Comparative Study Of Prostatic Volume And Uroflowmetry In Benign Prostatic Hyperplasia Patients With Lower Urinary Tract Symptoms

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Abstract
Objectives: To compare the influence of inner gland ratio with total gland volume of the prostate in patients with benign prostatic hyperplasia and its relationship with lower urinary tract symptoms.

Material and methods: We prospectively studied 40 clinically diagnosed cases of benign prostatic hyperplasia who were examined at the surgical out patient clinic or those who were evaluated as inpatients and scheduled for prostatectomy.

Results: In this study 30% of the total patients showed a peak flow rate of more than 15 gm/sec and 70% of the patients had peak flow rate less than 15 gm/sec signifying abnormal peak flow rate. The correlation between peak flow rate and outer gland volume was statistically significant (p=<0.01). The correlation between inner gland volume and peak flow rate which was statistically highly significant (p=<0.001).

Conclusion: In patients with lower urinary tract symptoms, knowing the relationship between outer and inner gland prostate volume and its relationship with peak flow of urine output can help to predict the degree and cause of obstruction. Larger the size of the gland, lower the peak flow rate. Higher the inner and outer gland ratio, higher is the possibility of having benign prostatic hyperplasia as the cause of urinary obstruction.

INTRODUCTION
Lower urinary tract symptoms are one of the commonest presentations in urology clinics. Benign prostatic hyperplasia has been known as a cause of urinary dysfunction and the most common disease affecting the aging men. Fifty percent of men aged 51 to 60 years and 90% of men over aged 80 years have histological evidence of benign prostatic hyperplasia (1). Clinical diagnosis of benign prostatic hyperplasia is made by the assessment of urinary symptoms, prostate size or volume and reduced urinary flow rate. Histopathologically benign prostatic hyperplasia characterized by an increased number of epithelial and stromal cells in the periurethral transition zones of the prostate.

The etiology of benign prostatic hyperplasia is not clear but androgens, estrogens stromal epithelial interaction, growth factors and neurotransmitters may play a role, either alone or in combination in the initiation of prostatic growth. Prostatic hyperplasia increases the resistance to the flow of urine. Compensatory changes in the urinary bladder function, along with age related changes in the nervous system function lead to urinary frequency, urgency and nocturia, the most troublesome benign prostatic hyperplasia related complaints. The complex symptoms commonly referred as prostatism is not specific for benign prostatic hyperplasia. Aging men with a variety of lower urinary tract pathologies may exhibit similar symptoms. Although non-specific causes of symptoms can be excluded in a significant majority of these patients on initial clinical evaluation including digital rectal examination, additional diagnostic tests are necessary in quite a number of patients where the diagnosis is still unclear.

Ultrasound of the prostate is the investigation that enables us to visualize the prostate gland directly and is one of the commonest diagnostic modalities performed now a days. It can be done using the suprapubic abdominal approach as
well as transrectal approach.

Watanabe et al first clinically applied transrectal ultrasound of the prostate in 1971 (1). Since then it is rapidly advancing with growing acceptance and importance in diagnosis and management of prostatic diseases. Transrectal ultrasound is an accurate means of assessing prostatic volume and is superior in this regard to abdominal ultrasound (2). Among several methods the diameter method is the most commonly used for determination of prostate volume. It comprises measurements of height (H), width (w) and length (L) and volume is calculated using the formula $\frac{1}{2} (H \times W \times L)$ (3).

Urodynamic studies in patient with lower urinary tract symptoms are used for objective assessment of the urinary bladder and bladder outlet behaviour. However, to decide what is abnormal it seems mandatory to agree on what can be considered normal (4). Although urodynamic studies are frequently used to evaluate voiding disorders in an elderly men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia, (5) only a few studies have included sufficient age-matched controls.

In the studies done by Robertson et al and Wyndaele of young adults, most urodynamic parameters showed large variations (6,7,8). Different and changing flow patterns, low minimal flow rate, large bladder capacity, bladder over activity and residual urine volume which are all usually considered signs of pathologic conditions, were seen. Urodynamic findings revealed a reduced urinary flow rate and increased residual urine volume with advancing age. This warrants a careful interpretation of the urodynamic variables in elderly subjects.

The above mentioned studies support the statement of Wyndaele et al since normality in urodynamic variables may include so many different features, the interpretation of urodynamic evaluation should be made with caution. To decide what is abnormal, it is important to know what can be considered normal in elderly men. Only after fully understanding the range of values seen in the normal population we can be sure of our observation of the ‘abnormal’ is genuine and relevant to clinical management (9). The association of benign prostatic hyperplasia and aging has been demonstrated repeatedly in autopsy studies (10). The prostate undergoes significant growth during fetal development, puberty and in most men during late middle age. Logistic growth analysis of benign prostatic hyperplasia lesions removed by enucleation at John Hopkins University Hospital demonstrated that the growth of benign prostatic hyperplasia is most likely initiated before the age of 30 years (10).

