ROLE OF TRANSITION ZONE INDEX IN ASSESSING BLADDER OUTFLOW OBSTRUCTION DUE TO BENIGN PROSTATIC HYPERPLASIA

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DECLARATION

I solemnly declare that this dissertation titled "**ROLE OF TRANSITION ZONE INDEX IN ASSESSING BLADDER OUTFLOW OBSTRUCTION DUE TO BENIGN PROSTATIC HYPERPLASIA"** was prepared by me in the Department of Urology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai under the guidance and able supervision of Prof. R. Jeyaraman, M.Ch , Professor & Head of the Department, Department of Urology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai. This dissertation is submitted to the Tamil Nadu Dr.MGR Medical University, Chennai in partial fulfillment of the university requirements for the award of the degree of M.Ch. Urology.

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CERTIFICATE

This is to certify that the dissertation titled "**ROLE OF TRANSITION ZONE INDEX IN ASSESSING BLADDER OUTFLOW OBSTRUCTION DUE TO BENIGN PROSTATIC HYPERPLASIA**" submitted by **Dr.ARUN KUMAR.K** appearing for **M.Ch. (Urology)** degree examination in August 2012, is a bonafide record of work done by him under my guidance and supervision in partial fulfillment of requirement of the Tamil Nadu Dr.M.G.R. Medical University, Chennai. I forward this to the TamilNadu Dr.M.G.R. Medical University, Chennai.

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INTRODUCTION

Benign Prostatic Hyperplasia

Historically, Benign prostatic hyperplasia(BPH) has been a major focus of urologic practice and surgery. Benign Prostatic Hyperplasia is correctly defined as histological enlargement of the prostate gland from progressive hyperplasia of stromal and glandular prostatic cells. Clinical BPH refers to the lower urinary tract symptoms(LUTS) associated with benign prostatic enlargement causing varying degrees of bladder outlet obstruction.

However a simplistic causal relationship among prostatic enlargement, progressive obstruction, lower urinary tract symptoms(LUTS), retention and complications of retention has been challenged by recognition of the incomplete overlap of prostatic enlargement with symptoms and obstruction. This caused a shift in the application of various modalities of BPH management with current focus on medical management rather than surgical therapy.

Benign prostatic hyperplasia is a pathological process which contributes to, but is not the sole cause of lower urinary tract symptoms(LUTS).It is now clear that a significant proportion of patients who present with LUTS suffer from age related detrusor dysfunction

independent of benign prostatic enlargement(1).While evaluating men with LUTS, we can stratify them into mild, moderate and severe symptomatic groups according to a standardized symptom questionnaire like the IPSS (International Prostate Symptom Score)(2).

Bladder Outlet Obstruction(BOO) may itself induce a variety of neural alterations in the bladder which may contribute to symptoms. Men with benign prostatic enlargement presumably have an increase in the total prostate volume because of BPH. BPH may or may not produce clinically significant LUTS and may or may not produce urodynamically proven bladder outlet obstruction.

Histologically BPH is characterized by an increased number of epithelial and stromal cells in the periurethral area of the prostate. The precise molecular etiology of this hyperplastic process is uncertain. The observed increase in cell number may be due to epithelial and stromal proliferation or to impaired programmed cell death leading to cellular accumulation (3).Androgens, estrogens, stromal-epithelial interactions, growth factors and neurotransmitters may play a role either solely or in combination in the etiology of this hyperplastic process(3).

McNeal demonstrated that BPH first develops in the periurethral transition zone of the prostate. However, the transition zone also enlarges

with age unrelated to development of nodules. The size of the prostate does not correlate with degree of obstruction. Thus, other factors like dynamic urethral resistance prostate capsule and anatomic pleomorphism are more important in production of clinical symptoms than the absolute size of the gland (4).

While evaluating LUTS with the standardized questionnaires, in addition to mere enumeration of symptoms by frequency of occurrence; the bother associated with symptoms, interference with activities of daily living and the impact on quality of life are important distinguishing characteristics(2).

Recent studies have shown that there exists only a weak relationship between prostate size, severity of BOO and severity of symptoms (5,6). The complex of symptoms referred to as LUTS is not specific for BPH. Aging men with a variety of lower urinary tract pathological processes may produce similar symptoms. The diagnostic challenge is to establish that the symptoms are in fact, a result of BPH. This is the primary focus of initial evaluation and diagnostic testing of prostate.

Digital Rectal Examination(DRE) establishes the approximate size of the prostate gland, although its reliability across observers is

considered poor (7). In addition, DRE underestimates the size of the prostate by 25 to 50% when compared with ultrasonogram(7). Ultrasound, either transabdominal or transrectal are more accurate in assessing prostate size(8).

Transrectal ultrasound (TRUS) volume measurements using prostate ellipsoid volume formula are the most widely accepted measure of prostate volume with reasonable statistical performance when measured by several well trained examiners(9).TRUS measured prostate volume has been found to increase slowly and steadily with advancing age(10). MRI prostatic volume is 10% larger when compared to TRUS. The total prostate volume increases from 25ml in 40 yr old patients to 45ml in 70 yr old patients. The transitional zone volume increased from 15 to 25 ml for similarly aged men (11).

Infravesical obstruction can be measured only by invasive pressure flow studies. Uroflowmetry or free flow rates promise at best an indirect measure for the probability of obstruction being present. It is commonly accepted that a maximum flow rate of greater than 15ml/sec indicates low probability of obstruction when compared with a flow rate of less than 10 ml/sec which indicates high probability (12). However, its utility is low as flow rate is dependent on voided volume. There is no single

universally accepted nomogram. A high degree of day to day variability and diurnal variation further reduces its usefulness in defining disease.

Pressure flow studies are most useful for distinguishing between urethral obstruction and impaired detrusor contractibility(13).The inclusion of pressure flow studies in preoperative evaluation and indications for surgery reduced the failure rate from 28 to 12%(14). Due to absence of strong correlation between symptom scores, maximal flow rate and prostate volume, recent attention has been focused on co-relations between the transition zone of the prostate and physiologic measures of obstruction. Kaplan and co-authors first reported a strong co-relation between transition zone volume and symptoms along with peak urine flow and unexpectedly also with detrusor pressure at peak flow(15). Invasive pressure flow studies are not performed in community based studies and thus comparative data from population based studies are not available.

Data from Olmstead county study suggest no stronger co-relation between symptoms and peak flow rate with transition zone volume than with total prostate volume (11). The TZ index weakly correlated with AUA symptom index and peak flows in a large BPH treatment trial(16).

Therefore the correlation between non invasive markers of BOO in BPH are modest in community based population studies and weak in BPH trial populations. We thus decided to restudy the role of transition zone index in the Indian population in comparision with other noninvasive markers of obstruction like uroflowmetry, postvoid residual urine, prostate volume and detrusor wall thickness. The performance characteristics of transition zone index when compared to the gold standard pressure flow studies was also analysed.

AIMS AND OBJECTIVES

- The primary objective of our study was to evaluate the role of transition zone index in assessing bladder outflow obstruction due to benign prostatic hyperplasia.

- The secondary objective was to determine correlation of transition zone index with IPSS score, Abrams-Griffith number and urinary flow rates

REVIEW OF LITERATURE

Benign Prostatic Hyperplasia (BPH) is correctly defined histologically as enlargement of the prostate gland from progressive hyperplasia of stromal and glandular prostatic cells. Clinical BPH refers to the lower urinary tract symptoms(LUTS) associated with benign prostatic enlargement causing varying degrees of bladder outlet obstruction.

Etiology

BPH is characterized histologically as a progressive enlargement of the prostate gland resulting from a nonmalignant proliferative process that includes both epithelial and stromal elements. Growth results from proliferation of fibroblasts or myofibroblasts and epithelial glandular elements near the urethra in the transition zone of the prostate gland. The hyperplastic process is multifocal and exhibits a variegated histology with variable proportions of stromal nodules and glandular hyperplasia(17).

Endocrine factors

Androgens are not only required for normal proliferation and differentiation but also to actively inhibit cell death. In experimental BPH produced by androgens, despite a significant increase in gland size, there

is actually a reduction in the rate of DNA synthesis (18). It is known that the prostatic levels of dihydrotestosteroneand androgen receptors remain high with aging despite the fact that peripheral levels of testosterone are decreasing. Ninety percent of prostatic androgen is in the form of dihydrotestosterone which is more potent and binds with greater affinity to the androgen receptor. The hormone receptor binds to specific DNA sites in the nucleus which results in increased transcription of androgen dependent genes and ultimately stimulation of protein synthesis (19). Androgen withdrawal may exert its effect on prostate through vascular effects, inactivation of key androgen dependent genes like PSA and activation of key genes involved in programmed cell death (20).

Apoptosis

Programmed cell death is a physiologic mechanism crucialto the maintainence of normal glandular homeostasis. Apoptosis occurs without activation if the immune system but requires RNA and protein synthesis. Following castration,active cell death is increased in luminal epithelium as well as in distal region of ducts which is modulated by the TNF-β family of cytokines (21).

Embryonic Reawakening Theory

The prostatic stromal and epithelial cells maintain a paracrine type of communication. BPH may be due to a defect in the stromal component that normally inhibits cellular proliferation, resulting in a loss of the normal braking mechanism. The process of new gland formation in the hyperplastic prostate suggests a “reawakening” of embryonic processes in which underlying prostatic stroma induces epithelial cell development (22).

Growth Factors

Growth factors are small peptide molecules that stimulate, or in some cases inhibit, cell division and differentiation processes. Cells that respond to growth factors have on their surface receptors specific for that growth factor that in turn are linked to a variety of transmembrane and intracellular signaling mechanisms. Interactions between growth factors and steroid hormones may alter the balance of cell proliferation versus cell death to produce BPH. Lawson's group was the first to demonstrate that extracts of BPH stimulate cellular growth. This putative prostatic growth factor was subsequently found on sequence analysis to be basic fibroblastic growth factor (b-FGF) (23).

