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Original Research Article

Correlation between prostate specific antigen and prostate volume with disease symptom severity assessed by international prostate symptom score

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ABSTRACT

Background: Benign prostatic hyperplasia (BPH) is clinically defined as prostate adenoma, resulting in bladder outlet obstruction (BOO), which may eventually harm the bladder and even kidneys. For differential diagnosis of male LUTS, uroflowmetry can be used together with non-invasive ultrasound to ascertain the flow rate and IPP. PSA is also an important indicator for differential diagnosis. International prostate symptoms score (IPSS) is used to assess the severity of the symptoms for clinical BPH. There is also a recommendation to consider the quality of life (QoL) index, where a QoL score of ≥3 is considered as worrisome.
Methods: This was a retro-prospective study based on secondary and primary data collection and analysis, pertaining to BPH patients who visited the study site previously as well as those who are coming for regular follow-up since 2019. Patient enrolment was done at a teaching hospital Shree Krishna Hospital affiliated to the Pramukh Swami Medical College, Bhaikaka University, Karamsad. About 100 patients presenting with lower urinary tract symptoms (LUTS) and histo-pathologically proven cases of BPH were enrolled to pursue research objectives. All patients were followed up to a period of 3-months after initiating the treatment and disease severity through IPSS and quality of life upon completion of treatment were also assessed.
Results: PSA is also an important indicator for differential diagnosis, which is generally less than 1 µg/l in patients in absence of clinically confirmed BPH. In our study, mean prostate volume was reported to be 43.46±19.35 cc. A positive correlation was observed between prostate volume and serum PSA with disease severity.
Conclusions: Our study evaluated the IPSS to predict the disease severity and correlated it with quality of life, prostate volume and serum PSA. Our findings were in line with currently available evidences, and suggested that QoL, prostate volume and serum PSA are better predictors of disease severity, IPSS.

Keywords: BPH, IPSS, Prostate, Prostate volume, PSA

INTRODUCTION

Benign prostatic hyperplasia (BPH) is clinically defined as prostate adenoma, resulting in bladder outlet obstruction (BOO), which may eventually harm the bladder and even kidneys.[1] The condition is generally characterized by the slow progression due to which patients start getting used to the symptoms. As a result, patients may not experience any lower urinary tract symptoms (LUTS), rather present with sudden acute retention of urine, painless gross haematuria, raised prostate-specific antigen (PSA) levels or even urinary infection.[1,2] Clinically confirmed diagnosis for BPH can be made with noninvasive ultrasound, which helps measure intra-vesical prostatic protrusion (IPP). The test offers 100% specificity and positive predictive value for the diagnosis of prostate adenoma. For differential diagnosis of male LUTS, uroflowmetry can be used

together with non-invasive ultrasound to ascertain the flow rate and IPP.[3] PSA is also an important indicator for differential diagnosis, which is generally less than 1 µg/l in patients with no prostate cancer, prostatitis or clinical BPH. In patients with confirmed clinical BPH, further assessment of voiding function and storage function is important to ascertain any possible harm to the bladder and kidneys.[4]

International prostate symptoms score (IPSS) is used to assess the severity of the symptoms for clinical BPH. There is also a recommendation to consider the quality of life (QoL) index, where a QoL score of ≥3 is considered as worrisome. Grade 1a prostates are considered clinically least obstructive, whereas grade 3a prostates are considered most obstructive. Accordingly, grade 1c prostate can be managed by a medical therapy with 5-α reductase inhibitors, whereas grade 3a prostates need to be managed with a surgical intervention using transurethral resection for removal.[5,6]

Aims and objective

To study the correlation between serum prostate specific antigen levels and prostate volume with disease symptom severity as assessed by the international prostate symptom score (IPSS).

METHODS

Study design

Retro-prospective study based on secondary and primary data collection and analysis, pertaining to BPH patients who visited the study site previously as well as those who are coming for regular follow-up from January 2019 to December 2021.

Study Site

Patient enrolment was done at a teaching hospital Shree Krishna Hospital affiliated to the Pramukh Swami Medical College, Bhaikaka University, Karamsad, District Anand in the state of Gujarat, India.

