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Benign prostatic hyperplasia morphological parameters for assessing risk of acute urinary retention

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Abstract

Aim of the study: To evaluate objective measurements of morphological changes of the prostate in Benign Prostatic Hyperplasia (BPH) as predictors of acute urinary retention (AUR).

Methods: Overall 169 consecutive patients older than 50 years of age were prospectively divided into group A ($n = 61$); men with acute urinary retention (AUR), or group B ($n = 108$); men with different degrees of lower urinary tract symptoms (LUTS). Transrectal ultrasound (TRUS) measurements of total prostate volume (TPV), transitional zone volume (TZV), ratio of TZV to TPV (TZV/TPV), and vesico-urethral angle (VUA) were recorded. Group B patients also had post-void residual (PVR) and maximum flow rate (Q-max) recorded. TZV/TPV and VUA were correlated with Q-max and PVR, and a comparison was made between the two groups.

Results: Group A had significantly larger TPV ($p = 0.03$) and TZV/TPV ($p = 0.04$) compared to Group B. VUA in Group A had a significant correlation with AUR ($p = 0.02$). In Group B, both TZV/TPV and VUA had significant correlation with PVR and Q-max. A TZV/TPV cutoff ratio of 0.67 as a predictor of AUR had a 68% overall accuracy with sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 88%, 53%, 44%, and 97%, respectively. VUA of $< 90^\circ$ as a predictor factor of AUR had a 67% overall accuracy with sensitivity, specificity, PPV and NPV of 88%, 50%, 44%, and 97%, respectively.

Conclusion: Morphological changes in BPH can be objectively quantified using ultrasound by TZV/TPV and VUA. These parameters may potentially serve as predictors of AUR in patients with BPH.

Keywords: Prostate, Morphology, Urinary retention

1 Background

Bladder outlet obstruction (BOO) caused by benign prostatic enlargement (BPE) due to histologic benign prostatic hyperplasia (BPH) is common in men older than 50 years [1]. BPE is thought to be key mechanism in causing lower urinary tract symptoms (LUTS), which negatively impacts on quality of life in elderly men if left untreated. BOO due to BPH can, eventually, progress to

acute urinary retention (AUR). Therefore, any predictive model which can identify those at higher risk of developing AUR would be of clinical use to forewarn patients, and even counsel them to choose the most suitable line of treatment. Patients with morphological parameters that may predict a high chance of AUR may benefit from active treatment rather than watchful waiting.

BPH arises from enlarging spherical masses of glandular and stromal tissue from the glands surrounding the prostatic urethra. The transitional zone (TZ) and median prostatic lobe enlargement are the main prostatic areas that see such morphological changes [2]. Although it is

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an imperative initial investigation, digital rectal examination (DRE) has been shown to underestimate prostate size during routine physical examination and assessment for these changes [3]. The widely held belief that prostate size may not necessarily correlate with urinary flow rate or post-void residual (PVR) [2, 4–6] has resulted in some urologists paying little attention to prostate volume estimation during evaluation of patients with BOO. However, other studies have shown a more promising relationship between prostate volume and various symptom questionnaires [3, 7–10]. On the back of these findings, the degree of median lobe enlargement may be an important factor influencing the degree of obstruction secondary to BPH and therefore the clinical symptoms.

The aim of our study is to evaluate the objective measurements of morphological changes of prostate in patients with BPH that may predict the risk of development of AUR in these patients in a non-invasive fashion.

2 Methods

Between October 2019 and November 2021, we assessed 169 consecutive men aged ≥ 50 years of age who presented at their first visit with LUTS or AUR. We prospectively divided them into group A (n = 61; men with AUR), or group B (n = 108; men with variable degrees of LUTS).