Other Signaling Pathways

Sympathetic signaling pathways are important in the pathophysiology of LUTS. There is increasing evidence that sympathetic pathways may be important in the pathogenesis of the hyperplastic growth process. Alpha blockade, in some model systems, can induce apoptosis. Alpha-Adrenergic pathways can also modulate the smooth muscle cell phenotype in the prostate. All the components of the renin-angiotensin system (RAS) are present in prostatic tissue and may be activated in BPH (24,25).

Anatomy of BPH

The proposed organization of the fetal, newborn, and adult prostate into discrete lobes has been regarded with skepticism .With a focus on the development of benign prostatic hyperplasia (BPH), Franks conceptualized a prostate with an inner (urethral) and outer glandular configuration (26). McNeal and Lowsley suggested that the urethral (inner) glands should be considered separately from the prostate and its intrinsic architecture (22,27). However, the major physiologic and biochemical similarities of these glands and those of the prostatic parenchyma weigh against this concept. Tissell and Salander, who used meticulous dissection techniques, observed subdivisions of the prostate

gland that had several similarities to those reported by McNeal, but they interpreted these as evidence for the existence of prostatic lobes(28).McNeal observed that the urethra separates the prostate into ventral (fibromuscular) and dorsal (glandular) portions. McNeal separated the glandular prostate into four distinct regions: peripheral zone, central zone, transition zone, and periurethral gland region. The peripheral zone constitutes approx 75% of the glandular prostate.Its ductal system enters the urethra along the posterolateral recesses of the urethra and extends from the verumontanum distally to the prostatic apex. The wedge-shaped central zone, the base of which is positioned superiorly at the bladder neck, occupies approx 20% of the glandular prostate. Its ductal network closely follows the ejaculatory ducts to the urethra and empties adjacent to orifices of the ejaculatory ducts on the apex of the verumontanum(22). The transition zone, accounting for 4–5% of the adult glandular prostate, is not well defined in the prepubertal prostate. It consists of two modest lobules of paraurethral tissue anterior to the peripheral zone. Its ducts empty in the posterior lateral recess of the urethra just proximal to peripheral zone ducts. The transition zone is lateral to McNeal's preprostatic sphincter, a smooth muscle cylinder enveloping the proximal urethra from the bladder neck to the base of the verumontanum. The last anatomically discrete area within the glandular prostate is the periurethral

gland region, which represents less than 1% of the total volume of the glandular prostate. Its ductal network represents a more proximal extension of the networks of the peripheral and transition zone areas. These regions have differing acinar, stromal, and cellular configurations. McNeal postulated that the anatomic and histologic similarities of the peripheral andtransition zones and periurethral gland region were attributable to a common urogenital sinus embryonic origin (22).The anterior fibromuscular stroma forms an apron that extends distally, covers the entire anterolateral aspect of the glandular prostate, and is responsible for the anterior convexity of the prostate gland. It represents approximately one-third of the tissue within the prostate capsule (29). This unusually distinct area, composed predominantly of smooth muscle fibers, maintains continuity proximally with the detrusor muscle fibers of the bladder neck. Contraction of the circular smooth muscle of the bladder neck and preprostatic sphincter assists in the elimination of secretions within the prostatic urethra; this smooth muscle probably forms the major working element of the internal urethral sphincter. The anterior and anterolateral aspects of the prostate contain smooth and skeletal muscle, joining the fibers of the external sphincter and augmenting urinary control (30).

McNeal demonstrated that BPH first develops in the periurethral transition zone of the prostate. Although early TZ nodules appear to occur either within or just adjacent to preprostatic sphincter, as the disease progresses and the number of small nodules increase, they can be found in any portion of the transition zone or periurethral zone. However, the transition zone also enlarges with age unrelated to development of nodules. The size of the prostate does not correlate with degree of obstruction. Thus, other factors like dynamic urethral resistance prostate capsule and anatomic pleomorphism are more important in production of clinical symptoms than the absolute size of the gland (4,22).

Natural history of BPH

The first pathologic evidence of BPH occurs in less than 10% of men in the 31- to 40-yr-old group(26,31). Thus, either the initiating factor is present in most men of this age and only clinically evident in a few, or young men with recognizable BPH have a discrepancy between physiologic and chronologic aging. Evidence of histologic and anatomic BPH increases with age; by the ninth decade approx 90% of men have histologic evidence of BPH, and more than half have anatomic evidence of BPH (31). The initial lesion of BPH typically occurs in the periurethral area proximal to the verumontanum. Although descriptions of the ductal

and glandular structure of this area vary, it is generally agreed that BPH arises from an inner set of prostatic ducts and glands that reside within the urethral wall or adjacent to it. The paraurethral portion of this tissue comprises approx 5% of the normal gland and is designated the transition zone. However, once the process is initiated, all elements of the normal prostate, both stromal and glandular, participate to a variable degree in its progression. Glands in the hyperplastic nodules have the capacity to bud and form new ducts and acini; in contrast to normal tissue, these new glandular elements grow toward each other. Both the average weight of the prostate and the incidence of prostatectomy by decade suggest that once BPH develops, it is progressive in most men (32).

Effect of BPH on the bladder

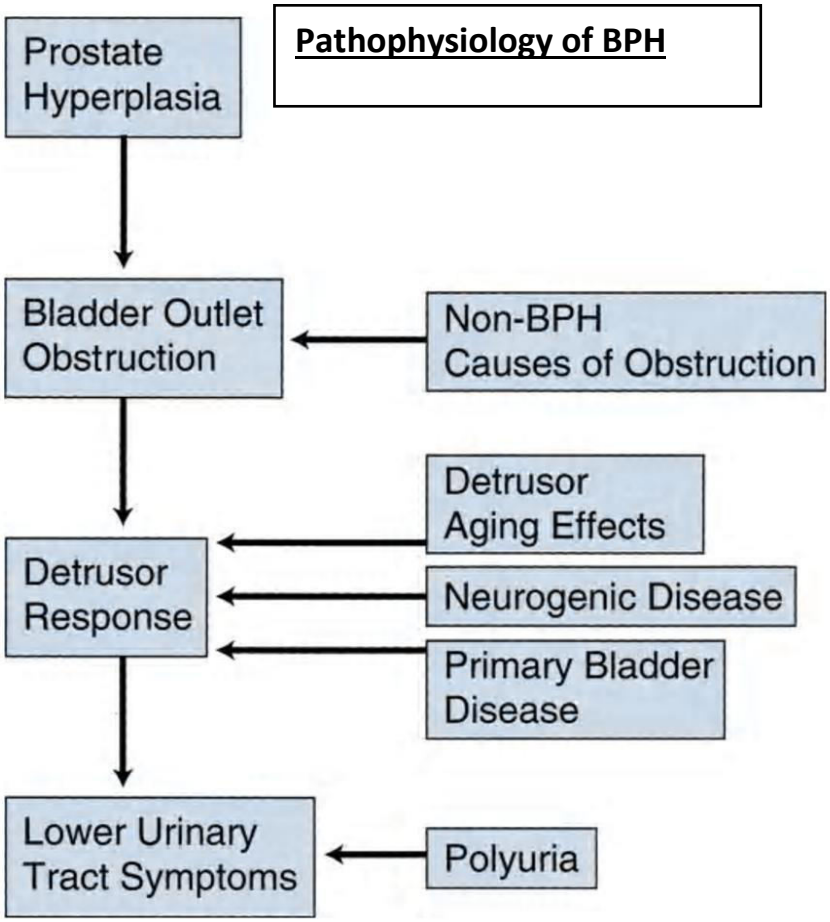
The development and progression of mechanical obstruction from the prostatic mass has been the traditional focus regarding the sequelae resulting from BPH. The perception that the mass and configuration of the hyperplasia dictated the degree of outflow blockage undoubtedlyresulted from early experience treating patients with acute and chronic urinary retention. Renal failure, urinary tract infection, and calculi were common indications for various approaches to relieve bladder neck obstruction. The reversal of these serious secondary

phenomena and restoration of improved voiding patterns reinforced the mass concept. Failures in both of these therapeutic goals were overshadowed by the frequent correction of the problems that existed. In the last 20 years, intrinsic prostatic tension from contracting prostate stromal smooth muscle and/or extrinsic tension on the BPH prostate mass by a contracting prostate capsule have been proposed as having potentially important roles in primary or persistent bladder outlet obstruction(33, 34, 35).The proposed role of stromal smooth muscle-mediated increased intrinsic prostate tension has been reinforced substantially by in vitro physiologic and, to a lesser degree, by clinical observations with both α-adrenergic agonists and antagonists(34). The proposed role of peripheral capsular tension on bladder outlet obstruction is supported by the results of transurethral incision(36). Although α - agonist mechanisms may adversely impact voiding in a variety of ways that may complement the effects of BPH treatment, these secondary phenomena are unlikely to play a direct role in the primary BPH-mediated effects on voiding.

BPH-mediated bladder outlet obstruction results in a series of changes in bladder tissue mass, composition, and function. It also affects blood supply and nerve status and function. The degree and persistence of the obstruction is thought to play a pivotal role in the subsequent

anatomic and functional bladder effects. Obstruction can be the primary source of physiologic change, with results varying from hyper function and hyperirritability to nonfunction or atony. Evaluation of this spectrum of functional states can be difficult and confusing. Consequently, evidence of bladder changes associated with outflow obstruction is derived largely from observations in animals. In general, partial bladder obstruction initially results in reversible detrusor hypertrophy and increased bladder weight (37). The increased muscle mass is associated with increased intravesical pressure (38). The human models develop a thickened, trabeculated bladder in response to outflow obstruction. Moreover, obstruction is associated with increased collagen deposition and decreased compliance(37). Rabbits with bladder outlet obstruction show changes in detrusor muscle myosin phenotype, suggesting a trend to a dedifferentiated phenotype(37).The anatomic and physiologic alterations that occur in response to obstruction probably play a major role in the specific bladder and renal changes that occur in individual patients. Currently, loss of bladder compliance is most likely the principal factor in producing upper urinary tract functional and anatomic damage. Cellules, saccules, and diverticula are recognized related anatomic bladder changes that develop and progress unpredictably and may have clinical significance. Based on their extensive experience with the

pathophysiology of obstruction-induced bladder changes, Levin et al. suggested that bladder outlet obstruction should be relieved as soon as possible after diagnosis to maximize the opportunity for bladder recovery (37).