Study sample

About 100 patients presenting with lower urinary tract symptoms (LUTS) and histo-pathologically proven cases of BPH were enrolled to pursue research objectives. Data pertaining to patient age, gender, PSA levels, prostate volume, symptoms of BPH patients and their quality of life before and after any medical/surgical intervention was collected for study purpose.

All consecutive patients in the outpatient department of the Surgery or patients getting admitted with LUTS in the department of surgery, were potentially screened for inclusion/exclusion criteria. Those qualifying for the inclusion criteria were explained about the study objectives and their consent was sought for enrolment. All patients were followed up to a period of 3 months after initiating the treatment and quality of life upon completion of treatment was also assessed.

Inclusion criteria

Patients with lower urinary tract symptoms, biopsy proven BPH, age >40 years were included.

Exclusion criteria

Patient with ongoing medical management, HPE proven prostatic cancer, patients with acute prostatitis, patients with per urethral catheter in situ were excluded.

Study variables

The international prostate symptom score (IPSS) has seven multiple choice questions. The International Union Against Cancer and the World Health Organization have also recommended an additional (eighth) question related to the perceived quality of life by the BPH patient (Table 1) A) mild: score between 0 to 7, B) moderate: score between 8 to 19, C) severe: score between 20 to 35.

Ethical consideration

All the suspected LUTS/BPH patients were explained about the study objectives and given participant information sheet (PIS) in local language. They were informed about the risks and benefits that might get incurred during the study. While screening and obtaining patient related data from hospital records, due diligence was exercised to ensure privacy and confidentiality of the participants. The patient-related information was retrieved with reference to their hospital patient ID and patient name or any such information that my reveal patient identity was omitted during the data collection process. No extra charges were applied to participants if they participated in the study; no compromise had been made on the treatment part if they did not agree to the participation. If participants accepted to participate in the research, they signed an informed consent form. The study proposal was presented to the meeting of the ethics committee of HM Patel Centre for Medical Care and Education, Karamsad. The present study was approved via letter reference number IEC/BU/137/Faculty/08/120/2022 dated 07/07/2022.

RESULTS

Considering 60-year is the widely accepted age cut-off for senior citizen, we analyzed data to understand patient distribution by this cut-off. Descriptive statistics found that about 29% and 71% patients were <60 and ≥60-year of age, respectively. Further in this section, we will use 60-year age cut-off for analysing study variables and/or to explore any possible statistical association.

Table 1: Patient responses were recorded with regards to following study variables including IPSS.

Patient hospital ID				**Serum prostate-specific antigen**		**ng/ml**	
Patient age				**Prostate volume (on USG)**		**ml**	
Patient symptoms on presentation							
In the past month	**Not at all**	**<1-5 times**	**<Half the time**	**About half the time**	**>Half the time**	**Almost always**	**Score**
Incomplete Emptying	0	1	2	3	4	5	
Frequency	0	1	2	3	4	5	
Intermittency	0	1	2	3	4	5	
Urgency	0	1	2	3	4	5	
Weak Stream	0	1	2	3	4	5	
Straining	0	1	2	3	4	5	
	None	1 time	2 times	3 times	4 times	5 times	
Nocturia	0	1	2	3	4	5	
Total score							
	Delighted	**Pleased**	**Mostly satisfied**	**Mixed**	**Mostly dissatisfied**	**Unhappy**	**Terrible**
If you were to spend the rest of your life with your							
Urinary condition just the way it is now, how would you feel about that?	0	1	2	3	4	5	6
Outcome of treatment at discharge							

Table 2: Disease severity based on IPSS (before treatment).

IPSS categories	No. of cases (N=100)	Percentage
Mild (IPSS 0 to 7)	26	26.0
Moderate (IPSS 8 to 19)	43	43.0
Severe (IPSS 20 to 35)	31	31.0

As per Table 2, about 31% patients reported IPSS score between 20 to 35, classified as 'severe' disease condition. Around 43% were found to have 'moderate' disease severity and a quarter (26%) of patients were having 'mild' disease severity before treatment.

Most patients (98%) reported 'mild' disease severity on IPSS at 3-month follow-up. Only two patients reported 'moderate' severity and none reported 'severe' at 3-month follow-up. This suggests considerable improvement from 43 and 31 patients reporting 'moderate' and 'severe' disease condition on the IPSS at baseline.

