Ultrasonographic Correlation of Intravesical Prostatic Protrusion with Post-void Residual Urine among Patients with Benign Prostatic Hyperplasia in Calabar, Nigeria-a Pilot Study

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ABSTRACT

Bladder outlet obstruction due to benign prostatic hyperplasia (BPH) is a distressing situation, impacting negatively on patients' quality of life, so early detection is apt. Ultrasonography is a viable alternative to an invasive pressure flow meter for predicting bladder outlet obstruction. There is a dearth of work on the use of intravesical prostatic protrusion (IPP) as an ultrasonographic parameter in Nigeria and there might be racial variations similar to the observation with prostate volume. This study aims to sonographically assess the grade of IPP associated with significant post-void residual (PVR) urine volume. Sixty-three consecutive newly diagnosed BPH patients referred from the general outpatient department were recruited into the study over 18 months. Sonoscape A8 Ultrasound machine was used for the Trans-abdominal pelvic assessment. The measured IPP was graded as <5mm (I), 5-10mm (II) and >10mm (III) and the PVR urine volume as <50ml, 50 -100ml and >100ml. The prostate volumes were also stratified into four before correlating all the parameters. A post-void residual urine volume of 100ml was chosen as the threshold that defines obstruction due to the patients' average age (61.69 years). It was observed that 39.68% of all the patients had significant PVR urine volume. Across all prostate volume groups, only grade III IPP (>10mm) caused a significant mean PVR urine volume (111.76ml). Grade III was responsible for most of the significant PVR urine volume and 96.83% occurred at a prostate volume greater than 40ml.

Keywords: Ultrasonography, Benign Prostatic Hypertrophy, Prostatic Protrusion, Post-Void Urine Volume

INTRODUCTION

Benign prostatic hyperplasia (BPH), usually commences from the age of 40 years and is characterized by the formation of large, fairly discrete nodules in the periurethral region of the prostate gland. BPH results in enlargement and increase in the stromal smooth muscle tone of the gland which subsequently leads to bladder outlet obstruction (BOO). BOO is said to occur when there is a significant residual urine volume in the bladder immediately after voiding. The cut-off value for this significant volume is observed to be age-related and has been debated to be either above 50mls or 100mls. BOO patients may present in the clinic with a complaint of lower urinary tract symptoms (LUTS), haematuria or symptoms of urinary tract infection, bladder calculi and renal failure.[1] BOO significantly affects the quality of life, so early detection and intervention will help to preserve normal bladder function.[2] Most patients with LUTS due to BPH are initially seen by the general practitioners or primary care physicians and a lot of them initiate the medical treatment of the condition.[3-5] Management guidelines have been developed for BPH and all physicians need to be abreast with the protocol. Monitoring of BPH progression includes predicting which of the patients will develop BOO or acute urinary retention. An ideal diagnostic tool for predicting BOO should be non-invasive, cheap, reproducible and give prompt results.[6] Pressure flow studies are the gold standard for BOO assessment but they are invasive and can be complicated by urinary retention and gross haematuria.[7] These necessitated the search for non-invasive options. Ultrasonography is a viable alternative and its various parameters have been assessed for their accuracy mainly in Asia and some parts of Europe and America.[8-10] Though all the ultrasound parameters predict BOO to varying degrees, intra-vesical

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prostatic protrusion (IPP) and detrusor wall thickness (DWT) were found to be better tools than the prostate volume (PV), bladder wall thickness (BWT) and others by a majority of studies.[6,10] Results from other countries might not be applicable in Nigeria, because of the observed ethnic or racial variation in normal prostate volumes.[11,12] This variation might also exist for the grade of IPP associated with significant PVR urine volume. This has made it imperative for different ethnic nations and homogeneous groups to conduct local studies to develop their normal values of measured ultrasound parameters. The trans-abdominal approach will be utilized because it has been reported to be as accurate as the trans-rectal approach in measuring the prostatic volume.[13,14] This approach is also more acceptable by patients with low pain threshold and anal lesions like haemorrhoid, fissure or fistula-in-ano. Furthermore, though catheterization is more accurate in measuring the PVR urine volume, it is not the best option in terms of care and comfort.[15] Again, trans-abdominal ultrasonography has proven to be a reliable, alternative method of measuring PVR urine volume and thankfully it is not intrusive or invasive.[16] The ellipsoid formula for calculating volumes installed in the machine is reputable for estimating PVR urine volume,[17] as it is for prostate volume and the pre-void urine volume. Due to the pre-void volume of urine affecting the ultrasonographic evaluation of the bladder and prostate volumes, IPP and DWT, these parameters were obtained when the bladder was distended with 250-400ml of urine, for an accurate assessment and ease of comparison of results. The lower limit was chosen because the DWT is said to decrease continuously with increasing bladder filling up to 250ml and remains stable thereafter until maximum bladder capacity.[18] The upper limit prevents over distension which may displace and distort the prostate, making it volume assessment inaccurate.[14] In the same vein, measurement of IPP becomes unreliable above the upper limit but its estimation below 400ml correlates well with that obtained through the trans-rectal route.[19] This upper limit also prevents an uncomfortably full bladder which results in false positive, significant PVR urine volume, even in healthy young men. Eriz *et al.* advised that the pre-void volume should not be equal or greater than 540ml.[20] There is a dearth of data on the ultrasound assessment of IPP, particularly in correlation with an elaborate stratification of prostate volume into four groups among Nigerian men. This study aims to sonographically evaluate the IPP, PV and PVR urine volume in BPH and correlate these parameters. The grade of IPP with the propensity to result in BOO will then be determined.