The initial evaluations included medical history, DRE, complete physical examination, urinalysis (UA), total serum prostate specific antigen measurement (PSA) and serum creatinine (SCr). For men in group B, PVR, voiding diary and uroflowmetry assessment was performed. Plain X-Ray of Kidney-Ureter-Bladder (KUB) was used to assess for any bony abnormalities or presence of obvious urolithiasis. Transabdominal ultrasonography was used to assess upper and lower urinary tracts and for

post-void residual (PVR) measurement. In both groups, trans-rectal ultrasonography was used to measure the total prostate volume (TPV), transitional zone volume (TZV), and vesico-urethral angle (VUA) by two different operators. However, in group A, a Foley catheter was placed to relieve AUR first, then the bladder was refilled with 200 °c of normal saline before starting the transrectal ultrasound examination (Table 1).

Men who were aged < 50 years, those with a history of prostate cancer, bladder mass (other than prostatic lobe) or bladder stones, history of urethral stricture, previous pelvic surgery or trauma, previous prostate surgery, current urinary tract infection, and neurological diseases (such as Parkinson’s disease or cerebrovascular accident) were excluded from this study. Radiological findings of the urinary tract revealed 4 (7.4%) patients with renal stones, and 2 (3.7%) patients with renal cysts. These patients were included in final analysis.

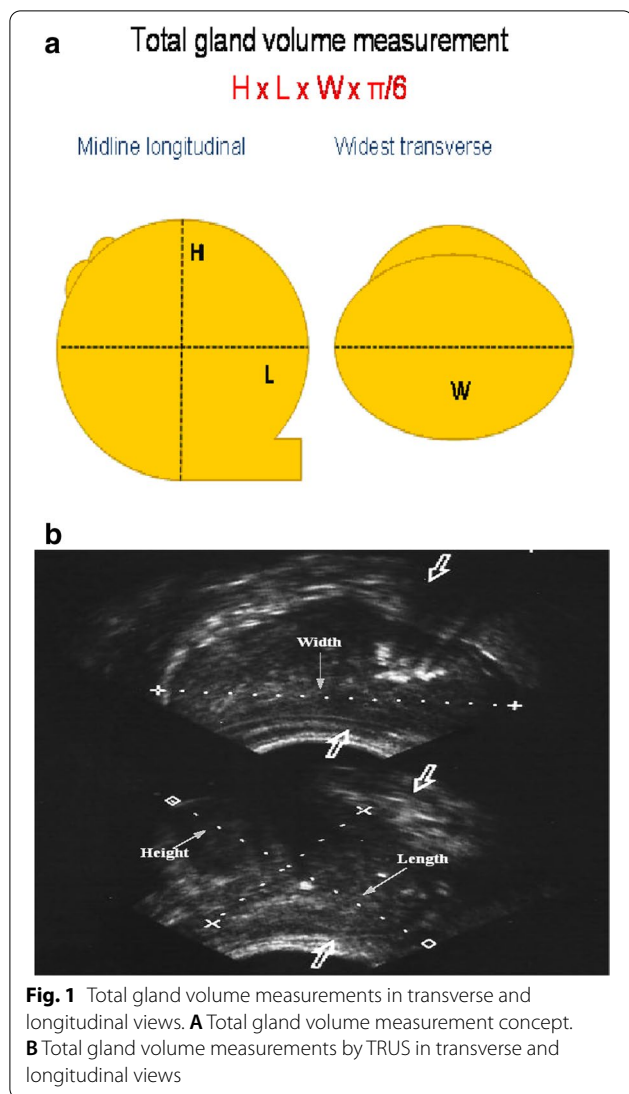
TRUS was performed using the B-K medical Hawk ultrasound scanner type 2102, and transrectal multiplanar probe 6–10 MHz B-K medical type 8551.

TPV and TZV were separately measured using height × width × length formula, where width was calculated from transverse view, and height x length were calculated from longitudinal view of the gland, Figs. 1 and 2. VUA was measured in a midline longitudinal plane between the proximal prostatic urethra and the trigone, Fig. 3.