As per Table 3, in less than 60 years, approximately half of the participants (44.8%) had 'mild' disease severity, while 27.6% had 'moderate' and 27.6% had 'severe' disease severity. Whereas nearly half of the participants (49%) over the age of 60 had 'moderate' severity (49.3%), followed by 'severe' severity (32.4%). Around 18% were 'mildly' affected. The Chi^2 test revealed that disease severity is statistically associated to patient's age ($p<0.05$).

As per Table 4, QoL analysis revealed that about third (34%) of all participants rated their experience ranging between 'mostly dissatisfied' or 'unhappy' to 'terrible'. Nearly 30% rated their experience with the disease symptoms to be 'mixed'. About same proportion of patients (29%) rated their QoL experience to be 'mostly satisfied' or 'pleased'. And 8% patients reported it to be 'delighted'.

Table 3: Disease severity based on IPSS (before treatment) by age.

Age		IPSS (before treatment)			Total	P value
		Mild (IPSS 0 to 7)	**Moderate (IPSS 8 to 19)**	**Severe (IPSS 20 to 35)**		
<60	N	13	8	8	29	0.02
	%	44.8	27.6	27.6	100.0	
≥60	N	13	35	23	71	
	%	18.3	49.3	32.4	100.0	
Total	N	26	43	31	100	
	%	26.0	43.0	31.0	100.0	

Table 4: Quality of life by age.

Quality of life		Age			P value
		<60	≥60	Total	
Delighted	N	1	7	8	0.02
	%	3.4	9.9	8.0	
Pleased	N	11	5	16	
	%	37.9	7.0	16.0	
Mostly satisfied	N	3	10	13	
	%	10.3	14.1	13.0	
Mixed	N	7	22	29	
	%	24.1	31.0	29.0	
Mostly dissatisfied	N	4	16	20	
	%	13.8	22.5	20.0	
Unhappy	N	3	10	13	
	%	10.3	14.1	13.0	
Terrible	N	-	1	1	
	%	-	1.4	1.0	
Total	N	29	71	100	
	%	100.0	100.0	100.0	

QoL by age analysis found statistically significant association between patients' age and their quality-of-life experiences ($p<0.05$). Overall findings revealed that patients with age ≥60-year doesn't have satisfying quality of life experiences under the given disease condition. The analysis revealed that about half (51.6%) of the patients <60-year age reported their QoL experiences ranging from 'delighted', 'pleased' or 'mostly satisfied', compared to only 31% from the patients aged ≥60-year. On the contrary, only quarter of the patients (24%) from <60-year age-group reported their QoL experiences ranging from 'mostly dissatisfied' or 'unhappy' to 'terrible', compared to 38% from the patients aged ≥60-year.

A total of 100 patients were given treatment for a period of three months followed by which quality of life was re-assessed. The findings revealed that almost 96% patients reported their health-related QoL ranging from 'delighted', 'pleased' to 'mostly satisfied'. While only 4% patients reported their QoL experiences to be 'mixed', there were no patients reporting their experiences to be 'mostly dissatisfied', 'unhappy' or 'terrible'.

Table 5: Pre-post comparison of quality-of-life paired samples statistics.

Quality of life	N	Mean	SD	P value
Before treatment	100	3.8000	1.51090	<0.001*
Follow-up at 3-month	100	1.2800	0.76647	

As per Table 5, the pre-post comparison for patients' QoL experiences found statistically significant ($p<0.001$) association, with patients' experiences improving considerably at 3-month follow-up, as none of the patients reported their experiences to be 'mostly dissatisfied', 'unhappy' or 'terrible', compared to 34% patients reporting similar experiences before treatment.

Table 6: Descriptive statistics for study variables.

Study Variable	N	Minimum	Maximum	Mean	Std. deviation
Age	100	36.00	91.00	66.4100	11.25651
Prostate volume (cc)	100	7.60	110.00	43.4580	19.35444
Serum PSA (ng/ml)	100	0.05	10.28	2.8187	1.98582
IPSS (before treatment)	100	2.00	30.00	14.7700	7.91349
IPSS (after treatment)	100	1.00	8.00	3.2200	1.92054
QOL score (before treatment)	100	1.00	7.00	3.8000	1.51090
QOL score (after treatment)	100	.00	3.00	1.2800	.76647

As per Table 6, the descriptive analysis of study variables found mean age of participants to be 66.4±11.25 years. Mean prostate volume and serum PSA were found to be 43.46±19.35 cc and 2.82±1.99 ng/ml, respectively. Mean scores for IPSS decreased considerably from 14.77±7.91 at baseline (before treatment) to 3.22±1.92 at 3-month follow-up post-treatment. This decline was also supported by patients' experiences of health-related quality of life, for which the mean scores decreased from 3.8±1.51 at baseline (before treatment) to 1.28±0.77 at 3-month follow-up post-treatment.