Other Causes of LUTS

Other causes of these symptoms gleaned from the history include urinary tract infection, prostatic obstruction, BPH, bladder cancer, prostate cancer, urolithiasis, urethral stricture disease, and neurological causes (e.g, Parkinson disease, cerebrovascular accident). In patients

experiencing urinary frequency or polyuria, the symptoms may be caused by nonurological conditions, such as polydipsia, diabetes mellitus and diabetes insipidus. Similarly, nocturia may be associated with factors other than prostatic obstruction or BPH, including detrusor overactivity, sensory urgency, abnormal drinking patterns, congestive cardiac failure, venous insufficiency, or polydipsia. The use of prescription drugs and over the counter medications should be discussed because some medications affect detrusor contractility (eg, anticholinergics) or increase bladder outflow resistance (eg, alpha agonists). Bladder diaries and symptom questionnairesare useful as adjuncts to information acquired in the history (34).

NON INVASIVE ASSESSMENT OF BENIGN PROSTATIC HYPERPLASIA-

Digital Rectal Examination (DRE)

A DRE and a focused neurologic examination should usually be performed to detect prostate or rectal malignancy, to evaluate anal sphincter tone and to rule out any neurologic problems that may cause the presenting symptoms(36). In addition, examination of the external genitalia is indicated to exclude meatal stenosis or a palpable urethral mass, and an abdominal examination is necessary to exclude an

overdistended, palpable bladder. The presence of induration is as important a finding as the presence of a nodule and should be correlated with a serum PSA value so that the need for prostatic biopsy can be assessed.

DRE establishes the approximate size of the prostate gland. In patients who choose or require either medical or invasive therapy, estimation of prostate size is important to select the most appropriate pharmacologic or technical approach. Prostate size does not correlate precisely with symptom severity, degree of urodynamic obstruction, or treatment outcomes (7). If a more accurate measurement of prostate volume is needed to determine whether to perform open prostatectomy rather than transurethral resection of the prostate (TURP), ultrasound (transabdominal or transrectal) is more accurate than cystourethroscopy. It is now established that a larger gland is associated with a greater risk of disease progression and AUR (39).

Symptom Scores in LUTS

Questionnaires are especially useful in evaluating patients in that they offer the patient and the physician an opportunity to efficiently record the nature, frequency of occurrence, severity, and degree of bother of the patient's LUTS. Merely reading the questionnaire makes the

patients think more intently about their symptoms, but not all patients are compliant. Some do not answer the questions at all; others answer them without even thinking; and some do not understand the questions and answer them incorrectly. It is important, therefore that the patients be specifically queried for the accuracy of their answers.

The International Prostate Symptom Score(IPSS) also known as the American Urological Association Symptom Index has been recommended for the assessment of severity of patients' LUTS. The IPSS was developed by the Measurement Committee of the AUA (2). Each question on the IPSS can yield 0 to 5 points, producing a total symptom score that can range from 0 to 35. This seven-question set is internally consistent (Cronbach's alpha, 0.85) and reliable (test-retest correlation, 0.93). The index correlates strongly with patients' global ratings of their urinary difficulties (r = 0.78) and is sensitive to treatment response. The AUA score can be divided into "mild," "moderate," and "severe" symptom categories (2).Symptom impact on a patient's lifestyle must be considered as well. An intervention may make more sense for a moderately symptomatic patient who finds his symptoms very bothersome than for a severely symptomatic patient who finds his symptoms tolerable. Although the IPSS correlates well with quality of

life measures (40), there is still a need for sensitive BPH-specific quality of life instruments.

The Overactive Bladder Symptom Score, the Urgency Perception score and the Urgency Perception scale are the 3 questionnaires that focus on urgency associated symptoms, and these are useful in determining patient response to treatment. In addition, the Patient Global Impression of Improvement questionnaire is a simplistic assessment of how the patient feels after treatment, and it does not evaluate LUTS specifically. The King's Health Questionnaire which is not a symptom score, focuses on the bother owing to LUTS and incontinence and on overall quality of life, including personal, social, and emotional perspectives(41).

Some questionnaires double as outcome instruments in assessing response to treatment. For example, LUTS Outcome score is used in patients receiving treatment for LUTS, and it combines subjective and objective parameters(42). This score may easily be ciphered with the data derived from the IPSS, uroflow, postvoid residual volume, voiding diary, and a single question regarding whether treatment administered resulted in cure, improvement, or same or worse status.

The voiding diary is an essential part of the workup; the time and volume of each void and a description of associated LUTS should be

noted. The voiding diary differs from a simple frequency-volume chart in that it not only incorporates frequency, voided volume, urge episodes, pad usage, and fluid intake but also includes data related to patient activities and allows patients to have a more thorough self-evaluation of their LUTS. Above all, the voiding diary allows the physician to assess a patient's voiding patterns (i.e., frequency, nocturia, incontinent episodes) during his ordinary life activities. The maximum voided volume gleaned from the diary is useful as a guide for determining the optimal infusion rate during cystometry and for estimating the minimum volume that should be infused. For routine clinical practice, a 24hr voiding diary will suffice(43).

Serum Prostate-Specific Antigen

Prostate cancer can lead to LUTS by producing bladder outflow obstruction similar to BPH. Moreover, prostate cancer commonly coexists with BPH. In most men with a 10-year or greater life expectancy, the knowledge of concomitant prostate cancer may well alter management of the BPH component. The detection of a large nodular prostate cancer on DRE would no doubt alter therapy; however, the "early detection" of small volume prostate cancer in an 80-year-old man is unlikely to increase life expectancy. A PSA test and DRE increase the

detection rate of prostate cancer over DRE alone. Therefore, measurement of the serum PSA value should be performed in patients in whom the identification of cancer would clearly alter BPH management (44). There is significant overlap between the serum PSA values of men with BPH and men with clinically localized prostate cancer. Twenty-eight percent of men with histologically proven BPH have a serum PSA greater than 4.0 ng/ml (36). Serum PSA trends over time (PSA velocity), measurement of free versus complexed PSA, and PSA density may help to improve the specificity of PSA in men with BPH.

In the absence of prostate cancer the PSA value can provide a guide to prostate volume and also provide an indication of the likelihood of response to pharmacotherapy with a 5α-reductase inhibitor.

Uroflowmetry

Uroflowmetry involves the electronic recording of the urinary flow rate throughout the course of micturition. It is a common, noninvasive urodynamic test used in the diagnostic evaluation of patients presenting with symptoms of BOO. The results of uroflowmetry are nonspecific for causes of the symptoms. For example, an abnormally low flow rate may be caused by an obstruction (e.g., hyperplastic prostate, urethral stricture, meatal stenosis) or by detrusor hypocontractility. The Agency for health

care policy and research (AHCPR) Guideline Panel concluded regarding uroflowmetry that (36):

The peak flow rate (PFR; Qmax) more specifically identifies patients with BPH than does the average flow rate (Qave).

Flow rate recording is the single best noninvasive urodynamic test to detect lower urinary tract obstruction. Current evidence, however, is insufficient to recommend a given “cutoff” value to document the appropriateness of therapy.

A Qmax of less than 15 mL/s does not differentiate between obstruction and bladder decompensation.

The Fourth International Consultation on BPH concluded that flow rate measurement represents a reproducible way to quantify the strength of the urinary stream and, when used in combination with symptom scores for a small subset of patients (20%), has a high probability of correctly characterizing whether there is BOO (44).

Scott and coworkers (1967) and Shoukry and associates (1975) found that Qmax correlated better than symptoms with the presence or absence of obstruction as determined by pressure-flow studies(45,46).Qmax appears to predict surgical outcome in some studies.

In one study reported by Jensen and coworkers (1984), 53 patients underwent prostatectomy based on clinical indication alone. All three groups according to level of Qmax experienced improvements in their symptom score after surgery, but the group with a Qmax less than 10 mL/s before treatment had a better overall subjective outcome as assessed by global subjective judgment(47).Very low rates do not appear to portend poor treatment outcome. In one study of 84 patients undergoing surgery for symptomatic BPH, patients with a preoperative Qmax less than 7 mL/s improved symptomatically as much as patients with a Qmax greater than 7 mL/s(48).

Postvoid Residual Urine

Postvoid residual (PVR) urine is the volume of fluid remaining in the bladder immediately after the completion of micturition. Studies indicate that PVR urine normally ranges from 0.09 to 2.24 mL, with the mean being 0.53 mL (49). Seventy-eight percent of normal men have PVRs of less than 5 mL, and 100% have volumes of less than 12 mL (50). The AHCPR BPH Guideline Panel reached the following conclusions regarding PVR (36):

Residual urine volume does not correlate well with other signs or symptoms of clinical BPH

Large residual urine volumes may predict a slightly higher failure rate with a strategy of watchful waiting. However, the threshold volume defining a poorer outcome is uncertain.

Residual urine volume can be measured with sufficient accuracy noninvasively by transabdominal ultrasonography. The measurement variation caused by the method is less than the biologic range of PVR variation.

The Fourth International Consultation on BPH, initially recommended PVR determination in the initial assessment and during monitoring of patients under watchful waiting or other conservative treatment regimens (44).