SUBJECTS AND METHODS

This was a prospective observational study at a Secondary health care facility run by the Military in Calabar, Cross River state, Nigeria. The city accommodates a Teaching hospital and two public Secondary health facilities where BPH patients can be treated. The sample size for the pilot study was determined from the mean annual prevalence rate of BPH in a previous study in the city. Four hundred and sixty-three patients had confirmed diagnosis of BPH in 8 years giving an average prevalence rate of approximately 58 patients annually.[21] Five more subjects were added to this to make it 63. The 63 men aged 40 years and above, were newly diagnosed with BPH through a combination of digital rectal examination, PSA levels and sonographic features of the prostate gland. They were recruited from a single centre, over a study period of 18 months, between November 2015 and April 2017. They presented at the general outpatient clinic where the general practice physicians evaluated them. The severity of symptoms was assessed with the international prostate symptom score (IPSS) and digital rectal examination was done to assess the contour, consistency, nodal enlargement and prostate size to make a clinical diagnosis of BPH. They were subsequently sent for laboratory investigations which included prostate-specific antigen (PSA), serum electrolyte, urea and creatinine, full blood count and urinalysis.

Those with PSA levels and findings on digital rectal examination suggestive of BPH were then referred to the Radiology department for routine trans-abdominal ultrasonography. Informed consent was obtained from those who met the inclusion criteria before they were recruited into the study.

Inclusion criteria

Clinical diagnosis of BPH, PSA <4.0 ng/mL, absence of sugar, protein, nitrite or leukocyte esterase on urinalysis, normal values of full blood count and serum electrolyte, urea and creatinine and patients not yet on treatment.

Exclusion criteria

Associated Urethral stricture, Diabetic Mellitus, patients on 5 alpha-reductase inhibitors and alpha-blockers, neurological disorder, chronic renal insufficiency, prior pelvic or urinary tract surgery, prostatic or vesical carcinoma and bladder calculi.

Technique

The trans-abdominal ultrasound scans were carried out in the Radiology department using 3.5Hz curvilinear transducer of a Sonoscape A8 Ultrasound machine. The patients were instructed to drink water and were scanned when they had a moderate urge to void urine to guarantee a reasonable level of bladder filling. The patients laid in the supine position on the couch and were scanned through the supra-pubic region after application of the coupling gel. The pre-void urine volume was first measured to confirm that it was between 250 and 400mls to optimise the evaluation of the ultrasound parameters. The echotexture, outline and volume of the prostate gland were then assessed in transverse and sagittal planes. This was followed by the measurement of the IPP in the mid-sagittal plane. Finally, the patient was allowed to micturate and the PVR was assessed immediately after voiding.

The urine volume were obtained by measuring the length, width and height of the bladder lumen and prostate gland. The lengths of these organs were measured in the sagittal plane, while their width and height were measured in the transverse plane. The IPP was also measured in the midline sagittal plane. IPP is the perpendicular height of the prostate gland, from a line drawn where it adjoins the base of the bladder as shown in figure 1a and 1b. The PVR urine volume was measured immediately after voiding not exceeding 5 minutes to prevent significant refilling of the bladder. The measured IPP and PVR urine volume were put into three groups according to international standards and previous studies. The IPP grades are, I(<5mm), II(5-10mm) and III(>10mm), while the stratification for PVR urine volume was <50ml, 50-100ml and >100ml. Most of the previous studies divided the prostate volume into three or two groups. The three grade systems are <20ml, 20-40ml and >40ml or ≤30ml, 31-80ml and ≥81ml while the common two grading systems are <30ml and ≥30ml or <40ml and ≥40ml. For this study, the measured prostate volume was divided into four; 20-40ml, 41-60ml, 61-80ml and >80ml categories to capture all previous grading. These measured sonographic variables were correlated with each other and the results presented as means, frequencies and percentages.