**MATERIALS AND METHODS**

Forty consecutive patients aged 50-86 years (mean 67.95 years) with a clinical diagnosis of BPH who were examined at the surgical outpatient clinic or those who were evaluated as inpatient and planned for prostatectomy were included in this study. Informed consent was obtained from all patient selected for the study. All patients included in this study were clinically evaluated mainly focusing on their urinary tract symptoms, history of catheterization or previous procedures and treatment history. Digital rectal examination was done and size of the prostate was estimated along with its consistency and fixity of rectal mucosa with the gland. In addition, examination of external genitalia was done to exclude meatal stenosis or a palpable urethral mass.

Uroflowmetry was performed in all patients and voiding volume, peak flow rate, average flow rate, hesitance time and voiding time were recorded. The patient whose voided urine volume was less than 150 gm were excluded from the study. The patients were advised to come in empty bladder soon after the uroflowmetry. Post-void residual urine was determined by using transabdominal ultrasound measurement using the formula for elliptical volume (transverse dimension x antero-posterior dimension x cephalocaudal dimension x $\frac{1}{2}$). The patients with less than 50 ml of post-void volume were excluded from this study.

Transrectal ultrasonography of the prostate was performed in all patients using a 7.5 MHz transrectal probe in Sonoace 8800 Medison ultrasound machine. Prostate size was measured by planimetric ultrasound with the patient resting in lateral decubitus position. The central and total prostate volume was measured directly from planimetric sections and peripheral prostate volume was defined as their differences. The central zone refers to the sonographically lucent region in the central part of cross-sectional images of the prostate. In addition to assessing the echogenicity pattern of the prostate gland, three measurements were made to calculate the total prostatic volume and central zone volume. The anteroposterior and transverse diameters were measured at the maximal dimensions, whereas the superior-inferior diameter was measured as the maximal length from the base to the apex in the midline sagittal plane. The hypoechoic central zone volume was caliper measured by one operator on static films from these baseline images, which were
optimized to measure total prostatic volume. Total prostate volume was manually reread in a similar manner and volumes were calculated with the prolate ellipsoid formula, Volume = \( \frac{1}{2} \times \text{transverse} \times \text{antero-posterior} \times \text{superior-inferior} \). Random samples of 40 prostate ultrasound films were reread. All patients included in the study underwent prostatectomy either by transurethral resection method or open retro pubic approach. Following surgery, the resected tissues were sent for histopathological examination to exclude those patients with prostatic carcinoma. Patients clinically diagnosed as benign prostatic hyperplasia and planned for prostatectomy (transurethral/open) were included in this study, whereas patients with histopathologically proven prostatic carcinoma and patients taking 5-alpha reductase blockers were excluded from this study.

**PATHOPHYSIOLOGY**

The clinical symptoms of benign prostatic hyperplasia are not simply due to a mass related increase in urethral resistance. A significant proportion of the symptom are due to obstruction and age induced detrusor dysfunction along with a variety of neural alterations in the urinary bladder and prostate. The obstruction induced changes in detrusor function compounded by age related changes in both bladder and nervous system function leads to urinary frequency, urgency and nocturia, the most troublesome benign prostatic hyperplasia related complaints.

**DIAGNOSTIC TESTS**

A detailed medical history focusing on the urinary tract and a digital rectal examination (DRE) are the preliminary evaluations which establishes the working diagnosis of benign prostatic hyperplasia. An urine analysis and measurement of serum creatinine should be performed in all patients. Several additional tests may be required or useful prior to formulating the final clinical impression and treatment plan. These include urodynamic evaluation, intravenous pyelography, cystourethroscopy, serum prostate specific antigen measurement and imaging studies to assess the volume of prostate and residual urine.

Ansari MA et al conducted a study to evaluate the usefulness of MR imaging in assessing the severity of urinary outlet stenosis in comparison with uroflowmetry and to evaluate what findings are related to the degree of urinary outlet stenosis. They found that the inner gland ratio, extent of prostate protrusion into the urinary bladder and presence and absence of surgical capsule are the most important factors to assess in the MRI evaluation of bladder outlet stenosis. The probability of outlet stenosis increases in patients with two or more of these findings. MR imaging is useful for the evaluation of bladder outlet obstruction in patients with non-stromal hyperplasia.