PVR measurement can be performed by noninvasive (ultrasound) and by invasive (catheterization) methods. The most common method is by ultrasound. Invasive techniques are accurate if performed correctly but carry a small risk of discomfort, urethral injury, UTI, and transient bacteremia (which has not been quantified in the literature). The test-retest reliability of PVR volume is poor, regardless of the techniques used. Although repeated measurements may minimize the error, this is either costly (noninvasive techniques) or uncomfortable (invasive techniques) for the patient. Birch and coworkers (1988) reported that of

30 men with PBH, 66% had wide variations in PVR when three measurements were done on the same day. In 34% of patients, there was no difference among the three measurements. In 58%, at least two volumes were significantly different. In 8% of patients, all three were different. In most patients, two measurements were statistically similar whereas the third one yielded quite different results. They also found no correlation between the amount of residual urine and any cystoscopic or urodynamic findings, symptoms or the presence or absence of a history of UTIs(51).

Most clinical studies demonstrate minimal correlation between PVR and baseline measurements of symptoms, flow rate, or urodynamic measures of obstruction (52).

However, Neal and associates (1987) found a significant association in 253 men between PVR, age, “below normal” Qmax, and high urethral resistance. Low voiding pressure, however, did not correlate well with PVR. The authors concluded that outflow obstruction is related to the development of increasing amounts of PVR urine(53). In the AUA Outcome Study, Barry and colleagues (1993) found a significant correlation between high PVR and low flow rates but no correlation with IPSS(54).

High PVR does predict a slightly higher failure rate for watchful waiting. In summary, PVR is best viewed as a “safety parameter.”Men with significant PVRs should be monitored more closely if they elect nonsurgical therapy.

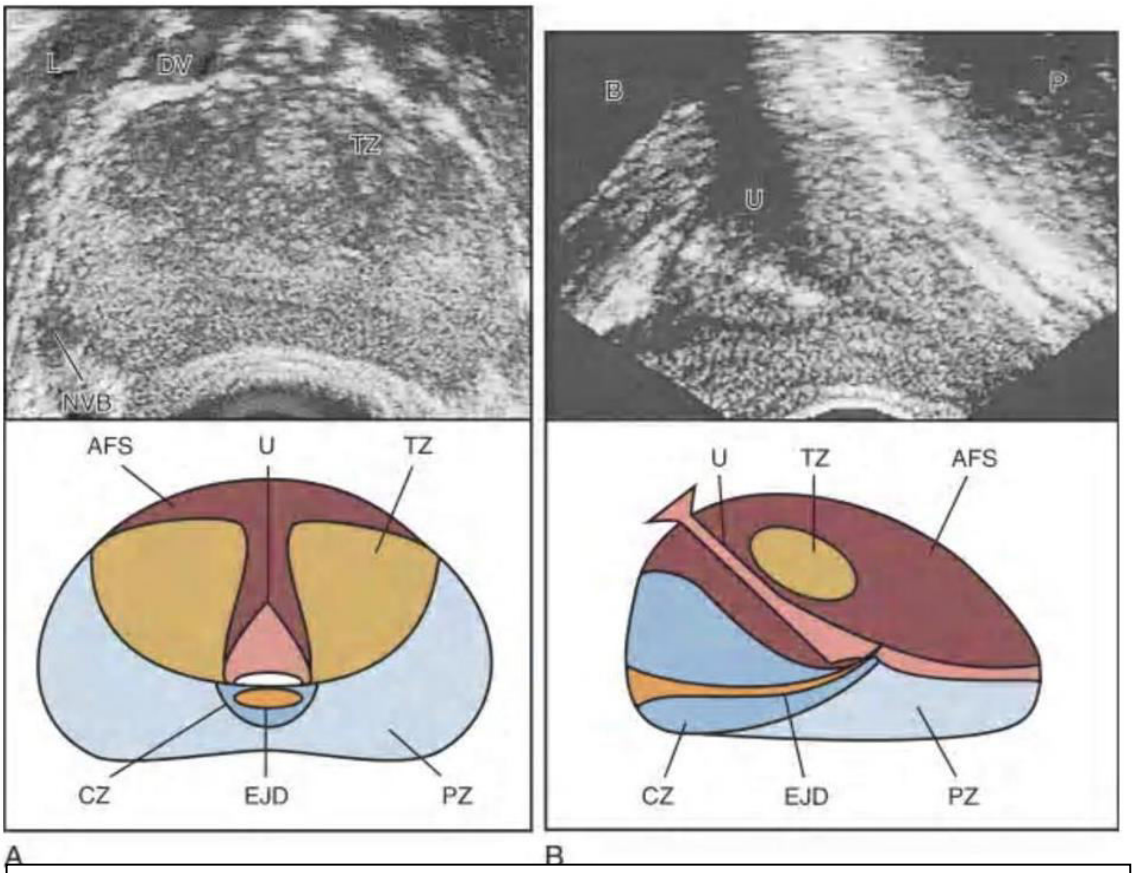
Ultrasound of the Prostate

TRUS of the prostate, first described by Wantanabe and colleagues in1968, was expanded to routine clinical use with improvements in ultrasound technology and the introduction of the TRUS-guided systematic sextant biopsy protocol by Hodge and associates (55). TRUS technology has become a mainstay of many image-guided prostate interventions, including prostate biopsy, brachytherapy, cryotherapy, and high-intensity focused ultrasound (HIFU), as well as being used in the evaluation of appropriate patients for treatment of benign prostatic hyperplasia.

Ultrasonographic Anatomy of the Prostate

The prostate lies between the bladder neck and the urogenital diaphragm, just anterior to the rectum, an ideal position to be imaged via TRUS. The prostate gland is traditionally described based on a pathologic zonal architecture. These divisions consist of the anterior fibromuscular stroma (AFS) that is devoid of glandular tissue, transition zone (TZ), central zone (CZ), periurethral zone, and peripheral zone (PZ). Unfortunately, these regions are not visible sonographically as distinct

entities. Figure showing the normal TRUS anatomy of the prostate and also the zonal anatomy at the level of verumontanum.

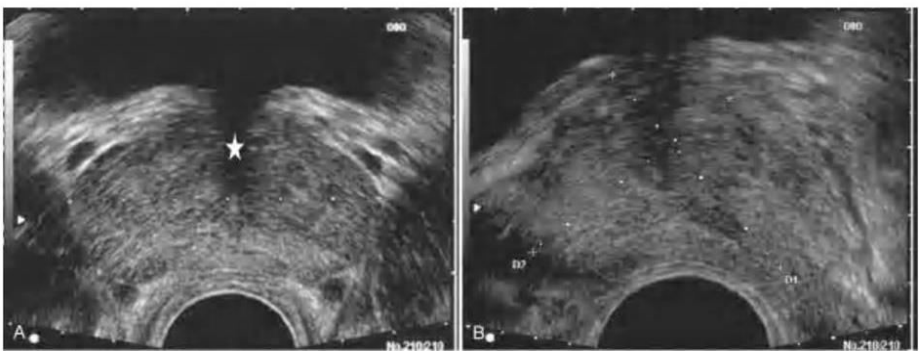


TRUS anatomy of prostate: AFS- anterior fibromuscular stroma , CZ-central zone, PZ-peripheral zone, TZ-transition zone, U-urethra, B-bladder, EJD-ejaculatory duct

However, the TZ may often be discernible from the PZ and CZ, particularly in glands with significant BPH. Located posteriorly, the normal CZ and PZ, from which a majority of adenocarcinomas arise, have a homogeneous echogenic appearance whereas the anteriorly situated TZ is more heterogeneous. Frequently, calcifications along the surgical capsule known as “corpora amylacea” highlight the plane

between the PZ and TZ (56).The prostatic urethra traverses the length of the gland in the midline and thus must be imaged in the sagittal plane to be simultaneously viewed along the entirety of its course. The distended urethral lumen has a hypoechoic appearance whereas periurethral calcifications may produce a thin echogenic outline. The smooth muscle of the internal sphincter extends from the bladder neck, encircling the urethra to the level of the verumontanum. These muscle fibers may be visualized sonographically as a hypoechoic ring around the upper prostatic urethra, giving it a funneled appearance proximally as it arises from the bladder neck. On reaching the verumontanum the urethra angles anteriorly and runs through the remainder of the gland to exit at the apex of the prostate. This angle gives the prostatic urethra an anteriorly concave appearance when viewed along its entire course in the sagittal plane.

Figure showing Gray scale TRUS image of prostate showing the centrally running urethra.



Midline hypoechoic urethra represented as a star

Prostate Volume Calculation

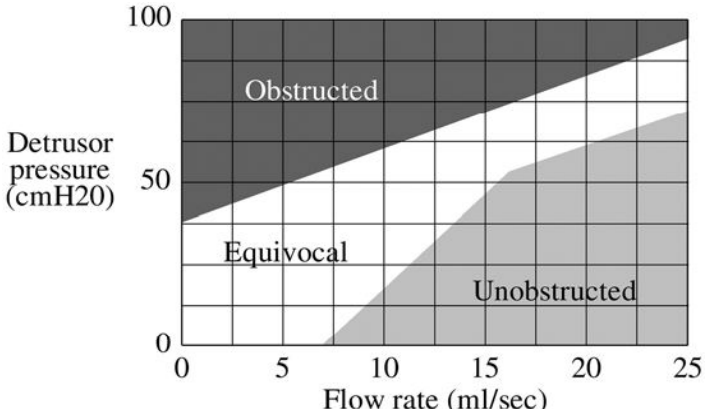
Prostate volume can be calculated through a variety of formulas. Volume calculation requires measurement of up to three prostate dimensions. In the axial plane, the transverse and anteroposterior (AP) dimensions are measured at the point of widest transverse diameter. The longitudinal dimension is measured in the sagittal plane just off the midline because the bladder neck may obscure the cephalad extent of the gland. Most formulas assume that the gland conforms to an ideal geometric shape: either an ellipse ($\pi/6$ × transverse diameter × AP diameter × longitudinal diameter), sphere ($\pi/6$ × transverse diameter^3), or a prolate (egg shaped) spheroid ($\pi/6$ × transverse diameter^2 × AP diameter). Despite the inherent inaccuracies that arise from these geometric assumptions, all formulas reliably estimate gland volume and weight, with correlation coefficients greater than 0.90 with radical prostatectomy specimen weights, since 1 cm^3 equals approximately 1 g of prostate tissue(9). The mature average prostate is between 20 and 25 g and remains relatively constant until about age 50, when the gland enlarges in many men (57).

