includes medical history, validated symptom questionnaires (International prostate symptom score [IPSS]), physical examination, urinalysis, blood analysis, ultrasound of the prostate, uroflowmetry, and ultrasound measurement of post-void residual urine (PVRU).

All patients who had previously signed a specific informed consent were first diagnosed in the primary care setting. After an initial assessment checking whether the patient met the inclusion criteria, the GP performed a medical history and physical examination, including DRE. IPSS questionnaire was administered, including assessment of quality of life (QoL) item 8. The answer to this question reflects the patient's willingness to accept treatment to lessen their symptoms, and allows a physician's insight into how troubled the patient is by their symptoms. The first visit also included laboratory studies to determine PSA and creatinine (and others depending on the patient's history) and a urinalysis was considered necessary to screen for urinary tract infections, bladder cancer, and stones. An external ultrasonography exam, including a prostate planimetry and a PVRU, was performed by a radiologist.

With regard to the DRE, most GPs acknowledged that it is uncommonly performed in their practice, and they felt unable to assess prostate changes properly. The urologist proceeded to train them using both visual and simulation models until they seemed trained. Assuming that DRE tends to underestimate the true prostate volume, physicians had to classify patients into four groups according to their prostate volume (I: <30 cc; II: 30-50 cc; III: 50-70 cc; and IV: >70 cc.), defined by transverse and longitudinal diameters. Regarding the consistency of the prostate, three groups were defined: fibroelastic, adenomatous, and indurated. Any induration or palpable nodule was considered suggestive of prostate cancer, and the decision of performing a prostatic biopsy was left to the urologist.

In a second visit, after finishing the evaluation, the GP proceeded to classify the patient into a specific profile (mild, moderate, or severe BPH, with or without progression criteria) and recommended a treatment. This was written in a specific study form and sent for a centralised independent evaluation. Then, the patient was remitted to the urologist having the different tests done. Within a period not exceeding 21 days the urologist evaluated the patient, blinded to the GP recommendations. After evaluating the patient and performing a uroflowmetry, the urologist proposed a treatment, and the patient was started on it. These recommendations were also written and sent for a centralised independent evaluation (Figure 1).