RESULTS

The mean age of the 63 patients was 61.69 ± 9.82 years, with a range of 49-83 years. The age distribution of participants is shown in table 1. The overall mean PV was 56.18ml but most (36.51%) were between 20-40ml, followed by 41-60ml, which accounted for 33.33%. The grade of IPP increased as the mean PV increased from 38.59 to 64.44ml (table 2). The PV also correlated positively with the PVR urine volume. For the PVR urine volumes less than 50ml, the mean PV was 39.22 ± 11.60ml, for those between 50 -100ml, the mean PV was 55.94 ± 24.79ml and for those greater than 100ml, the mean PV was 74.68 ± 35.47ml. Grades I and II IPP had similar mean PVR urine volume values (between 77.00-78.00ml) which are within normal limits but this was high (111.76ml) for grade III (table

2). Table 3 summarises the number of patients in the 3 categories of PVR urine volume, according to their PV group and IPP grade. The 20-40ml PV was observed in 23 patients, 41-60ml in 21 patients, 61-80ml in nine patients and 10 patients had values greater than 80ml. It was also observed that 39.68% (N=25) had bladder outlet obstruction (PVR >100ml), 19.05% had equivocal PVR urine volume and 41.27% did not have obstruction. Generally, the grade of IPP increases with an increase in the PV and all those greater than 60ml had IPP above 5mm. The detailed frequency distribution of IPP grades amongst the PV's is highlighted in table 4. The frequency of obstruction amongst the IPP grades and PV groups are presented in table 5. Twenty percent of patients with grade I IPP, 25% of grade II and 60.71% of grade III had an obstruction. The rates of obstruction for patients with PV of 20-40ml, 41-60ml, 61-80ml and >80ml are 8.7%, 52.385%, 55.56% and 70% respectively.

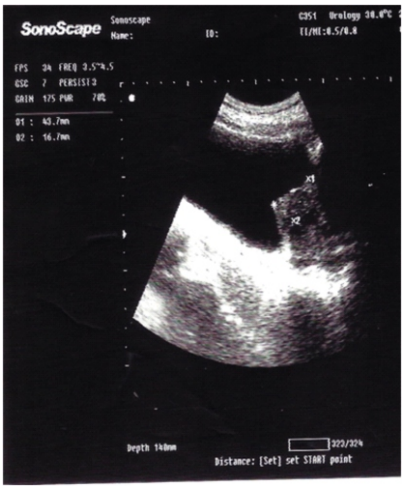

Figure 1a. Midline sagittal sonographic scan image, showing how to measure IPP; perpendicular height (line 2) from the line drawn across the base of the bladder (line 1).

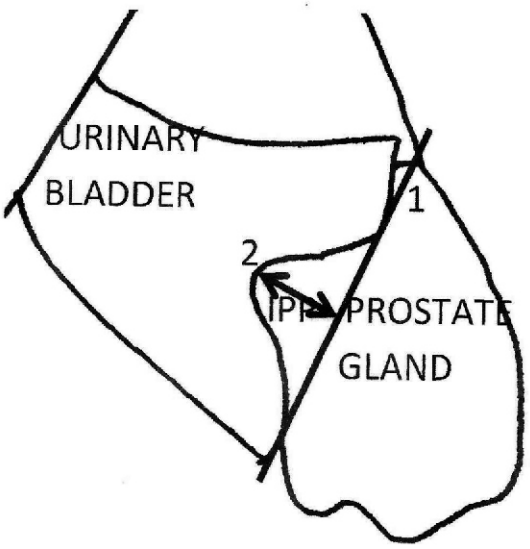

Figure 1b: Diagramatic representation of the ultrasound image showing how IPP (Intravesical prostatic protrusion) is measured.

Table 1. Age distribution of study population

Age group (years)	Frequency (n)
40-49	5
50-59	22
60 - 69	19
70 - 79	14
80 - 89	3
Total	63

Table 2. Mean PV and PVR urine volume in each grade of IPP

IPP (mm)	IPP grade	PV mean (ml)	PV range (ml)	PVR mean (ml)	PVR range (ml)
< 5	I	38.59±13.36	20.46-55.49	77.17±79.5	9.39-204.26
5-10	II	44.08±25.26	26.4-140	77.69±94.3	5.31-305
>10	III	64.44±31.28	26.9 -180	111.76±87.21	0-370

Table 3. Frequency distribution of patients according to their intravesical prostatic protrusion (IPP) grade, Prostatic volume (PV) and Post void residual (PVR) urine volume

IPP grade (mm)	PV group (ml)	Number of patients in the PVR groups (ml)			Total number
		<50	50 -100	>100	
I	20 - 40	2	1	-	3
(<5)	41 - 60	-	1	1	2
	61 - 80	-	-	-	0
	>80	-	-	-	0
II	20 - 40	10	1	-	11
(5-10)	41 - 60	4	-	3	7
	61 - 80	-	-	1	1
	>80	-	-	1	1
III	20 - 40	5	2	2	9
(>10)	41 - 60	2	3	7	12
	61 - 80	2	2	4	8
	>80	1	2	6	9
	Grand total number	26	12	25	63