Data were analyzed using SPSS software (Statistical Package for Social Science; SPSS Inc., IL, USA), Minitab Statistical Software (Copyright 2000, Minitab Inc.), and NCSS statistical system (2007). Comparison between groups was performed with application of Student’s T-test and ANOVA test. Accuracy was represented with sensitivity, specificity, positive predictive value (PPV),

Table 1 Comparison between two groups

Group	Age (years)	PSA (Ng/ml)	Gland (cc)	Adenoma (cc)	Angle	Foley
A: No. of cases:	61 patients					
Mean	61.721	3.46	42.262	27.770	117.902	-.44
SE of mean	0.9749	0.411	1.3983	1.1268	18.987	0.108
Median	61.000	2.60	40.000	27.000	95.00	-1.0
Minimum	50.0	0	27.0	14.0	48.0	-1
Maximum	74.0	12	74.0	54.0	910.0	1
B: no. of cases:	108 patients					
Mean	63.685	8.83	47.806	30.370	111.743	0.45
SE of Mean	0.7960	1.906	3.0687	2.3191	12.4218	0.084
Median	64.000	3.00	36.000	25.000	98.000	1.00
Minimum	45.0	0	19.0	5.0	46.0	-1
Maximum	81.0	101	166.0	130.0	810.0	1
F value	0.018	13.835	17.308	14.905	0.003	0.069
P value	0.83	0.000	0.000	0.000	0.953	0.793

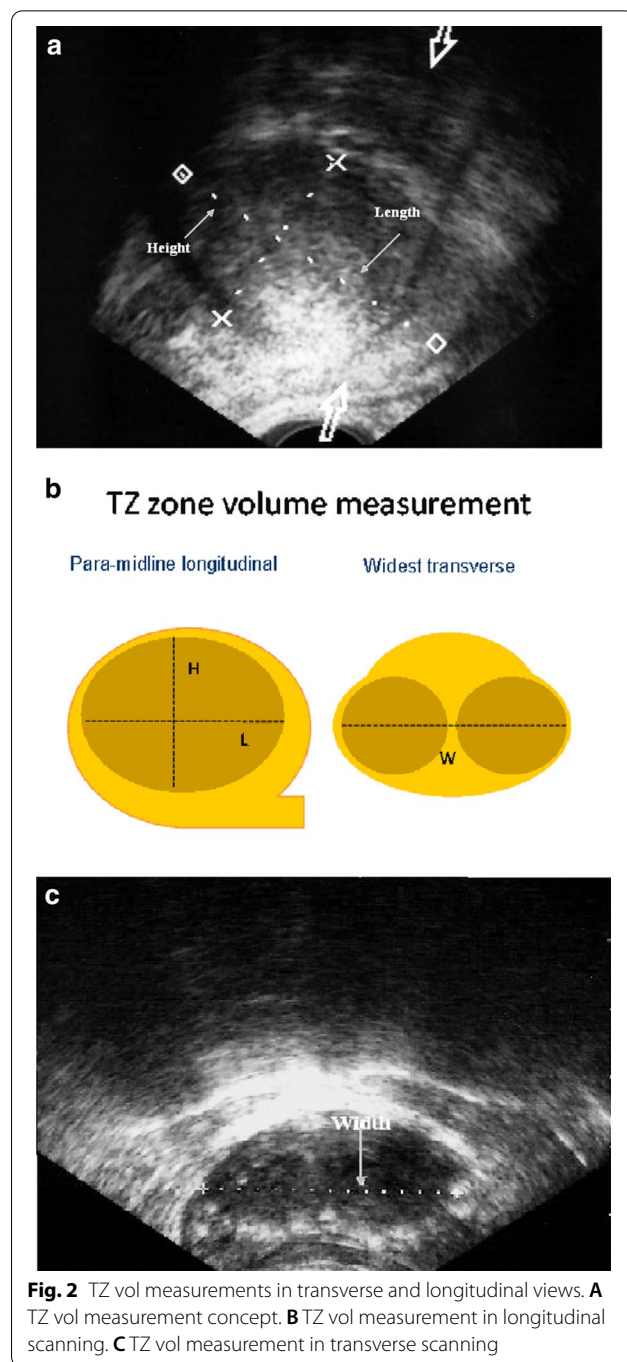


negative predictive value (NPV), and using ROC curve (Receiver Operator Characteristics curve). Correlation between various variables was established using Pearson's moment correlation coefficient (r). A probability value of (p) < 0.05 was considered significant.