**NORMAL PROSTATIC ECHO PATTERNS**

Three echo levels are seen on prostatic sonographic examinations:

- Isoechoic
- Hypoechoic
- Hyperechoic

In normal young men, the normal inner gland of the prostate has generally low echogenicity compared with the outer gland. As the transition zone enlarges a distinct demarcation between these regions become clear. The transition zone produces a hypoechoic images compared with the generally isoechoic peripheral zone. Hyperechoic structures are most common characteristic of fat, corpora amylacea or calculi.

**SONOGRAPHIC APPEARANCE IN BENIGN PROSTATIC HYPERPLASIA**

The typical sonographic features of benign prostatic hyperplasia is enlargement of the inner gland which remains relatively hypoechoic to the peripheral zone. The echo patterns depends on the admixture of glandular and stromal elements because nodules may be fibroelastic, fibromascular, hyperadenomatous and fibroadenomatous. With increasing enlargement, the hypoechoic transition zone compresses the central and peripheral zones. The margin separating the hyperplasia from the peripheral zone is considered to be the surgical capsule. Ultrasound can also analyze the effect of the hyperplasia on the anterior urethra and assess median lobe enlargement. Other sonographic appearances of benign prostatic hyperplasia (BPH) include calcifications and rounded hypoechoic nodules called BPH nodule.
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Figure 1
Figure 1: Normal prostate by transrectal ultrasonography.

Figure 2
Figure 2: Benign prostatic hyperplasia including rounded hypoechoic nodules called benign prostatic hyperplasia nodule (arrow).

MEASUREMENTS OF PROSTATE VOLUME

Transrectal ultrasonography (TRUS) is now accepted as an accurate means of assessing prostate volume and is regarded superior to abdominal ultrasonography in this regard (17). There are three methods commonly used to estimate the prostate volume.

Step planimetry method, which calculates volume from the sum of sequential horizontal areas measured from the base to apex.

Diameter method which comprise measurements of height (H), width (W) and length (L) and volume is calculated using the formula $\frac{1}{2} \times H \times W \times L$ (5).

Ellipsoid method is a method available on some ultrasonography scanners that allows the operator to delineate the prostate contour transversely at the mid-gland and then define a hypothetical axis of rotation for that area with distance markers.

UROFLOWMETRY

One of the simplest and most useful urodynamic investigations is the measurement of urinary flow rate using a flow meter. In 1979, Turner Warwick et al (18) first described how the intravenous urogram might be converted to an urodynamic study by incorporating the measurement of the flow rate while the bladder is emptied at the end of the examination. This correlation of the flow rate with the post-micturition bladder residual volume adds useful information about bladder obstruction. Flow rate measurements are used now in a similar manner during ultrasonography of the lower urinary tract (19, 20). The need for reliable objective criteria for lower urinary tract symptoms is underscored by the fact that usual clinical indexes such as symptomatology, prostate size and degree of bladder trabeculation, correlate poorly with objective evidence of outflow obstruction (21, 22). The gold standard to evaluate grade of lower urinary tract symptoms is urodynamic studies with pressure-flow analysis (23). Uroflowmetry is regarded as one of the most useful urodynamic techniques for objective assessment of obstructive uropathy (14). For decades, uroflowmetry has played a major role in the evaluation of voiding complaints and helps in making decision about the need for therapeutic intervention to relieve lower urinary tract symptoms (23). Single episode of uroflowmetry may not be sufficiently reliable for the determination of lower urinary tract symptom due to benign prostatic hyperplasia because many patients are unable to relax and void in the normal fashion while at the clinic. Moreover, since variability between consecutive flow measurements and cicardian changes may be found in various voiding parameters and specifically in peak flow rate, any decision based on a single-flow measurement is questionable (26). To minimize this effect a homely and real life situation should be provided to the patients so that free uroflow values are obtained under normal conditions. Also, as we move into an era when alternatives to surgery are increasingly used to treat BPH, the times has come to consider the minimum diagnostic criteria that should be established before any medical or surgical treatment is recommended (27).

RESULTS

In this study 30% of the total patients showed a peak flow rate of more than 15 gm/sec. and 70% of the patients had peak flow rate less than 15 gm/sec. signifying abnormal peak flow rate. Twenty five percent of this patients (n=10) showed significantly low flow rate. There was a negative
correlation between peak flow rate and inner and outer gland volume that means larger the gland size lower the peak flow rate. The correlation between peak flow rate and outer gland volume showed \( r \)-value equal to -0.398 \((p<0.01)\) which is statically significant. The correlation between inner gland volume and peak flow rate in similar way showed negative correlation with \( r \)-value -0.540 \((p<0.001)\), which is highly significant. Correlation of inner and outer gland volume was obtained and found positively correlated with \( r \)-value +0.812 \((p<0.001)\) which is highly significant. There was a negative correlation between peak flow rate and inner and outer gland volume that means larger the gland size lower the peak flow rate \( (= -0.398 \text{ and } p=0.011) \). Using a maximum urine flow cutoff value of 15 ml/sec or less for predicting bladder outlet obstruction sensitivity and specificity were 73\% and 60\% respectively. The sensitivity and specificity for predicting obstruction using a prostate volume of 40 gm or more were 66\% and 64\% respectively. The correlation between peak flow rate and prostate volume obtained in this study is more significant than other studies done previously.