Table 4. Frequency distribution of IPP grades amongst the prostatic volume

PV (ml)	Frequency distribution of IPP grades % (N)			Total % (N)
	I	II	III	
20-40	13.04(3)	47.83(11)	39.13(9)	100(23)
41-60	9.53(2)	33.33(7)	57.14(12)	100(21)
61-80	0.00(0)	11.11(1)	88.89(8)	100(9)
>80	0.00(0)	10.00(1)	90.00(9)	100(10)

Table 5. Distribution of obstruction amongst the IPP grades and PV groups

Frequency distribution of patients with obstruction in the PV groups and IPP grades % (n/N)				
	Prostate volume			
IPP Grade	20-40ml	41-60ml	61-80ml	>80ml
I	0.00(0/3)	50.00(1/2)	0.00(0/0)	0.00(0/0)
II	0.00(0/11)	42.86(3/7)	100.00(1/1)	100.00(1/1)
III	22.22(2/9)	58.33(7/12)	50.00(4/8)	66.67(6/9)

n= number of obstructed cases. N= total number of patients in the group.

DISCUSSION

A 100ml was chosen as a significant PVR urine volume to define BOO in this study, because of the average age of the patients. Among the three grades of IPP, this study revealed that only those >10mm (grade III) had a significantly high mean PVR urine volume (111.76ml) above the threshold for obstruction. This is higher than the observed cut-off value of 5mm by Reis LO *et al*, 5.5mm by Reddy SVK *et al.*, and 8.5mm by Keqin Z *et al.* who carried out their research in Asia and Latin America.[10,22,23] This study has revealed a racial variation in the IPP grade that is most likely to cause BOO, so 10mm should be used as the cut-off value for Nigerian men. IPP greater than 10mm has found relevance in patient stratification, for managing BPH and projection of its treatment outcomes. BPH patients with this grade of IPP were shown to have three times the probability to use medication than those of lower grades, and they also experience a higher rate of progression, clinically.[24,25]

The index study also shows a positive correlation between PV and IPP which is corroborated by other researchers, though the mean PV varied in the different studies.[22,26,27] Similarly, it was observed that the size of prostate gland affects the PVR; the mean PVR urine volume increased as the mean PV increased. A detailed look at the results showed that obstruction occurred among all grades of IPP but the frequency increased with an increase in PV within each grade. This study showed that 38 patients (60.31%) had grade III IPP which agrees with the 59.5% observed by Reis et al, but higher than the findings of Lee A *et al.* (31.15%), and Topazio L *et al.* (21.54%).[10,27,28] Grades I and II were observed in 7.94% and 31.75% of the patients, respectively. Grade III is responsible for 76% (N=19) of 25 patients who had obstruction, while grades II and I contributed 20% (N=5) and 4% (N=1) respectively. While evaluating each group, it was revealed that, 80% of patients with grade I did not develop obstruction which is similar to the finding of 79% by Chia et al who worked with a sample size of 200 over 30 months study period and 80.49% by Reddy SVK *et al.* who got 164 patients in 32 months.[29,22] Grade III IPP has the highest rate (50%) of obstruction in this index study, similar to, but with a much lower margin than the studies of Chia *et al.* (94%) and Reddy SVK *et al.* (83.3%).[29,22]

This study demonstrated a positive correlation between the mean PV and the degree of IPP; the higher the PV, the higher the grade of the IPP. Patients with low PV (20-40 ml), have the highest frequency (13.04%) of grade I IPP and the lowest rate of grade III IPP (39.13%). Conversely, those with prostate volume >80 ml, have the highest rate of grade III(90%) and no grade I(0%) IPP. It was also observed that PV influenced the possibility of obstruction within each grade of IPP. No obstruction occurred among patients with PV <40ml in grades I and II IPP. This study shows that it was only in grade III, obstruction occurred across all the PV groups, with the lowest rate of 22.22%, seen within 20-40ml group. These findings have shown that correlating the PV and the IPP give a better sonographic evaluation of BOO in BPH.

The limitation of this study is the sample size which might increase the margin of error.

CONCLUSION

Ultrasonographic assessment of the IPP is simple and reliable in patients with BPH having LUTS. Grade III IPP (>10mm) was responsible for most of the significant PVR urine volume (BOO) in men with a mean age of 61.69 years. PVs greater than 40ml, were responsible for most (96.83%) of the obstructions.

RECOMMENDATION

Ultrasonographic assessment of the IPP should be included in the protocol for evaluating patients with BPH presenting with LUTS. Further studies are recommended with larger sample size, possibly multicentre based, to draw more affirmative conclusions and to develop ultrasonographic IPP measurement as a predictive tool for BOO.

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