PRESSURE FLOW STUDIES

Pressure-flow studies consist of the simultaneous measurement of bladder pressure, abdominal pressure, and uroflow. The patient has a full bladder, and a free (uncatheterized) urine flow rate is obtained.

A small (7–8 Fr) dual-lumen catheter is placed in each urethra; one lumen is used to measure bladder pressure and the other is used to infuse room temperature water or saline. A rectal catheter is placed to measure abdominal pressure. Detrusor pressure is obtained by subtracting the abdominal pressure from the total bladder pressure. Electromyography(EMG) of the external urethral sphincter is usually also recorded by means of patch or needle electrodes on the perineum. A high detrusor pressure–low flow pattern indicates bladder outlet obstruction, whereas a low pressure–low flow pattern indicates impaired detrusor contractility. The EMG recording indicates the degree of external sphincter activity and is most useful in identifying a lack of sphincter relaxation during voiding (dynamic obstruction).There are a variety of ways in which the results of pressure-flow studies may be interpreted. In general, a detrusor pressure of more than40 cm H2O with a uroflow less than 12 mL is considered obstructed; a detrusor pressure of less than 30 cm H2O with a uroflow less than 12 mL indicates impaired detrusor

contractility; and detrusor pressures between30 and 40 cm H2O with a uroflow less than 12 mL is indeterminate (58).Another common way to analyze these studies is to plot the detrusor pressure at maximum flow vs the maximum flow rate. The Abrams-Griffiths nomogram is then used to divide results into obstructed, unobstructed and equivocal categories (figure).



Pressure-flow studies are advantageous because they can be used to differentiate detrusor hypocontractility from bladder outlet obstruction. They are considered the gold standard for the diagnosis of bladder outlet obstruction and are widely used for both clinical and research purposes. However, they are invasive, time-consuming, labor-intensive, and proneto measurement error. Two or three consecutive studies must be performed because the results of a single test are highly variable(59). There tends to be a decrease in obstructive parameters with successive tests so that as many as 28% of patients will be redefined into a less obstructive Abrams-Griffiths category if the first study is compared with

subsequent studies(60). Furthermore, interpretation of the tests is not always straightforward, resulting in high intrainterpreter and inter inter preter variability (60).

VIDEOURODYNAMICS

Videourodynamic studies involve the measurement of urodynamic parameters along with the simultaneous fluoroscopic imaging of the bladder and urethra. For these studies, contrast material is infused in to the bladder instead of saline or water. In some instances, fluoroscopy is simply added to the pressure-flow study as described previously. In other cases, a triple-lumen bladder catheter is used, with the third, proximal lumen used to measure intraluminal urethral pressure. During filling, the proximal urethral pressure transducer (which is marked with a radiopaque marker) is positioned at the area of maximum resting urethral pressure (the external sphincter), and the distal transducer remains in the bladder to record intravesical pressure. This technique gives a more direct measurement of external sphincter activity than EMG electrodes. Some urodynamicists also omit the rectal catheter and simply measure total vesical pressure and urethral pressure. By adding fluoroscopic imaging to the measurements of pressures and flow rates, videourodynamic testing can be used to identify the location of bladder outlet obstruction (bladder neck, prostate, external urethral sphincter, bulbar urethra). Furthermore,

other abnormalities such as vesicoureteral reflux or urinary incontinence are easily demonstrated. The obstruction can be confirmed fluoroscopically by observing a narrowing of the urinary stream. This technique correlates well with results of pressure-flow studies and is less prone to technical difficulty(61).Despite the apparent advantages of videourodynamic studies, there has been no systematic evaluation of the utility of these studies in the evaluation of men with LUTS.

CYSTOMETRY

Cystometry is routinely performed as part of a pressure-flow or videourodynamics study. Pertinent abnormalities on cystometry include detrusor instability and diminished bladder compliance. Detrusor instability(DI) can be documented in approx 50% of men with LUTS and40% of men with documented obstruction(62). In patients who have DI before surgery, up to half may continue to have DI after prostatectomy, a suboptimal result(62). Unfortunately, there are currently no clinical or urodynamic criteria to determine which patients with bladder outlet obstruction and DI will do well after relief of the obstruction, and which patients will continue to have DI. Diminished bladder compliance has been demonstrated in 25–35%of men with bladder outlet obstruction(62). Older patients and those with severe obstruction demonstrate more significant compliance abnormalities than

patients who are younger and have less obstruction (62). This loss of compliance appears to be a generic response of the detrusor to obstruction (63). This finding is quite important because severe compliance abnormalities are clearly associated with the development of hydronephrosis and postrenal azotemia (63). Surgical intervention should be strongly considered for patients with significantly diminished compliance and bladder outlet obstruction. Such patients should have close urodynamic follow-up to assess for improvements in compliance following relief of the obstruction.

SYMPTOMS AND URODYNAMIC FINDINGS

Bladder outlet obstruction from BPH may result in medical conditions(urinary retention, renal insufficiency, bladder stones, recurrent urinary tract infections) that warrant surgical therapy. However, most men with prostatism do not have such conditions but instead have bothersome voiding symptoms. Numerous studies have failed to show any type of reproducible urodynamic finding that correlates with specific symptomatic complaints(64). Therefore, validated symptom scores for BPH are helpful to quantitate symptoms and assess response to therapy but cannot be used to diagnose bladder outlet obstruction. Urodynamic studies and symptom assessments appear to measure separate aspects of

lower urinary tract function that are probably related to some degree, but the nature of that relationship has not yet been defined.

PREDICTIVE VALUE OF URODYNAMICS

It is clear that 20–50% of men with LUTS do not have bladder outlet obstruction (62). Because the decision to perform surgery is often based on symptoms alone, one would expect that an equivalent proportion of patients undergoing surgery would also be unobstructed. If relief of obstruction equates with symptomatic success, one would expect limited symptomatic relief in those who are unobstructed preoperatively, but the literature on this point is inconclusive. A variety of studies have stratified symptomatic outcome based upon preoperative uroflowmetry results. Jensen and co-workers performed a prospective study of 139 men undergoing prostatectomy and found that those with a preoperative Qmax of greater than 15 mL/s had an increased likelihood of symptomatic treatment failure at 6 months (47). Pressure-flow studies have been extensively evaluated as potential predictors of treatment response following surgery (TURP or open prostatectomy).Some evidence exists that urodynamic data may yield relevant prognostic information. Abrams et al. reported a 72% success rate (symptomatic and flow rate improvement), which increased to 88% if pressure-flow criteria were

used to select patients for surgery (14).However, this study has been criticized for the unusually high failure rate (28%) in the initial group. Rollema et al. reported a better symptomatic outcome in 19 preoperatively obstructed patients when compared with 10 unobstructed patients (65). Interestingly, 3 of the10 unobstructed patients reported significant postoperative improvement despite no demonstrable urodynamic changes. Data from these studies indicate that a policy of reserving surgical therapy for patients with demonstrated obstruction in preoperative pressure-flow studies may improve treatment outcomes, although most of these studies indicate a significant benefit to unobstructed patients as well. Kaplan et al. performed a retrospective review of 121 patients after TURP, with a mean follow-up of more than4 years (62). There was no correlation with level of satisfaction with therapy and the presence or absence of bladder outlet obstruction on preoperative urodynamic tests (62). In another prospective study of 56 patients, Roehrborn et al. reported no association between degree of preoperative obstruction and 6-month symptomatic response following TURP (66).

INDICATIONS FOR URODYNAMIC STUDIESIN MEN WITH LUTS

To date, no urodynamic criteria have been found that predict treatment response to medical therapy for men with LUTS. The role of routine urodynamic testing before surgery is controversial. Urodynamic testing does appear to lower the surgical failure rate to some degree. Furthermore, although a significant number of unobstructed patients benefit from surgery, in such cases it is unclear what is being treated. Alternative therapies such as anticholinergic agents or biofeedback-assisted pelvic floor muscle exercises may be equally beneficial and less morbid. However, the cost of performing routine urodynamic testing before surgery in all patients would be significant. The decision to obtain urodynamic studies must be individualized, but the eventual decision is largely based on the treatment philosophy of the physician.

Men with persistent symptoms following surgical treatment to relieve bladder outlet obstruction should be studied. Such patients may have persistent obstruction, detrusor hypocontractility, detrusor instability, or diminished bladder compliance(67). Similarly, those with known or suspected neurologic disease may exhibit a wide range of urodynamic abnormalities. Proceeding with TURP or open prostatectomy

in these patients should be done only after other potential sources of voiding dysfunction have been identified and treated. Men with previous pelvic radiation or major pelvic surgery should also undergo urodynamic testing because these treatments may result in impaired bladder storage function, which could result in suboptimal results following surgery. In men with atypical clinical presentations (isolated symptoms of urgency and urge incontinence, severe symptoms and normal uroflow, young age), BPH-induced bladder outlet obstruction is less likely to be the cause of the symptoms, and it would therefore seem prudent to make the diagnosis clearly before proceeding with surgical therapy.