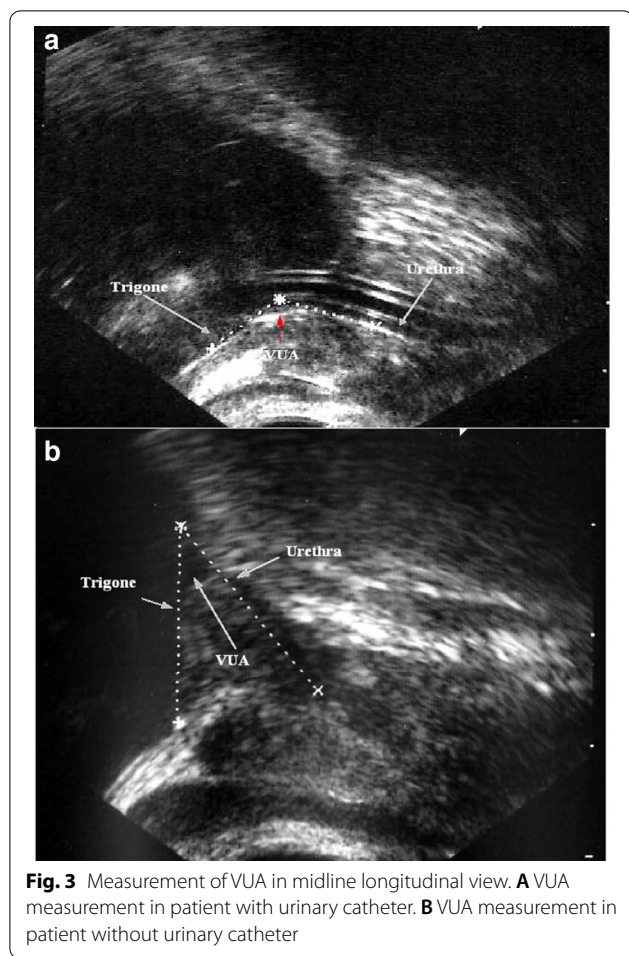
Sample size was calculated using G*power software program. Previous studies were used as references to determine the sample size (Mullhal et al., 2003). At power of 85%, sample size was calculated as 169 patients for the whole study.

3 Results

The clinical variables for the two groups are summarized in Table 1 Compared with group B, Group A patients had significantly higher PSA ($p < 0.001$), TPV



($p = 0.03$), TZV ($p = 0.003$), and TZV/TPV ($p = 0.04$). There was a significant correlation between the VUA and AUR ($p = 0.02$) (Table 1). There was no significant correlation between TPV and Q-max ($p = 0.9$), or TPV and PVR ($p = 0.94$) in Group B. However, TZV/TPV was significantly correlated with PVR ($p = 0.006$) and Q-max ($p = 0.002$). Likewise, VUA was significantly correlated with PVR ($p = 0.05$) and Q-max ($p = 0.001$).



TZV by itself was also significantly correlated with PVR ($p = 0.001$) and Q-max ($p < 0.001$) (Table 2).

We calculated a VUA cutoff value $< 90^\circ$ as a risk factor for AUR with an overall accuracy of 67%, with sensitivity, specificity, PPV, and NPV of 88%, 50%, 42%, and 97%, respectively. We also calculated a TZV/TPV cutoff ratio of 0.67 as risk factor for AUR with an overall accuracy of 68%, with sensitivity, specificity, PPV and NPV of 88%,

53%, 44%, and 97%, respectively. In sub-analyses comparisons, we found that PSA value ≥ 2.6 ng/ml provided the highest overall accuracy of 72% in predicting AUR, with sensitivity, specificity, PPV and NPV of 88%, 55%, 50%, and 98%, respectively. Also, we calculated a cutoff value for age ≥ 61 years as a risk factor for AUR with an overall accuracy of 62%, with sensitivity, specificity, PPV, and NPV of 74%, 31%, 28%, and 87%, respectively.

