

IPSS Score Proves Its Clinical Relevance in Benign Prostate Hypertrophy Diagnosis and Follow-Up

I. Miklos^{1,2}, H. D. Mureşanu¹, A. I. Greluş^{1,2}, I. Ioiart¹

¹ Urology Clinic, Arad County Emergency Hospital, Arad, Romania

² "Vasile Goliş" Western University of Arad, Romania

Abstract

Introduction and Objectives. The benign hypertrophy of prostate (BPH) is a benign tumor of the prostate characterized by the appearance of LUTS (lower urinary tract symptoms). In Romania there are about 200 000 men registered under treatment, but the number of patients could exceed 900 000. The aim of the study was to re-evaluate the clinical relevance of the IPSS score in the BPH diagnosis and assessment of the quality of life during patients' follow-up.

Materials and Methods. Between October 2015 - September 2016 we conducted a population-based descriptive cross-sectional survey designed to assess the prevalence of clinical BPH amongst male adults in Arad County, Romania. The study group included male adults over 45 years; patients with any type of neoplasia were excluded. Additionally, 19 healthy patients were included in a control group. All patients were interviewed for LUTS using the IPSS questionnaire, and investigated for PSA level in conjunction with DRE (digital rectal examination) and transabdominal prostate ultrasonography.

Results. We selected 181 patients with BPH. The mean age of patients with BPH was 68.31 ± 5.54 years, the youngest subject being 53 years old and the oldest 83. Most patients were enrolled between 61-70 years and 60.77% (n = 181). Our study show that the rate of BPH in Arad County using IPSS questionnaire were 2.00% in 51-60 age group, 30.0% in the 61-70 age group and 21.00% in > 70 age group. The prevalence of BPH based on DRE and abdominal ultrasound is 4.00% in the 51-60 age group, 41.5% in the 61-70 age group and 23.00% in > 70 age group.

Conclusions. The IPSS score is an important factor both in the diagnosis of BPH patients for correct assessment of symptom severity and an indirect indicator in assessing the quality of life of patients both prior to treatment and in subsequent periodic evaluations.

Key-words: 5-alpha-reductase inhibitors, alpha-blocker treatment, BPH, IPSS, LUTS, phytotherapy

Correspondence to: Dr. Miklos Imola, M.D.

Urology Clinic, Arad County Emergency Hospital

2-4 Andrenyi Karoly Str., code 310037, Arad, Romania

Tel/Fax: +40773342983

e-mail: miklosimola@gmail.com

Introduction and Objectives

The benign hypertrophy of prostate (BPH) is the histopathological diagnosis of prostate adenoma, which is a benign tumor of the prostate characterized by the proliferation of prostatic stromal and epithelial cells and by the appearance of LUTS (lower urinary tract symptoms).

Adenomatous prostatic growth is believed to begin at approximately age 30. An estimated 50% of men have histologic evidence of BPH by age 50 and 75% by age 80; in 40–50% of these men, BPH becomes clinically significant^[1,2].

In Romania there are about 200 000 men registered under treatment, but the number of patients could exceed 900 000. Despite the high incidence of BPH, the disease is underdiagnosed. Men tend to go to a doctor only when the symptoms become severe and affect their everyday life^[3].

Complications of the BPH occur less commonly but may include acute urinary retention (AUR), impaired bladder emptying, the need for corrective surgery, renal failure, recurrent urinary tract infections, bladder stones, or gross hematuria^[4,5].

The diagnosis of BPH is based on the current guidelines that includes anamnesis, IPSS questionnaire, clinical examination of the patient, digital rectal examination, transabdominal and transrectal ultrasonography, and determination of PSA.

Although the utility of the IPSS score in BPH diagnosis and subsequent assessments of the symptoms improvements is demonstrated by numerous studies, it is rarely used today in Romania due to the long waiting time in hospitals and the limitation of consultation time.

The aim of the study was to re-evaluate the clinical relevance of the IPSS score in the BPH diagnosis and assessment of the quality of life during patients' follow-up.

Materials and Methods

This study is a population-based descriptive cross-sectional survey designed to assess the prevalence of clinical BPH amongst male adults in Arad County, Romania. The study group comprises of male adults over 45 years who provided written consent to participate and fulfill the inclusion criteria. Patients with any type of neoplasia were excluded from the study. Additionally, 19 healthy patients were included in the study as a control group.