Role of transition zone index in BPH

The human prostate is composed of five histologically discernable zones. Hyperplasia of the transition zone compresses the central and peripheral zones into a structure termed the surgical capsule. In the adult human prostate the plane between the surgical capsule and transition zone is readily discernable on transrectal sonography or magnetic resonance imaging. The total prostate volume and transition zone index have been found to play an important role in BOO. Men with a total prostate volume >30ml have 3.5 times risk of having severe LUTS and 3-4 times the risk

of developing AUR. The value of volumetric measurements of the transition zone was recently reported in several studies.

Tempany et al analysed the different zonal volumes and their changes after treatment with finasteride and concluded that the transition zone was more affected by medical treatment than was the peripheral zone(68). Tewari et al analyzed the differences in TZ and total volume reduction among patients whose peak urinary flow rate improved after finasteride therapy. They concluded that pre-treatment TZ index may help in predicting improvement in Q max after finasteride therapy. Furthermore it has been studied that the relation between the TZ and total gland volume was reported to correlate better than total volume alone with other clinical and urodynamic variables. In addition the TZ index correlation with the extent of BOO especially when the TZI >0.5 and it is also a predictor for acute urinary retention (69).Ohtani et al has shown that TZ volume and TZ index were useful parameters in preoperative decision making with regard to TURP (70).

Need for new markers of Bladder Outlet Obstruction

If we direct indications for treatment solely on symptoms and the subjective decline of quality of life without assessing BOO, we will treat patients symptomatically (α-blockers) and after treatment failure

invasively (transurethral resection of the prostate). In that case, treatment of a symptomatic patient with BOO with a-blockers would make him asymptomatic but leave him obstructed with the consequence of ‘‘silent obstruction.’’ BOO, then, might lead to a damage of the lower and upper urinary tract. Patients with (unrecognised) BOO in the absence of LUTS should also get treatment because damage of the upper urinary tract is caused by BOO and not by LUTS which would be neglected. For these reasons, assessment of BOO and LUTS must be an essential part in the diagnosis of patients with BPH. Precise evaluation of BOO is only possible with pressure–flow studies; in the clinical routine, uroflowmetry, post void residual urine, and prostate volume are used to estimate BOO in men with BPH which have their own shortcomings. Thus there is a need for non invasive markers for BOO in men with BPH.

MATERIALS AND METHODS

Study design

Prospective cross-sectional diagnostic study

Study centre

The study was conducted at the Departments of Urology and Radiology, Madras Medical College and Rajiv Gandhi Government General hospital.

Period of study

The period of study was from August 2011 to February 2012.

Study population

A total of 50 patients were enrolled in the study.

Inclusion criteria

Men aged more than 50 years with lower urinary tract symptoms due to benign prostatic hyperplasia

Exclusion criteria

Patients with any of the below mentioned characteristics were excluded from the study

1. Prostate cancer
2. Stricture urethra
3. Neurogenic bladder
4. Prostatitis/active urinary infection
5. Previous prostate surgery
6. Pelvic irradiation

Methodology

50 patients were enrolled for the study. Informed consent was obtained after explaining the need for the procedure and possible complications. Approval by the Ethical committee of the institute where the study was undertaken was obtained prior to conduct of the study. At initial presentation, a thorough history was obtained and physical examination done.

The grading of prostatic size on rectal examination was done as follows:

Normal: encroaches 0-1cm into the rectal lumen

Gr 1: encroaches 1-2cm into the rectal lumen

Gr 2: encroaches 2-3cm into the rectal lumen

Gr 3: encroaches 3-4cm into the rectal lumen

Gr 4: encroaches more than 4cm into the rectal lumen

International prostate symptom score(IPSS) was completed and a blood sample for measuring the patient's serum PSA was taken. Patients underwent uroflowmetry using Status Meditech flow meter. Post void residual urine estimation was done at the end of uroflow using 3.5 mHz ultrasound array. Transabdominal sonography of the kidneys, bladder and prostate was performed using 3.5 – 5 mHz array. The bladder wall thickness (DWT) was measured between the two hyperechoic lines which represent the mucosa and the adventitia. Two different points were measured at a bladder capacity of 200-250ml and the mean of both obtained. Median lobe projection of the prostate into the bladder was measured in a sagittal scan at the same time.

TRUS was performed by the radiologist unaware about the findings of uroflowmetry and pressure flow studies. The prostate dimensions were determined using a 7.5mHztransrectal probe. The prostate was imaged from base to apex in two views – sagittal/ transverse, documenting the presence of prostatic abnormality and measuring the volume using the ellipsoid formula,i.e.,

Volume= Π/6 x (height x width x length)in ml

Calculating the volumes requires the assumption that both prostate and transition zones are ellipsoidal.

The transition zone(TZ) is identified as an area of heterogenous echogenicity compared to the hypoechoic peripheral zone (PZ).The TZ volume was calculated using the same formula and maximum diameters were used for each measurement. Transition zone index was defined as the ration between TZ volume and total gland volume (TZI= TZV/ PV). Urine culture and sensitivity were done and confirmed to be sterile prior to performing urodynamic studies.

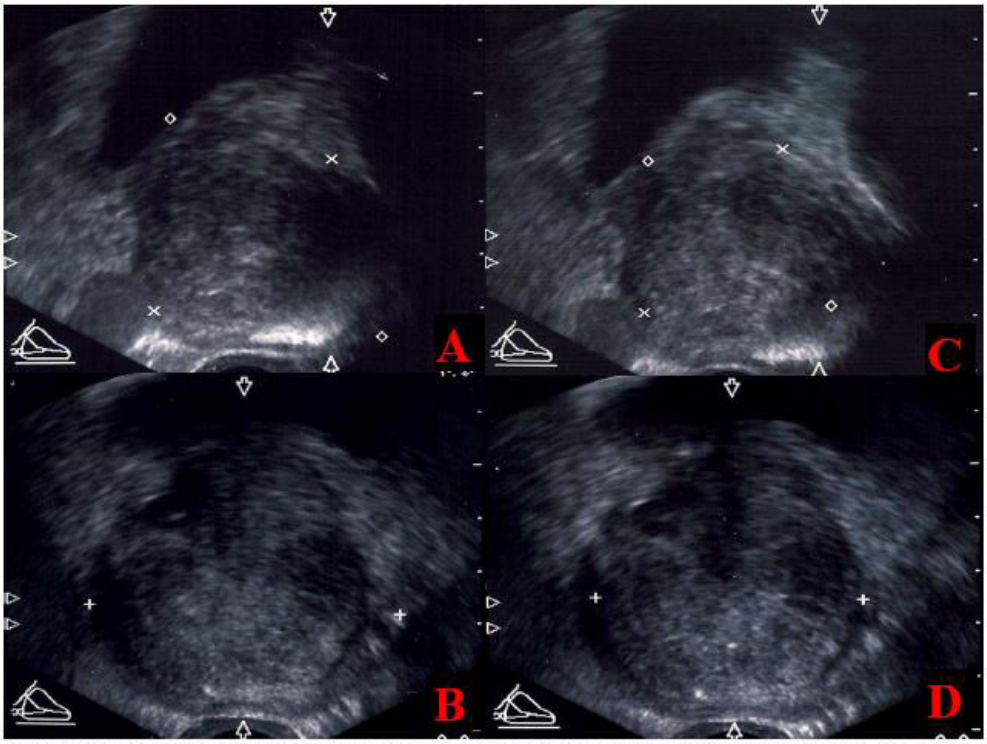


Fig. 1 Measurement of the prostate by transrectal ultrasound (A) Saggital section of the prostate, the distance between the "o's" is the length and the distance between the "x's" is the height. (B) Transverse section of the prostate, the distance between the "+'s" is the width. (C) Saggital section, the distance between the "o's" is the length, and the distance between the "x's" is the height of the transition zone. (D) Transverse section, the distance between the "+'s" is the width. The volume was calculated by the equation: 0.52 x length x height x width.

Urodynamic examination was done 1to 3weeks after the 1st visit. Urodynamic investigations were performed on a Laborie medical technology machine. Intravesical pressure was recorded by means of 5Fr

double lumen urethral catheter. Intraabdominal pressure was measured using 5Fr balloon catheter in the rectum. The pressure sensors were zeroed to atmospheric pressure before introducing them into the patient. The bladder was filled with saline at room temperature at the rate of 20-50ml/min. All studies were done with patients in sitting posture. Filling of the bladder was stopped when patient expressed a strong desire to void and filling catheter was removed. Patient was allowed to void in privacy in sitting posture. Voided volume and detrusor pressure at maximal flow rate were noted. The AG number was then calculated as, AG number=Pdet.Qmax – 2Qmax. Based on the AG number, patients were considered obstructed (AG>40) or non obstructed (AG<40).

STATISTICAL ANALYSIS

Descriptive statistics were used to illustrate the study population. All parameters were continuous variables and Pearson's coefficient of correlation was used for analysis. The statistical significance of these correlations was assessed using a two sided p-value. A p-value of <0.05 was considered statistically significant. The Chi Square test was used to assess the statistical significance of TZ index cut off value in predicting bladder outlet obstruction. A commercially available computer software package (SPSS version 10) was used for statistical analysis.

RESULTS

The duration of study was from August 2011 to February 2012.A total of 50 patients were included in the study.

AGE

The age wise patient distribution is shown in Table-1.most of the patients (48%) belonged to the age group of 61-65 years. The mean age of patients was 63.78 years and ranged between 52-78 years.

Table-1

Age group(yr)	Total
51-55	4
55-60	8
56-60	1
61-65	24
66-70	8
70-75	2
76-80	3

Duration of symptoms

All patients had symptoms of LUTS for a period ranging between 1-24 months, with a mean of 5.4 months. Table -2 shows distribution of duration of LUTS among patients.