**DISCUSSION**

The prevalence and incidence of clinical problems secondary to and associated with benign prostatic hyperplasia have been increasing as population ages. Autopsy data, summarized by Berry et al indicate that anatomic evidence of BPH is seen in approximately 8\% of men in their 30s, more than 40\% at 50-60 years of age, more than 70\% at 61-70 years of age and more 80\% above 80 years of age. (3a)

Although a poor correlation has been observed between symptoms and prostate size or histology in an individual patients, the proportion of the male population with clinically recognizable prostatism by a given age is about the same as the proportion with pathologic evidence of benign prostatic hyperplasia (52). Bosch and associates demonstrated that the observed prevalence of benign prostatic hyperplasia in the population could vary depending on the clinical definition used (30). The lowest prevalence rate of 4.3\% occurred using a clinical definition of prostate volume greater than 30 gm and an International prostate symptom score greater than 7, a peak uroflow less than 10 gm/sec, and the presence of post voided residual urine volume greater than 50 ml. One of the commonest problems seen in elderly people attending urology clinics is lower urinary tract symptom. These patients were sent to radiology department for ultrasound for the confirmation of the cause responsible for lower urinary tract symptoms. Benign prostatic hyperplasia is one of the common diagnosis made for these patients in radiology clinics. Benign prostatic hyperplasia is a disease process affecting the aging male. Prostatic carcinoma is another differential diagnosis to be thought of however, neoplasm affecting the prostate is much less than that of benign prostatic hyperplasia. The current scientific evidences suggest that benign prostatic hyperplasia and prostatic cancer are independent entities (31). However, there have been some studies to determine their interrelationship. Armenian and colleagues, in their prospective study of 345 patients with benign prostatic hyperplasia and a similar number of age-matched controls followed for 5 years, noted that deaths from prostate cancer occurred 3.7 times more frequently than in patients with benign prostatic hyperplasia (12). In a patient with lower urinary tract symptoms, knowing the relationship between outer and inner prostate gland volume and its relationship with peak flow of urine output can help to predict the degree and cause of obstruction. Larger the size of the gland lower the peak flow rate. It will help clinicians to determine the severity of the symptoms and line of managements.. Higher the inner and outer gland ratio, higher is the possibility of having benign prostatic hyperplasia as the cause of urinary obstruction. Hyperplasia of the prostate gland is a progressive condition with an onset in the early thirties and worsening with age. There are no good epidemiological studies of the incidence of clinical prostatism at different ages. However it has been shown that 50\% of men aged 51-60 years and 90\% of men over age of 80 years have histological evidence of benign prostatic hyperplasia (3). In our study almost half of the patients were in their 7th decade and only 2.5\% of the patients were more than 80 years of age. Symptoms of benign prostatic hyperplasia may be obstructive or irritative in nature. Among the obstructive symptoms, a decreased in force and caliber of the urinary stream due to urethral compression is one of the early and constant features of benign prostatic hyperplasia. Nocturia was another commonest symptom in this study, and all patients except two had this symptom.

Prostate volume is reportedly an important contributing factor to decrease peak flow rate. In this study 30\% of the total patients showed a peak flow rate of more than 15 gm/sec. Seventy percent of the patients had peak flow rate less than 15 gm/sec signifying abnormal peak flow rate. Twentyfive percent of the patients showed significantly low peak flow rate. There was a negative correlation between peak flow rate and inner and outer gland volume. Larger the gland size lower the peak flow rate. Our study demonstrated a highly significant correlation between peak flow rate and transrectal ultrasonogaphy (TRUS) determined prostate
volume. Using a maximum urine flow cutoff value 15 ml/sec or less for predicting bladder outlet obstruction sensitivity and specificity were 73% and 60% respectively. Sensitivity and specificity for predicting obstruction using a prostate volume of 40 gm or more were 66% and 64% respectively (a).

CONCLUSION

In patients with lower urinary tract symptoms, knowing the relationship between outer and inner gland prostate volume and its relationship with peak flow of urine output can help to predict the degree and cause of obstruction. Larger the size of gland lower the peak flow rate. It will help clinicians to determine the severity of the symptoms and line of management to undergo. Higher the inner and outer gland ratio, higher the possibility of having the cause to be obstructive due to benign prostatic hyperplasia.

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