Our study was performed during a one year peri-

od, between October 2015 and September 2016, with a follow-up every six months. We selected 181 patients with BPH irrespective of age, social status or ethnicity.

All patients were interviewed for LUTS using the IPSS questionnaire, and investigated for PSA level in conjunction with DRE (digital rectal examination) and transabdominal prostate ultrasonography. The diagnostic criteria for clinical BPH were prostatic volume of ≥ 25 mL with moderate/severe IPSS (IPSS ≥ 8). For BPH current guidelines we indicated specific treatments with: alpha-blockers, 5-alpha-reductase inhibitors, phytotherapeutic agents or surgery. Every six months the patients were clinically examined and IPSS score was calculated.

All statistical analyses were conducted using Statistica version 7 (StatSoft Inc., Tulsa, OK, USA). In all of the cases, a p value < 0.05 was considered significant. The inter-group homogeneity of age among different groups was checked using a Kruskal-Wallis test with tied ranks. Based on the absolute value of serum PSA, the men were stratified as having low PSA levels (up to 2.5 ng/mL), intermediate PSA levels (above 2.5 to 10 ng/mL), and high PSA levels (above 10 ng/mL), respectively. Chi2 tests were next applied on the distribution of PSA classes and specific treatment classes, respectively, across the prostate pathologies investigated, with the frequency observed in controls being used as a benchmark.

The study is conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, respects ethical demands that require research with human subjects. Before starting the study, we obtained the agreement of the Ethics Committee of the Arad County Emergency Hospital and the Western University "Vasile Goldis" in Arad.

Results

Over a one-year period we consulted over 400 patients in our clinic. We selected a total of 181 patients who fulfilled the inclusion criteria for BPH. Additionally, 19 healthy patients were included in the study as a control group.

Stratification according to age was performed for the BPH and control group. Ages of the participants ranged from 51 to 85 years with a mean of 68.31 ± 5.54 years. The major group of patients belong to 61-70 age, representing 60.77% from the group study. We identified only 4.97% patients with age under 60 years and 34.25% patients over 71 years. In control group the age average was 62.21 ± 3.10 . The major group of patients

belong to 61-70 age, representing 78.94% from control group.

We defined benign prostatic hypertrophy, as prostatic volume measured by transabdominal ultrasonography with a value > 25 g and / or IPSS score > 8 . PSA was routinely performed on every male over 50 years of age for the screening of prostate cancer.

We considered normal PSA level < 2.5 ng/mL according to EAU Guidelines. Patients with PSA level between 2.5-10 ng/mL have moderate risk to develop in the future prostate cancer, patients with PSA level > 10 ng/mL present high risk to develop prostate cancer and should undergo prostate biopsy to confirm/exclude this suspicion. Patients with PSA level > 10 ng/mL were referred to prostate biopsy.

Figure 1 presents the variations of the PSA values in BPH patients in comparison with the control group. For a better correlation we excluded the patients with the PSA level > 10 ng/mL, due to the possibility of the presence of prostate cancer. We can notice that the PSA levels are quite in value in BPH patients compared with control group.