4 Discussion

BPH is a progressive condition where approximately 15–20% of men may experience rapid progression over 4–5 years during watchful waiting, leading to moderate-to-severe symptoms, and eventual complications such as AUR [8]. Treatment of these patients should not be focused only on relieving their symptoms, but also improving their quality of life. Until now, urodynamic studies have been the only proven objective method of assessing BOO [9, 10]. The main disadvantages of urodynamic studies include the need for urethral and rectal catheterization, which may cause partial obstruction during micturition, the possibility of introducing an infection, and discomfort that may alter the micturition reflex [11, 12]. In addition, urodynamic studies are resource intensive, time consuming and can be an invasive and unpleasant experience for the patient. As a result, development of non-invasive methods of diagnosing BOO would be widely welcomed. Our study could be a step forward in achieving this, though searching for other steps will still be needed to optimise that goal. We evaluated the objective measurements of morphological changes of prostate in patients with BPH as possible predictors of BOO, and found that the VUA and the ratio of TZV/TPV may accurately predict AUR in this cohort of patients.

Previous studies showed a weak correlation between TPV and various parameters of BOO, as well as LUTS [5, 7, 13]. Thus, urologists have been interested in other parameters such as the TZV, the transition zone index (TZI), and the prostate configuration [14, 15]. Kaplan

Table 2 Pearson correlation of Group B variables with Q-max and PVR

	Foley	Angle	Adenoma	Gland	P.S.A	Age
Foley	1	-0.015	-0.155*	-0.026	-0.001	0.014
Angle	-0.015	1	-0.063	-0.071	-0.032	-0.083
Adenoma	-0.155*	-0.063	1	0.895**	-0.055	0.171*
Gland	-0.026	-0.071	0.895**	1	-0.082	0.147
P.S.A	-0.001	-0.032	-0.055	-0.082	1	0.071
Age	0.014	-0.083	0.171*	0.147	0.071	1

*Correlation is significant at the 0.05 level (2-tailed)

**Correlation is significant at the 0.01 level (2-tailed)

et al. concluded that TZV is a more useful, significant proxy of BPH size than TPV [15]. Furthermore, there is compelling evidence that TZI correlates significantly with evaluated parameters of BPH, and may be the best proxy for BPH size and evaluation of the worsening obstruction [15].

In the Medical Therapy of Prostatic Symptoms (MTOPS) trial, TPV, PSA, Q-max, PVR and age were important predictors of the risk of clinical progression of BPH [16]. Similarly, the Proscar® Long-term Efficacy and Safety Study (PLESS) proved that the risk of AUR and subsequent prostatic surgery was higher with increasing prostate size (≥ 40 ml) and PSA (>2 ng/ml) [17]. The Boston Health Professionals survey proved that age, international prostatic symptoms score (IPSS), and sympathomimetics were associated with a higher risk of developing AUR [18]. Among symptoms, sensation of incomplete emptying, a weak stream, and frequency were the best predictors of AUR, however, Q-max and prostate volume were not assessed in the study [18].

Clearly, there are no reliable non-invasive tests that could replace the traditional urodynamic studies. Several studies reported the importance of anatomic factors in evaluating men with LUTS. Keqin et al. concluded that the degree of intravesical prostatic protrusion (IPP), which is related to the VUA measurement in our study, is valuable in predicting BOO and detrusor function in men with BPH [19]. They reported that men with significant IPP may suffer from severe obstruction and impaired detrusor function [19]. In this study, they found that the incidence of AUR in the patients with a significant IPP versus those with non-significant IPP was 33.3% and 18.0%, respectively [19]. Chia et al. suggested that IPP causes a “ball-valve” type of obstruction, disrupting the funneling effect of the bladder neck and causing dyskinetic movement of the bladder during voiding [20]. They concluded that IPP is a much better predictor of BOO in comparison to other parameters such as age, symptoms, Q-max, PVR, or TPV [20]. Kojima et al. also suggested that IPP, as determined by transabdominal US, could be a useful non-invasive predictor of BOO [21]. Finally, Lim et al. correlated IPP, PSA and TPV with PFS, and found that only IPP was independently associated with BOO [22].