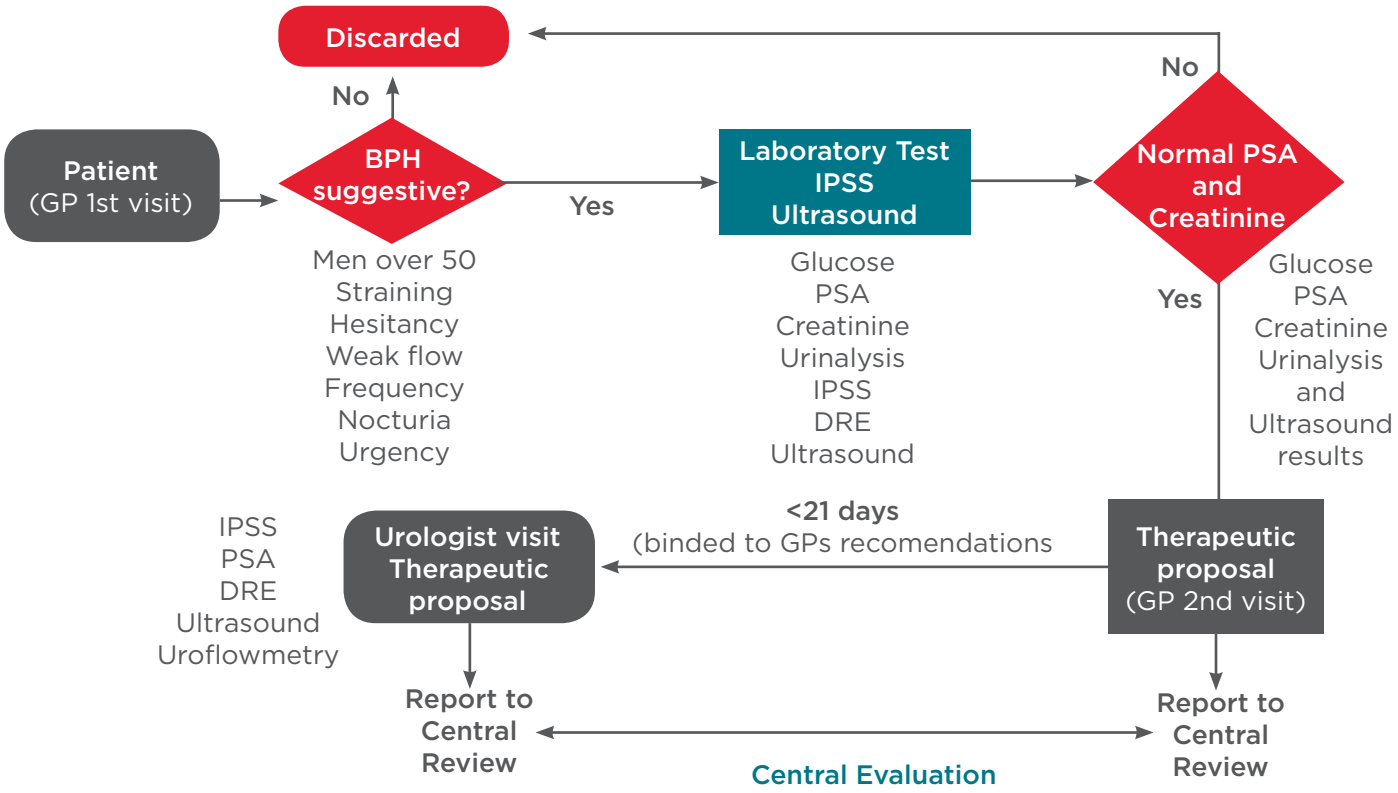


**Figure 1: Study flow-chart.**

BPH: benign prostatic hyperplasia; DRE: digital rectal exam; GP: general practitioner; IPSS: international prostate symptom score; PSA: prostate-specific antigen.

Each patient underwent a total of three visits (two with a GP and one with the urologist). Both diagnostics and treatment suggested by the GP were considered appropriated only if they met the inclusion criteria and coincided with the urologist recommendations, which were considered the gold standard. A difference of 25% between both recommendations was considered relevant because it could represent an undertreatment or an overtreatment. A sample size of at least 86 patients was considered appropriate to detect such a difference with a significance level of 0.05 and a power of 80%.

The statistical analysis was performed using SPSS 11 for Mac. Parametric tests for paired samples were applied to compare continuous variables adjusted to the normal distribution. Proportions were compared using chi-square test with Fisher correction. The agreement between GPs and the urologist were compared using the kappa statistic.

## RESULTS

Only four (50%) of the GPs (mean age: 44-years-old) agreed to participate in the study, so they were considered a 'motivated GPs' sample. Between January and June 2010, 136 patients were enrolled in the study. 19 (14%) of them did not attend the urologic office and were excluded. A total of 117 patients (351 visits) were diagnosed by the GPs as having BPH-related LUTS and, after completing the study protocol, were considered valids. For 31% of the patients the main cause of consultation was LUTS. The remaining cases were identified by asking patients, who were consulted because of other causes, about the presence of bothersome LUTS (Figure 2).

Out of the 117 patients identified as cases by GPs, the urologist confirmed 95 (81.2%). As was expected, the principal discrepancy was related to the DRE results. 22 patients were excluded by the urologist because they had a small volume with fibroleastic consistency. The urologist considered that LUTS should not be related to BPH. With regard to the IPSS score, a total of 23 patients (19.6%) were classified as having mild symptoms (IPSS 0-7); 81 (69.2%) moderate symptoms (IPSS 8-20); and the remaining 39 (33.3%) severe symptoms (IPSS 21-35). The mean IPSS score was 12.3. As it was expected, those who consulted by LUTS had a mean IPSS score higher (17.6) than those who did not (10.4), ($p<0.001$). Regarding QoL item, the mean score was 1.79, being higher among those who were consulted by LUTS (2.81) compared to those who were not (1.43) ($p<0.001$) (Table 2).