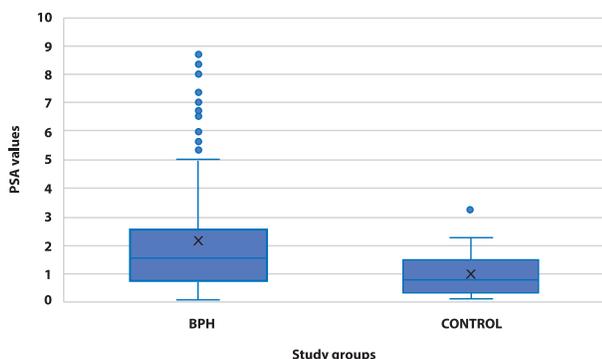


Figure 1. Variations of the PSA values in the examined groups

Table 1. The distribution of PSA levels versus prostatic volume and age groups

	Normal PSA < 2.5 ng/mL	PSA between 2.5-10 ng/mL	High PSA > 10 ng/mL
Prostate volume			
< 25 cm ³	86.36% (19)	13.64% (3)	0.00% (0)
25-30 cm ³	91.07% (51)	7.14% (4)	1.79% (1)
31-50 cm ³	67.95% (53)	30.77% (24)	1.28% (1)
> 50 cm ³	40.00% (10)	60.00% (15)	0.00% (0)
Age			
< 61 yrs	77.78% (7)	22.22% (2)	0.00% (0)
61-70 yrs	74.55% (82)	25.45% (28)	0.00% (0)
> 70 yrs	70.97% (44)	25.81% (16)	3.23% (2)
Provenience			
Rural	72.13% (88)	27.05% (33)	0.82% (1)
Urban	76.27% (45)	22.04% (13)	1.69 (1)

Data are presented for any PSA group as percentage (on the left) and absolute values (on the right).

Table 1 shows the distribution of PSA levels versus prostatic volume and age groups in BPH. Inclusion in this statistical analysis of BPH patients only, revealed very significant differences between PSA values among patients belonging to different prostate volume categories (Kruskal-Wallis test, $H = 18.892$, $p < 0.001$), but independently on the age category (Kruskal - Wallis test, $H = 0.266$, $p = 0.875$). In the first case, posthoc analysis revealed significantly higher values of this biochemical parameter for subjects with a prostate volume greater than 50 cm³ compared to subjects with prostatic volume less than 25 cm³ (Dunn test, $p = 0.036$). Low PSA values were specific to prostate volumes between 25 and 30 cm³ and these values were significantly lower compared to patients with prostate volume greater than 50 cm³ (Dunn test, $p < 0.001$). All the other patient groups regarding prostate volume expressed similar PSA values, without significant differences (Dunn test, $p \geq 0.052$). Our findings are in agreement with the literature data, which show that the PSA values directly correlate with prostatic volume.

According to the EAU Guideline 2017 for the management of LUTS, a validated symptom score questionnaire should be used for the routine assessment of male LUTS in all patients and same should be applied for re-evaluation of LUTS during treatment. Following the IPSS questionnaires data, we combined the main clinical and paraclinical features of our study group as they are presented in Table 2.

The main factors studied were the IPSS score, prostatic volume and PSA. We have noticed that the IPSS score is slightly increased by age. Further we applied the ANOVA test, which showed a value of $p = 0.046$, significant for these variation (Table 2). The analysis of variations in prostate volume by age, we did not show any statistically significant changes ($p = 0.26$), however a slight increase in mean prostate volume with aging may be observed (Table 2).

PSA values show statistically significant variations ($p = 0.034$) by age referred to the total number of patients. An increase in mean PSA values can be observed with age. Our results show that PSA has higher physiological values in the elderly compared to younger patients, with more severe prostate symptoms in the elderly (IPSS score = 12.88 ± 6.73), but the prostate volume is not directly influenced by the age of the patients.

Table 2. IPSS score and the clinical characteristics in the study groups

	Total patients (n=200)	51-60 yrs (n=13)	61-70 yrs (n=125)	> 70 yrs (n=62)	p value
IPSS score	11.42 ± 7.77	8.92 ± 8.22	10.96 ± 8.13	12.88 ± 6.73	p = 0.046
1-7	94 (47%)	9	65	20	
8-19	72 (36.5%)	3	40	29	
20-35	34 (16.5%)	1	20	13	
Prostatic volume (g)	35.71±16.49	28.84±9.6	34.42±16.5	39.75±16.89	p = 0.26
≤25	63	5	42	16	
>25	137	8	83	46	
PSA (ng/ml)	2.24 ± 3.17	1.59 ± 1.39	1.93 ± 1.72	3.00 ± 5.05	p = 0.034

IPSS: international prostatic symptom score; PSA: Prostate-specific antigen; BPH: benign prostatic hypertrophy; Values are presented as median and standard deviations or number of patients Value p was calculated by applying ANOVA assays