Table-2

Duration of symptoms	Number of pts
<=3 months	20
>12 months	1
3-6months	19
6-9 months	3
9-12 months	7

NATURE OF SYMPTOMS

Among the 50 patients, obstructive LUTS was noted in 42and irritative LUTS in 40. 64% had both obstructive and irritative symptoms. (Table-3)

Table-3

Irritative LUTS / **Obstructive LUTS**	**No**	**Yes**	**Total**
No	0	8	8
Yes	10	32	42
Total	10	40	50

IPSS

According to the IPSS scoring system,64% patients had moderate symptoms(score8-19) and 24% had severe symptom score(20-35). (Table-4)

On combining the patient symptoms with IPSS grades; patients in the mild grade had predominantly irritative symptoms. (Table-5) Ten patients in the severe IPSS grade had both obstructive and irritative LUTS.

Table-4

IPSS Grade	Total
Mild	6
Moderate	32
Severe	12
Grand Total	50

Table-5

IPSS grade	obstructive LUTS	irritative LUTS	Both irritative and obstructive LUTS
Mild	0	3	3
Moderate	9	4	19
Severe	1	1	10

RECTAL EXAMINATION OF THE PROSTATE

On examination 36 out of 50patients had only grade 1 prostatic enlargement.

Table-6

DRE PROSTATE	TOTAL
Grade 1	36
Grade 2	14
Grand Total	50

SERUM CREATININE

When patients symptoms were analysed according to their serum creatinine18% of patients with moderate symptoms and just 9% of patients with severe symptoms had azotemia. This shows that the severity of symptoms may not be indicative of the degree of compromise in renal function due to BPH (Table-7).

Table-7

S.Creatinine	IPSS mild	Moderate	Severe
<=1.6mg%	6	26	11
>1.6mg%	0	6	1
Total	6	32	12

PROSTATE SPECIFIC ANTIGEN

34% of patients with PSA > 1.5 ng/ml had severe symptoms, whereas, only 10% of patients with PSA <1.5ng/ml had severe symptoms(Table-8).

Table-8

PSA ng/ml	IPSS Grade			Grand Total
	Mild	Moderate	severe	
<1.5	4	15	2	21
1.5-4	2	17	10	29
Grand Total	6	32	12	50

POST VOID RESIDUAL URINE (PVR)

The PVR of patients studied ranged from 5 ml to150 ml (mean -46.2 ml).40% of patients had a PVR of > 50 ml. (figure-1)

Figure-1

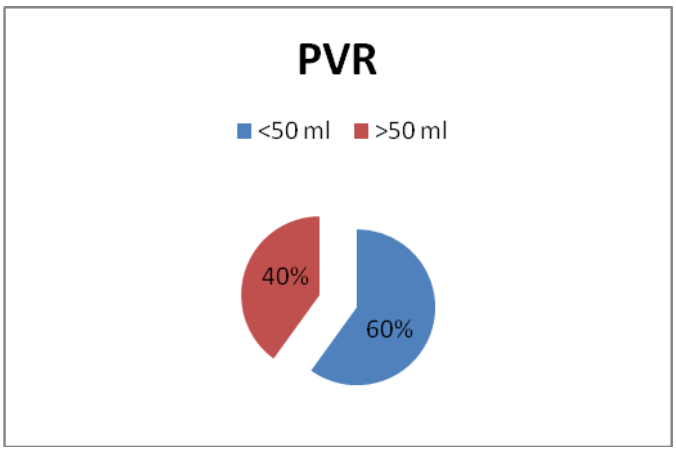


Table -9 shows the relationship of PVR to IPSS scores. None of the patients with mild symptoms had large PVR(>50 ml)whereas 50% of patients with large PVR had severe symptoms.

Table-9

PVR	IPSS mild	Moderate	Severe
<50ml	6	22	2
>50ml	0	10	10
Total	6	32	12

PROSTATE VOLUME ON TRUS

Only one patient with mild symptoms had a prostate volume > 30ml, while 84% of patients with severe symptoms had a prostate volume > 30ml. (Table-10)

Table-10

Prostate size	IPSS mild	Moderate	Severe	Total
<30ml	5	14	2	21
>30ml	1	18	10	29
Total	6	32	12	50

Table -11 compares the prostate volume on TRUS with grade on rectal examination. Only 48% of prostates that were grade 2 on rectal examination had a volume > 30ml.

Table-11

Prostate size	DRE Grade 1	DRE Grade 2	Total
<30ml	17	4	21
>30ml	19	10	29
Total	36	14	50

DETRUSOR WALL THICKNESS(DWT)

35 Out of 50 patients had a DWT < =5mm (figure-2). None of the patients with DWT > 5mmhad mild range IPSS scores, while only 26% of patients who were severely symptomatic had a DWT> 5mm.

Figure-2

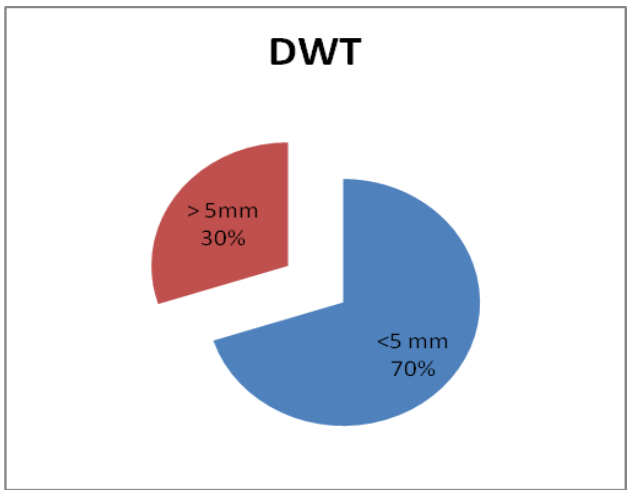


Table 12 shows relationship between DWT and PVR.73% of patients with a DWT> 5mm had a PVR> 50 ml.

Table -12

DWT	PVR <50ml	PVR > 50ml
<=5mm	26	9
>5mm	04	11
Total	30	20

UROFLOWMETRY

54% of patients had a peak flow rate < 10 ml/sec. There were nine patients who had a Qmax> 15 ml/sec.(figure-3)

93% patients with detrusor thickness> 5mm had a Qmax< 10ml (Table-13), while 48% of patients with Q max < 10 ml had a DWT<= 5mm.

Figure -3

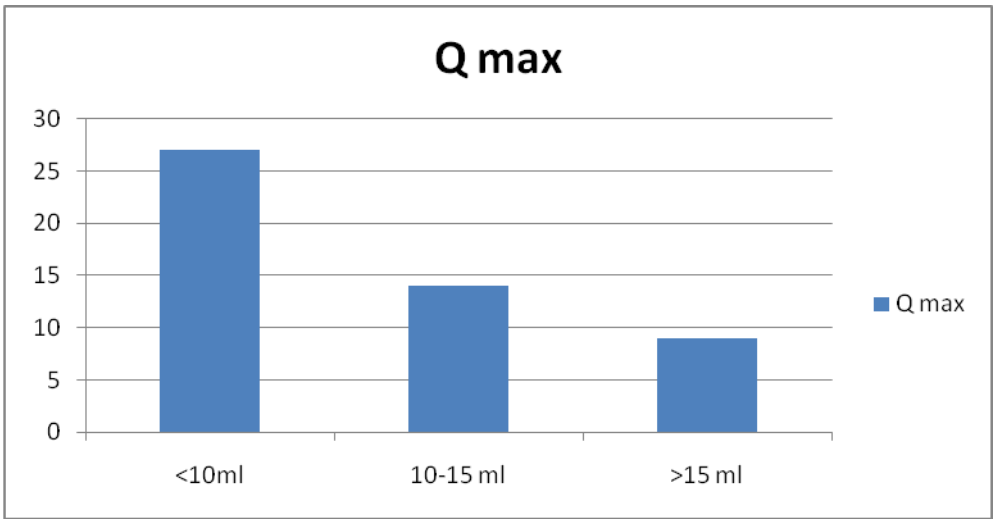


Table-13

DWT / Q max	<10	10-15	>15
<=5mm	13	13	9
>5mm	14	1	0
Total	27	14	9

Two thirds of patients with poor flow rates (<10ml) had a PVR > 50 ml, (Table -14); while all patients with Q max >15ml/sec had a PVR < 50 ml.

Table-14

Q max Group	PVR group		Grand Total
	<50ml	>50ml	
<10ml/sec	9	18	27
>15ml/sec	9	0	9
10-15ml/sec	12	2	14

ABRAMS GRIFFITH NUMBER (AG number)

There were 22 patients in the obstructed group (AG> 40) and 28 patients had an AG number <= 40 (figure-4).

Figure-4

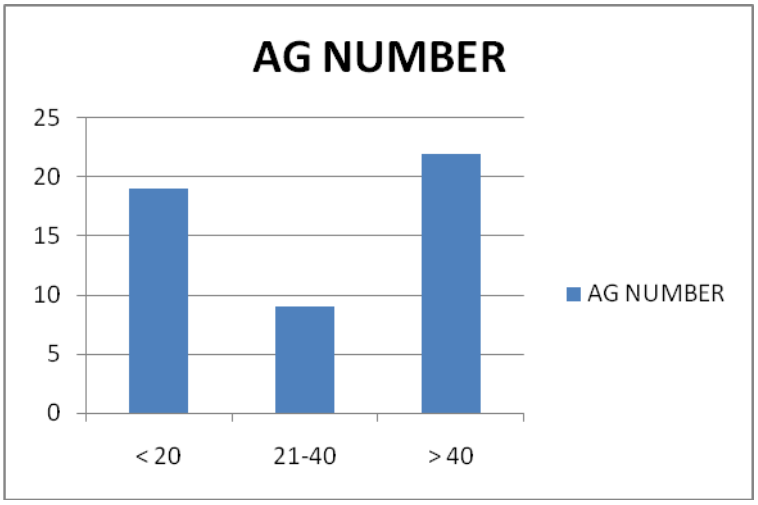


Table -15 shows that 21 out of 22 patients with bladder outlet obstruction had a Qmax< 10ml/sec. Only 6 patients out of 27(22%) had a Qmax< 10 ml/sec but were not obstructed on pressure flow studies (AG number < 40).