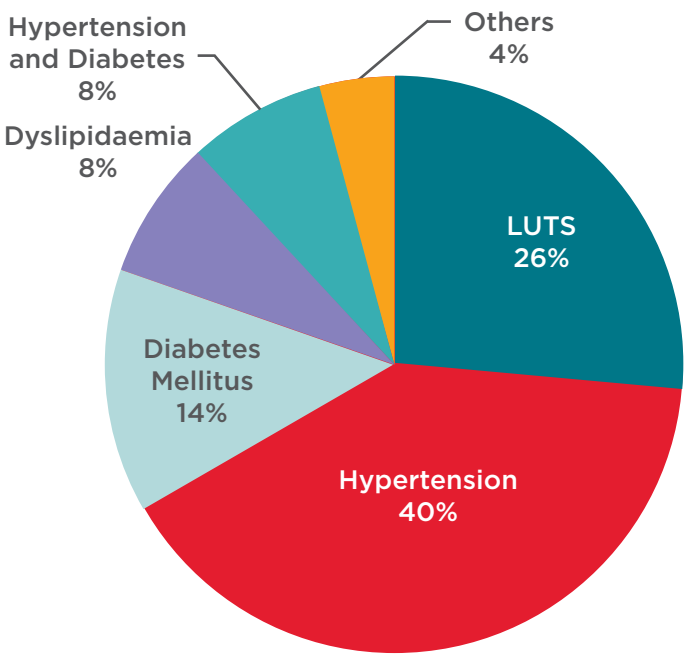


**Figure 2: Causes of consultation.**
LUTS: lower urinary tract symptoms.

A total of 39 patients (33.3%) had progression criteria defined as having a PSA ≥1.5 and a prostate volumen ≥30 cc. A strong correlation between symptom severity and progression criteria was observed: 3% in those with mild symptoms, 35.6% in those with moderate symptoms, and 78.5% in those with severe symptoms (Table 2). The sample PSA mean was 1.47 ng/ml and was correlated with the severity of symptoms (0.9 in mild symptoms, 1.52 in moderate group, and 2.19 in the severe group). A total of 43 (36.7%) patients had a PSA of ≥1.5 ng/ml (Table 2).

With regard to the assessment of prostate volume by DRE, an agreement was observed in 90 of 117 patients (76.9%) showing a kappa index of 0.63 (CI 95% 0.46-0.73), which can be considered good enough. The higher agreement was observed in the small volume prostate group. It was detected, an agreement of 84.8%, 86.1%, 58.8%, and 0% within volume I, II, III, and IV, respectively, although there were very few cases (3) in this last group (Figure 3).

Some differences were detected among the perceived severity of symptoms measured by IPSS scores in the same patient when visiting a GP or

a urologist. In 22 of 117 patients (18.8%) the IPSS score was different. This difference was considered significant and can only be related to the test reliability, as each patient was attended by the urologist in fewer than 21 days from their visit to the GP. In 13 cases (11%) the score shifted from mild to moderate symptoms. In the other 9 (7.6%) the score changed from moderate to severe symptoms. Given that these changes could have an influence on treatment decisions, we decided to take them into account for comparison only against those cases with perfect confidence in IPSS score between GPs and the urologist.

**Table 2: Comparative results of benign prostatic hyperplasia-related group versus other causes of consultation.**

| | Total | BPH-related LUTS | Other causes | P |
|---|---|---|---|---|
| N | 117 | 31 | 86 | |
| Age | 61.4 | 64.7 | 60.2 | p=0.006 |
| IPSS | 12.3 | 17.6 | 10.4 | p<0.001 |
| QoL | 1.7 | 2.8 | 1.4 | p<0.001 |
| PSA | 1.4 | 1.7 | 1.4 | p=0.091 |
| Prostate Volume | 38.5 cc. | 45.4 cc. | 35.8 cc. | p<0.001 |
| Q max | 15.7 ml/sg | 11.1 ml/sg | 17.3 ml/sg | p<0.001 |
| Progression Criteria | 39/117 (33.3%) | 13/31 (41.93%) | 26/86 (32.55%) | |
| Severity | | | | |
| Mild | 23/117 (19.6%) | 0/31 (0%) | 23/86 (26.7%) | |
| Moderate | 81/117 (69.2%) | 19/31 (61.3%) | 62/86 (72.1%) | |
| Severe | 13/117 (11.1%) | 12/31 (38.7%) | 1/86 (1.2%) | |

IPSS: international prostate symptom score; QoL: quality of life; PSA: prostate-specific antigen; BPH: benign prostatic hyperplasia; LUTS: lower urinary tract symptoms.

**Table 3: Treatment recommendations.**

| Clinical Profile | Recommended Treatment | % GP agreement | Most frequent GP deviation (%) | % Urologist agreement | Most frequent Urologist deviation (%) |
|---|---|---|---|---|---|
| Profile 1 | Observation | 93% | AB (7%) | 96% | AB (4%) |
| Profile 2 | AB | 84% | Observation (15%) | 75% | Observation (25%) |
| Profile 3 | AB | 87% | Observation (10%) | 82% | Observation (15%) |
| Profile 4 | 5ARI | 56% | AB (40%) | 90% | Combination (7%) |
| Profile 5 | Combination (AB + 5ARI) | 95% | AB (5%) | 95% | 5ARI (5%) |

AB: alpha-blockers; 5ARI: 5-alpha reductase inhibitors; GPs: general practitioners.