Table 3. Storage and voiding symptoms in BPH group compared to IPSS subscores

Patients groups	BPH (n=181)	Control (n=19)	P value
Main factors			
Age	68.31 ± 5.54	62.21 ± 3.1	< 0.005
Sub scores of IPSS			
Storage / irritative symptoms			
Increased micturition frequency	1.98 ± 1.76	0.49 ± 1.2	< 0.002
Increased micturition urgency	1.22 ± 2.21	0.19 ± 0.88	< 0.001
Nocturia	2.06 ± 1.33	1.05 ± 1.02	< 0.001
Voiding / obstructive symptoms			
Poor stream	3.56 ± 2.13	0.75 ± 1.53	< 0.001
Terminal dribbling	1.72 ± 2.1	0.23 ± 0.77	< 0.003
Hesitancy	2.19 ± 1.98	0.50 ± 1.32	< 0.001
Incomplete voiding	2.34 ± 2.20	0.43 ± 1.21	< 0.001
IPSS			
0	0	13	
1-7	75	6	
8-19	73	0	
20-35	33	0	
Prostatic volume	37.64±16.12	17.36±3.86	< 0.001
PSA (ng/ml)	2.38 ± 3.29	0.93 ± 0.83	< 0.001

Legend:
 BPH: benign prostatic hypertrophy; Control: group of clinically healthy control patients; IPSS: international prostatic symptom score; PSA: Prostate specific antigen
 Values are presented as median and standard deviations or number of patients Value p was calculated by applying ANOVA assays

To assess as accurately as possible the overall status of the patients included in the study, we emphasized the role of IPSS subclasses according to study group, prostate volume, and PSA values. These values are shown in Table 3.

Our study shows that the most common symptom among patients with BPH was poor urinary stream, showing a value of 3.56 ± 2.13, followed by incomplete

voiding of 2.34 ± 2.20 and hesitancy of 2.19 ± 1.98. All these scores are highly variable showing the symptom heterogeneity in BPH.

It can be noticed that no patient diagnosed with BPH had an IPSS = 0 score compared to the control group (n = 19), where 68.42% did not have prostate symptomatology but 31.58% had an IPSS score <8, rarely experienced LUTS without affecting their the

sleep or quality of life and without exceeding the IPSS score value of 2.

It can be observed that there are statistically significant differences between the two study groups, meaning that the frequency of LUTS, increase of prostatic volume and of PSA values are specific to BPH group.

Patients with BPH require regular monitoring for treatment adjustment and screening for prostate cancer, which may occur in a synchronous manner. We considered relevant performing the IPSS score both at diagnosis and follow-up every six months to observe the evolution of the BPH patients QoL (quality of life) under treatment. Patients were monitored in evolution every 6 months, where besides the standard clinical examination the IPSS score was also applied. The chart below shows the evolution of the IPSS score after the first 12 months of BPH treatment (Figure 2).

The data is presented as an average with a 95% confidence interval (error bars).

Post hoc analysis indicated a significant decrease in IPSS in BPH patients on medication, compared to those who did not receive any medication (patients under active surveillance) (HSD test for unequal samples for all treatments $p < 0.05$) (Figure 2).

Discussions

Benign prostatic hyperplasia (BPH) is the most common nonmalignant condition of the prostate developing in aging men. BPH is a major public health concern, causing high morbidity and worsening of men's quality of life (QOL).

The prevalence rates of BPH depend highly variable parameters. In Japan, these rates have been estimated on the basis of the results of community-based studies. Six percent and 12% of Japanese men in their 60s and 70s, respectively meet all of the following criteria for BPH: (1) an international prostate symptom score (IPSS) > 7 points; (2) prostate volume (PV) > 20 mL; and (3) peak urinary flow rate (Qmax) < 10 mL/s. Only 2%