Prostatic Urethral Angle (PUA) has also been described as an important factor in choosing the treatment modality and in predicting the response to treatment in patients with BPH/LUTS. Cho et al. demonstrated that PUA (which is defined as the angle formed by the proximal prostate urethra and distal prostate urethral) was inversely associated with the urinary flow rate, which can decrease by $>27\%$ as the PUA increases from 35° to 90° [23]. However, Ku et al. did not specifically find PUA to

be associated with the urinary flow rate, but a $PUA \geq 35^\circ$ was more likely to be associated with outlet obstruction than $PUA < 35^\circ$ in patients with LUTS/BPH [24]. The potential limitation of PUA as a predictor is that it may not reflect the anatomy of the prostatic urethra during voiding, since PUA is measured at resting phase and not during voiding phase, though this could also be considered a limitation to VUA measurement.

We found that TZV/TPV ratio and VUA had excellent predictive powers of worsening obstruction, especially as they are related to Q-max, but less so in case of PVR. TZV/TPV ratio of 0.67 or higher was a reliable predictor of AUR with an accuracy of 68%. We suppose that a $VUA < 90^\circ$ may be more reliable than previously studied IPP, or PUA, with an accuracy of 67%, however further comparative studies are needed to justify this assumption. In our sub-analyses, $PSA > 2.6$ ng/mL and $age > 61$ were also important and correlated with AUR. Others have also noted that patient age (>60) had a probability of 23% of AUR in the subsequent 20 years of follow up [25]. Previously at our institution, Massoud concluded that combination of patient age with quantified morphological prostatic changes could provide an accurate evaluation of the degree of obstruction and subsequent probability of AUR. In addition, TZV/TPV cutoff ratio of 0.6 in combination with age (>60) could predict AUR with an 85% accuracy [25]. Similarly, a $VUA < 90^\circ$ in combination with age had a 77% accuracy [25].

Our study was limited by the relatively small number of patients from a single institution and being operator dependent. We did not use IPSS or urodynamics during evaluation of our patients and as a result no direct comparisons could be made to these previously established standard-of-reference tests. A multi-institutional study with larger number of patients is needed to confirm our findings across different populations.

5 Conclusion

We demonstrated that morphological changes of prostate in men with BPH could potentially be objectively quantified with TZV/TPV ratio and VUA. These parameters were significantly correlated with the degree of BOO and seem to accurately predict the occurrence of AUR.

Abbreviations

AUR: Acute urinary retention; BPE: Benign prostatic enlargement; BPH: Benign prostatic hyperplasia; BOO: Bladder outlet obstruction; DRE: Digital rectal examination; IPP: Intravesical prostatic protrusion; LUTS: Lower urinary tract symptoms; NPV: Negative predictive value; KUB: Plain X-Ray of kidney-ureter-bladder; PVR: Post-void residual; PPV: Positive predictive value; PSA: Prostate specific antigen; ROC: Receiver operator characteristics; SCr: Serum creatinine; TPV: Total prostate volume; TZ: Transition zone; TZI: Transition zone index; TZV: Transitional zone volume; TRUS: Transrectal ultrasound; VUA: Vesico-urethral angle.

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Author contributions

AA, ME: Protocol/project development, Data Collection, Manuscript writing. AB: Data analysis. MS, AI, AIA: Data collection, Manuscript editing. AG: Data analysis, Manuscript editing. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations**Ethics approval and consent to participate**

Ethics approval and consent to participate: All procedures performed were in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all participating individuals in this study. Institutional Review Board, Faculty of Medicine, Minia University, Egypt, ethically approved the study on 22nd March 2021; Approval No. 10.3/2021.

Consent for publication

Not applicable.

Competing interests

No conflict of interest is declared by any of the authors.

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