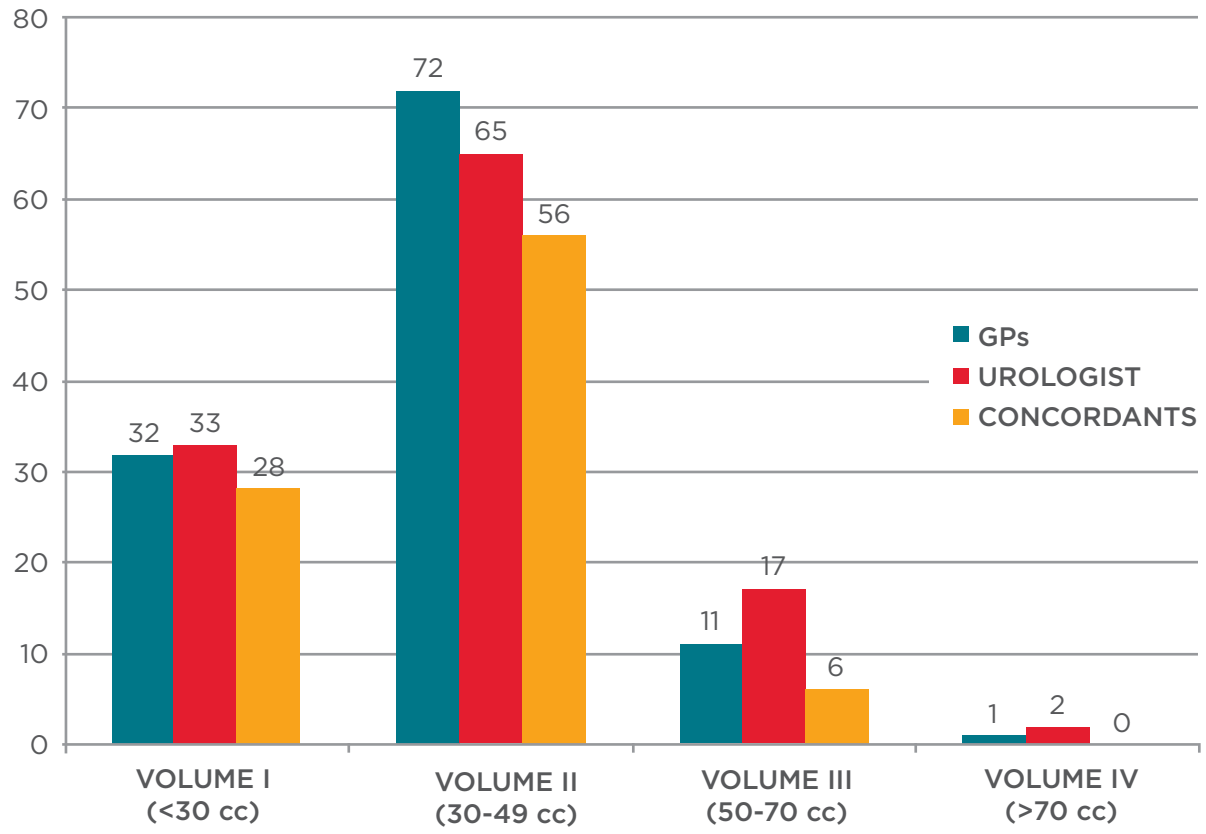


**Figure 3: Concordance of prostate volume estimated by DRE.**
GPs: general practitioners; DRE: digital rectal exam.

With respect to the therapeutic decision-making agreement, which was the primary goal of this study, and taking into account all patients, not only those considered cases by the urologist, an agreement was reached between GPs and the urologist in 84 out of 117 cases (71.79%), which corresponds to a kappa index of 0.595 (CI 95% 0.47-0.71) resulting in a moderate agreement. When we limited the comparison only to the 95 cases with coincident IPSS score, agreement was observed in 73 (76%) patients, kappa 0.651 (IC 95%=0.527-0.775), which can be considered a good agreement.

7 patients out of 95 (7.3%) would have been overtreated by the GPs given that they had mild symptoms and should have been managed conservatively. In 12 patients (40%) GPs proposed an AB when the consensus protocol suggested a 5ARI. The agreement was total in those patients where an AB was indicated and in those with severe symptoms in whom a combination therapy of AB and 5ARI was recommended (Table 3). In 34 (92%) out of 37 patients for whom the recommendation was to prescribe a 5ARI, alone or in combination, the urologist coincided 24 as monotherapy and 10 in combination. In the remaining three cases an AB was decided due to the prevalence of storage symptoms. The GPs only proposed a 5ARI to 23 out of 37 patients (62.1%) for whom it was recommended. In the other 14 patients, 13 cases were prescribed an AB and the remaining observation without treatment.