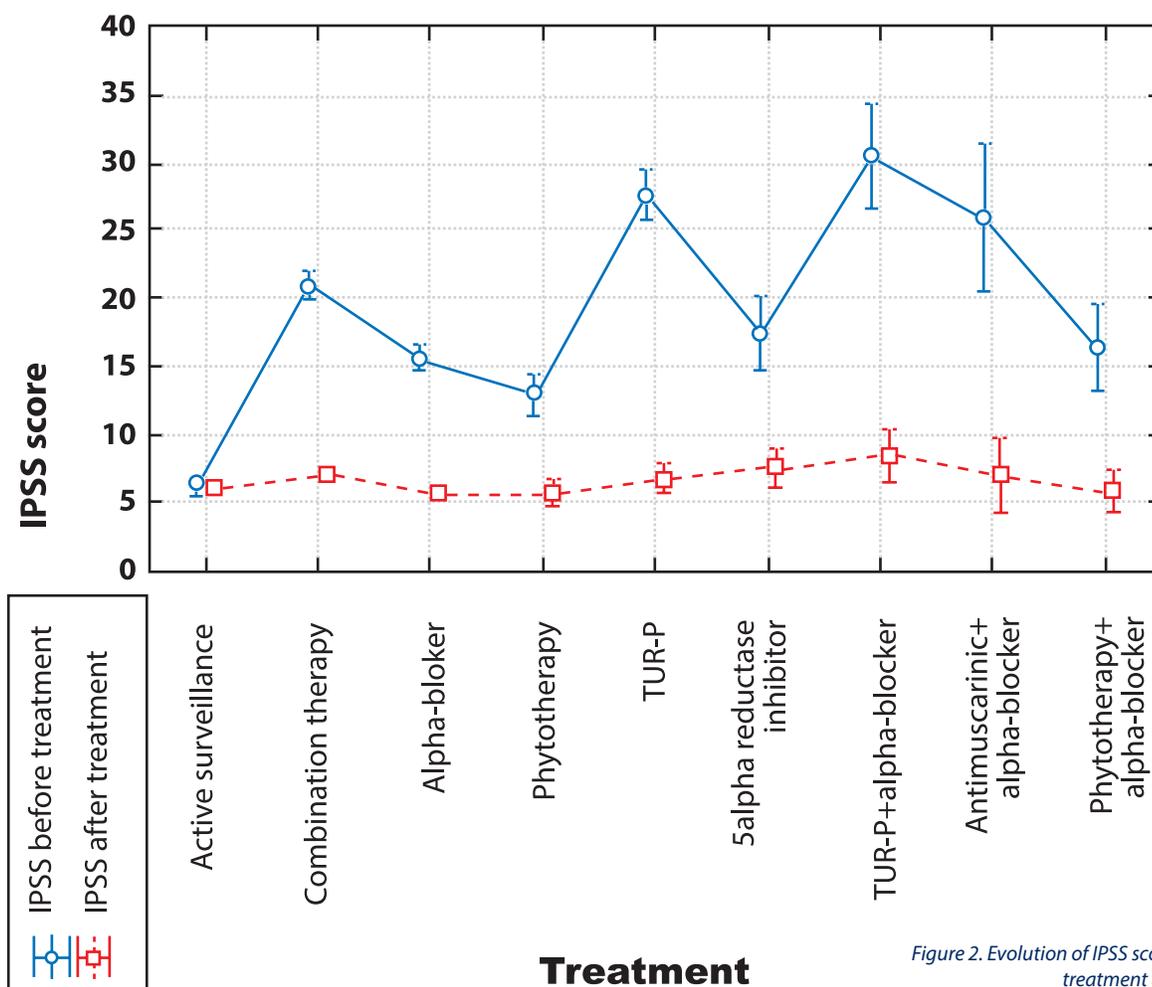


Figure 2. Evolution of IPSS score according to treatment after 12 months

of men in their 40s and 50s met the aforementioned criteria^[6,7,8].

A study realized by James Choi et al. in 2002 demonstrates that that age-matched Korean men with smaller prostates had a higher incidence of LUTS due to BPH in comparison to African-American, Caucasian, and Hispanic men^[9]. Korean men may be more prone to accepting LUTS as a normal part of the aging process and only the men with severe symptoms will seek evaluation and therapy. This theory was supported by recent data by Platz et al., which demonstrated that Korean men have a similar relative risk of having BPH related symptoms as Caucasian men but less likely to undergo BPH surgery^[10]. Higher incidence of BPH related symptoms in Asian men, however, was noted in another population-based study. Tsukamoto et al. reported that when comparing age-matched Japanese and Olmsted county men, Japanese men had worse BPH symptom scores^[11]. Furthermore, Japanese men tended to report 50% less bother by LUTS than American men with the same level of urinary symptoms, which may indicate a higher incidence than what is currently reported.

In our study (n = 181) the prevalence of BPH by age group showed that the mean age of patients with BPH was 68.31 ± 5.54 years, the youngest subject being 53 years old and the oldest 83. In the 51-60 age group there were 4.97% BPH patients. Most patients were enrolled between 61-70 years and 60.77% (n = 181), respectively. Patients over the age of 70 years were 34.35% (n = 181), two of whom were over 80 years of age.