Correlation analysis was done between prostate volume and serum PSA with IPSS to explore their possible correlation with disease severity. A positive correlation was observed between prostate volume and disease severity with r value of 0.750. Similar correlation was observed between serum PSA and disease severity with r value of 0.742. Given the p value of <0.05, it can be inferred that both prostate volume and serum PSA had statistically significant association with disease severity.

DISCUSSION

The distribution of IPSS before treatment revealed that 26%, 43% and 31% patients were experiencing mild, moderate and severe symptoms. However, at 3-month follow-up after treatment, almost 98% patients reported mild symptom experience on IPSS, with no one having severe symptoms. Mean scores for IPSS decreased considerably from 14.77±7.91 at baseline (before treatment) to 3.22±1.92 at 3-month follow-up post-treatment. About 27.6% and 49.3% patients reported 'moderate' disease symptoms before treatment on IPSS in the <60-year and ≥60-year age-groups, respectively.

PSA is also an important indicator for differential diagnosis, which is generally less than 1 µg/l in patients in absence of clinically confirmed BPH.[7] The descriptive analysis of study variables found serum PSA levels to be 2.82±1.99 µg/l. In our study, mean prostate volume was reported to be 43.46±19.35 cc.

Quality of life frequency distribution before treatment found that about third (34%) of all participants rated their experience ranging between 'mostly dissatisfied' to 'terrible'. The post-treatment analysis for QoL found that no patients reported their experiences to be 'mostly dissatisfied' to 'terrible'. Almost 96% patients reported their health-related QoL ranging from 'delighted', 'pleased' to 'mostly satisfied' at 3-month follow-up.[5] Mean scores decreased from 3.8±1.51 at baseline (before treatment) to 1.28±0.77 at 3 month follow-up post-treatment. The pre-post comparison for patients' QoL experiences found statistically significant (p<0.001) association, with patients' experiences improving considerably at 3-month follow-up. Fisher's exact test to determine association between disease severity (IPSS) and quality of life also found statistically significant association (p<0.001).

A positive correlation was observed between prostate volume and serum PSA with disease severity with r value of 0.750 and 0.742, respectively. For a unit increase in serum PSA in (ng/ml) and prostate volume, there is expected increase of 1.73 and 0.19 units in IPSS, respectively. We also run an analysis to explore whether age can be a predictor for prostate volume and serum PSA levels. However, our analysis found that age had mild positive correlation (r=0.227) with prostate volume and weak positive correlation (r=0.14) with serum PSA levels.

A study involving ~2,400 males from India with a mean age of 62.1±9.5 years and mean IPSS of 12.2±8.6 reported mean prostate volume of 21.6±10.63 cc, which is almost half the mean levels reported in our sample. This study found higher mean IPSS values despite lower prostate volume.[14]

There is also supporting evidence which suggests that males from South-East Asia have significantly lower prostate volumes as compared to their Western counterparts.[6] A study which compared mean prostate volume in Japanese and American males aged >40-year, reported that mean prostate volume were 20.3±10.6 ml in Japanese and 29.6±13.4 ml in American males.[15]

Limitation of this study includes size of sample, limitation of resources and less patient compliance with some of the patients. Further studies are required for the same in the future to evaluate various modalities in early diagnosis and treatment of BPH.

CONCLUSION

Our study evaluated the IPSS to predict the disease severity and correlated it with quality of life, prostate volume and serum PSA. Our findings were in line with currently available evidences, and suggested that QoL, prostate volume and serum PSA are better predictors of disease severity. For a unit increase in serum PSA in (ng/ml), there was expected increase of 1.73 units in IPSS. For a unit increase in prostate volume, there was expected increase of 0.19 units in IPSS.

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