## DISCUSSION

Shared care between GPs and urologists in the management of BPH is not a novel concept.[6] The high incidence of BPH-related LUTS makes it difficult for every individual presenting with prostatism to be assessed by a specialist. Coinciding with the rising number of office visits has been a dramatic shift in the assessment and treatment of LUTS, due to BPH increasing the role of primary care in its management.

Most CPGs assume that GPs can manage BPH patients as a urologist does. In Spain, the Spanish Association of Urology and the three existing scientific associations of GPs agreed and published

a conjoint document about criteria for referral to specialised care, in order to help in the management of these patients.[7]

The first issue to consider is the ability of a GP to properly diagnose a BPH patient; that is to say, to identify the true case of BPH. Medical history, symptoms assessment by IPSS questionnaire, and DRE and PSA measurement are diagnostic tests available for GPs that allow for a correct BPH diagnosis. Nevertheless, this requires not only the identifcation of the presence and severity of both storage and voiding symptoms, but also the interpretation of changes in prostate volume and consistency by DRE. Although ultrasonography may help in determining prostate volume, it cannot assess changes in consistency. Most GPs have problems interpreting DRE results.

This study shows that GPs can estimate prostate volume by DRE when the prostate is small, but have more difficulties as prostate volume increases. Assessing prostate consistency is important, not only to discard prostate cancer, but also to assign the appropriate treatment. In this study, almost 20% of BPH cases diagnosed by GPs were discarded by the urologist because of a normal DRE. Those patients underwent different tests to identify other possible causes of LUTS because it is important that other conditions associated with LUTS were excluded before a definitive diagnosis of BPH. Any oversight in this initial evaluation can potentially result in misclassification bias, misdiagnosis, and incorrect treatment of patients.[8]

The other important issue relates to the ability of GPs to establish the appropriate treatment recommendation. It has been published that GPs are less prone to treat patients compared to urologists. As it was not a goal of this study, and because only one urologist participated in the research, we could not verify this. Nevertheless, despite the small number of patients included and working with a consensuated protocol, GPs recommended active treatment in 7% of cases, when the protocol advised observation.

The presence of progression criteria in this study is small (33%) compared with that observed in urologic clinics where it reaches about 66%.[9] The explanation is that most patients were diagnosed proactively in a primary care setting, and therefore, only 30% of consultation causes were LUTS. In fact, progression criteria were observed in only 42% of these. This is an important issue because clinical progression, acute urinary retention (AUR), and prostate-related surgeries are important events that can be prevented or delayed by the early initiation of the use of 5ARIs alone or in combination with an AB.[10,11] An investigation in 28,903 patients concluded that every additional 30 days of 5ARI therapy reduced the likelihood of AUR and prostate surgery by 14% and 11%, respectively, while each 30-day increment of 5ARI therapy reduced BPH-related costs by 15%.[12]

Recent studies have shown that management of BPH may vary between the urologist and the primary care physician, including differences in their choice of therapy.[5,13] Urologists tend to treat more patients and to prescribe 5ARI and combination therapy, with an AB and 5ARI, significantly more often than primary care physicians. Primary care physicians, on the other hand, tend to prescribe nonselective ABs more often than urologists.[14] This has been demonstrated in our study despite the fact that the GPs were a highly selected and motivated group who participated in the protocol design. Certainly, most CPGs leave the choice between an AB or a 5ARI open in men with moderate-to-severe symptoms and progression criteria, but our consensus protocol clearly established the need to prescribe an 5ARI, alone or in combination. Only 60% of patients in whom a 5ARI treatment was recommended were prescribed by GPs. Therefore, almost 40% would have been on AB, suggesting that some may be undertreated and progression would contine; therefore, related costs were more likely to occur in such a percentage of patients. It is noticeable that there has been a complete concordance with regard to AB therapy.

Although decision agreement between GPs and the urologist was considered good enough, it is important to improve the ability of GPs to identify those patients at risk of progression, and treat them properly. Commensurate with the long-term preventive role of primary care, efforts can and should be made to treat the underlying condition of enlarged prostate as well as to manage the symptoms short-term. In all cases, the risks and benefits of each treatment need to be considered and discussed with the patient.

Some limitations of this study are that we have not taken into account differences in clinical practice between urologists as this was not the goal. Another would be the small number of patients

and GP participants recruited. But, on the other hand, we have to assume that the GPs were considered to be very motivated, and therefore, we could raise the question of what would have occurred if a larger number of less motivated GPs would have participated.

## CONCLUSIONS

In general, primary care physicians can manage BPH patients as urologists do, but it seems to be very important to educate the physicians regarding changes in the management of BPH as a progressive disease. Otherwise, it should not be assumed that they can manage all patients with BPH-related LUTS properly.

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