Unlike our results, a meta-analysis in China show the highest prevalence of BPH in the age group over 80 years representing 69.2%, and the lowest in the 40-49 age group by 2.9%^[12].

The World Bank data according to the WHO show that the life expectancy in South Korea and Japan are almost the highest in the world, with 82.16 years, irrespective 83.7 years. The life expectancy in 2014 in Romania and China was similar with 74.5-76 years^[13].

We consider that the differences between our data and other studies are due to ethnic, dietary and cultural variations in the populations.

In a multinational cohort study using the IPSS questionnaire, the rate of BPH in men between 40 and 79 was 14% in France, 18% in Scotland, 24% in Sweden, 38% in the US, and 56% in Japan^[14,15]. Another study, which detects the occurrence of BPH using the IPSS questionnaire and abdominal ultrasonography among men in Iran, found a 1.2% prevalence of the disease in

the 40-49 age group, 18.45% in the 50-59 age group, 26.8% at the group of 60-69 years and 36% in the group over 70 years^[16].

Arad County in 2013 has a population of 451 434 people, from which 48.30% were males (Romania INS, Tempo data base), and 4.87% of them were over 50 years^[17]. Relating to this data, our study show that the rate of BPH in Arad County using IPSS questionnaire were 2.00% in 51-60 age group, 30.0% in the 61-70 age group and 21.00% in > 70 age group.

In a study conducted in Ghana, BPH prevalence was 62%, being detected by digital rectal examination (DRE). The prevalence of BPH symptoms evaluated by IPSS score > 8 was 20%. In Ghana, PSA levels > 1.5 ng / ml; I mean prostate volume > 30 g were 36%^[18]. The South African Urology Association reported that 1:3 of men of > 45 years of age have moderate or severe LUTS, and 50% of men with symptomatic BPH^[19].

Our results show that the prevalence of BPH based on DRE and abdominal ultrasound is 4.00% in the 51-60 age group, 41.5% in the 61-70 age group and 23.00% in > 70 age group.

We can observe, that the association of the IPSS questionnaire with clinical examination and ultrasonography is very important thereby we can personalize the BPH treatment. Only the patients with moderate or severe IPSS need an aggressive therapy irrespective of the prostate volume (combination therapy or surgery) and patients with slight symptoms may benefit from alternative therapy (active surveillance, phytotherapy).

A nigerian study conducted during the period January 2013 to December 2013 about 103 men showed the mean age of the patients 62.6 yrs (range 21 – 85 yrs). Eighty patients (77.7%) had benign prostatic hyperplasia, 20 men had prostate carcinoma (19.4%) while 3 patients had prostatitis. The mean total IPSS was 15.3 (range 3 – 34). Seventy-two of the men, representing 69.9% had moderate symptoms while the mean prostate volume was 57.8 ml (range 20 – 195 ml). The Pearson correlation between prostate volume and IPSS = 0.13 with a p-value of 0.18. This study illustrates that there's no significant relationship between prostate volume and International prostate symptom score in African men with prostatic disease^[20]. Barry et al showed that at baseline symptom severity was not correlated with prostate volume^[21].

Our study shows statistical significant differences between prostate volume and IPSS score, the higher the prostate volume, the more severe the symptoms (p=0.015).

According with our study, Eckhard et al investigated the associations of symptoms and quality of life with age, prostate volume, and urodynamic parameters in a large group of strictly selected men with lower urinary tract symptoms. His conclusion was that except for nocturia, older men had higher voiding scores on the IPSS. Prostate volume and obstruction grade were not associated with high voiding scores on IPSS, but low detrusor contractility and low capacities were associated with the symptom index^[22].

Our study is in agreement with Eckhard results, showing that except for nocturia, voiding symptoms were more severe than storage symptoms in BPH patients.

Conclusions

The IPSS score is an important factor both for the diagnosis of BPH, for correct assessment of symptoms severity. IPSS can, although indirectly, be a very good indicator in evaluation of patients' quality of life both prior to treatment and in subsequent periodic evaluations.

Overall, our data suggest that IPSS score has an increased significance in diagnosis and follow-up of BPH patients and should be reconsidered in clinical practice.

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