Table-15

Count of AG number group	AG number Non obstructed	Obstructed	Equivocal	Grand Total
Q max Group	<20	>40	21-40	
<10ml/sec	2	21	4	27
>15ml/sec	6	0	3	9
10-15ml/sec	11	1	2	14
Grand Total	19	22	9	50

None of the patients with DWT more 5mm had an AG number of less than 20, while 14out 15 patients with DWT > 5mm had BOO

according to AG number signifying that DWT is a very good predictor of bladder outlet obstruction (Table-16).

Table-16

DWT / AG no.	<20	20-40	>40
<=5mm	19	8	8
>5mm	0	1	14
Total	19	9	22

Only one patient with AG number less than 20 had PVR more than 50 ml. 80% of patients with PVR more than 50 ml had AG number of more than 40.(Table-17) When correlating the IPSS grade to AG number 83% of those with severe symptoms were obstructed. However among those obstructed on pressure flow studies only 45% had severe range IPSS symptoms(Table 18).

Table-17

Count of PVR	AG number			Grand Total
PVR group	<20	>40	21-40	
<50ml	18	6	6	30
>50ml	1	16	3	20
Grand Total	19	22	9	50

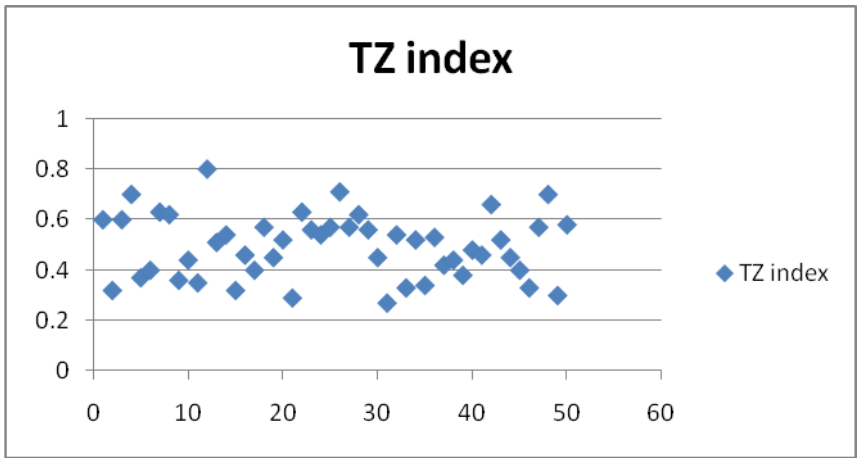
Table -18

IPSS Grade/ AG no.	<20	>40	21-40	Grand Total
Mild	6	0	0	6
Moderate	12	12	8	32
Severe	1	10	1	12
Grand Total	19	22	9	50

TRANSITION ZONE INDEX (TZI)

Figure-5shows the scatter diagram of TZ index in the study patients. Mean TZ index was 0.44. Transitional zone index if prostate volume < 30ml, was 0.3-0.63(mean-0.44) and if > 30ml it was 0.27-0.8(mean-0.53).

Figure-5



As shown in Table -19, the transition zone index value was statistically significant in differentiating obstructed from non obstructed patients. (p<0.001)

Table -19

Parameter	AG <=40	AG>40	p-value
Prostate volume, ml	28.35	45.46	<0.0005
Transition zone vol.,ml	11.7	26.4	<0.0001
TZ index	0.41	0.58	<0.0001

TZ Index cut off value for outlet obstruction

A TZ index value of greater than 0.45 had 100% sensitivity, 75%specificity,76%positive predictive value for diagnosing obstruction. Table-20 shows the statistical correlation of transition zone index value of 0.45 with the Abrams Griffith number. The p-value was highly significant (<0.001).

Table-20

TZI	AG number Group			Grand Total
	<20	>40	21-40	
<=0.45	16		5	21
>0.45	4	22	3	29
Grand Total	20	22	8	50

P<0.001 in chi square test

CORRELATION STATISTICS ON REGRESSION ANALYSIS

Table-21

r value/ p value	IPSS	PVR	Q max	PV	TZ vol	AG No.	PSA
T Z index	0.732/ <0.00001	0.51/ 0.0001	0.64/ 0.000001	0.09/ 0.03	0.58/ 0.0007	0.7/ 0.000001	0.39/ 0.005
PSA	0.44			0.54/ 0.0005	0.57/ 0.00001	0.64/ 0.000003	1
IPSS	1	0.65					
AG No.				0.45/ 0.001	0.61/ 0.00002	1	0.64/ 0.00003

IPSS, PVR, Peak flow rates, transition zone volume, AG number, serum PSA had strong correlations with the Transition zone index (table-21). The strongest correlation was with the IPSS score and Abram-Griffiths number (r=0.7) indicating good predictability for transition zone index in diagnosing bladder outlet obstruction.

DISCUSSION

The correlation between various BPH parameters and prostate size has been debated in the literature. The use of different symptom scores and various urodynamic parameters, including peak flow rate and post void residual urine (PVR) have contributed to a lack of consensus.

In our study, majority of patients had IPSS scores in the moderate range- mean score was 14.98 which are typical of men who visit our clinics. The mean age of patients was 63.7years, comparable to other studies, evaluating the role of transition zone (TZ)index; as both total prostate volume and transition zone volume increase with increasing age.

In the present study, serum PSA showed positive correlation with the IPSS scores(r=0.44). Serum PSA reflects the total gland volume more so for the TZ volume as it is produced by the TZ epithelial cells. Men with LUTS and higher PSA are therefore likely to have larger TZ volumes and hence more symptoms. The relationship between symptoms and total prostate volume (PV) in 803 patients have been described with no correlation detected (71). However in the present study, IPSS is strongly correlated with TZ volume, PV and TZ index.

Comparing the prostate grade on rectal examination with TRUS estimation of prostate volume, our study showed that they were poorly

correlated. BPH occurs in the TZ and rectal examination cannot assess the TZ. To avoid any evaluation bias, we measured the total PV/TZ volume using TRUS before performing pressure flow studies- the reference standard test.

Oelke et al studied 168 men with LUTS and concluded that Detrusor Wall Thickness (DWT) was the most accurate test to determine BOO, with a specificity of 95% and positive predictive value of 94% (72). However in the present study, detrusor wall thickness did not correlate with the severity of IPSS scores. DWT is also influenced by detrusor overactivity, incontinence, low compliance, dysfunctional voiding or detrusor hypocontractility. We had 30% of patients with DWT < 5mm with poor flow rates, indicating possible myogenic failure.

Uroflow and PVR

22 percent of patients with low flow rates were not obstructed on pressure flow studies; so uroflow is not specific for BOO. Likewise 20% of patients with PVR > 50 ml were not obstructed urodynamically. Residual urine or low Q max can be caused by BOO, detrusor underactivity or both indicating that these tests are poor predictors of obstruction.

While correlating IPSS grade to the AG number, we found that among those with BOO, only 45% patients had symptoms in the severe range; thereby indicating their unreliability in predicting BOO.

Transition zone index(TZI)

Greene et al noted that patients with clinical BPH had a TZ volume of 24.81+14.4 ml, in contrast to a volume of 6.14+3.2 ml in those without clinical BPH (73).Kaplan et al was the first to report TZ index as a more sensitive marker of BPH and showed TZI>0.5 to be an indicator of significant BOO (15). Kurita et al reported that men with a TZI >0.65had higher risk of developing acute urinary retention (74). Milonas et al reported that the highest risk of developing AUR was in patients with a TZI> 0.6 (75).The possible reasons for higher cut off of TZ Index in these series could be selection of men with AUR. Lepor et al reported that the total prostate volume, TZ volume and TZ index were not directly related to the symptom score and only weakly related to the flow rate (76). Discrepancy between the two reports was due to different inclusion criteria. The present study included men with BPH and LUTS like that of Kaplan et al and unlike that of Lepor et al (15,76).

Witjes et al in a prospective study on 150 patients found that TPV, TZV and TZI correlated equally well with age but weakly with pressure

flow studies (77). The problem with this study is that it consisted of men with a wide age range(30-85 years);prostate volume and symptom scores which could have resulted in the measured discrepancy.

Our results demonstrate a significant strong correlation between TZ index and IPSS score, uroflow, PVR, Serum PSA and AG number in men with LUTS due to BPH. Similar results were obtained in a study by Chen et al. They found that in elderly Asian men with BPH/LUTS, degree of BOO was significantly correlated with Total prostate volume and transition zone index, mean value being 0.46 in those with BOO (78). Intuitively these results are consistent with the hypothesis that the symptoms and urodynamic abnormalities associated with BPH are caused by mechanical or static compression by the prostate. Small prostates with smaller TZ volume may also result in severely symptomatic patients with markedly impaired flow rates and high voiding pressures.

It is conceivable that each patient may have a critical volume of TZ relative to the prostate; which results in bladder outlet obstruction. The strongest correlation of TZ index was with IPSS score(r=0.732) and AG number (r=0.7). Population and autopsy studies suggest a racial variance in prostate volume. In a study by Choi et al, they found that mean TZ index was significantly higher in Korean and Afro-American men (TZI=0.45) versus Caucasian and Hispanic men(TZI=0.39) (79).

We therefore decided to develop a cut off point for the TZ index which combines the greatest sensitivity with maximum specificity, i.e efficiency of a test. At a TZ index cut –off of >0.45, all patients with outlet obstruction were detected while the specificity remained high at 75%.(Table-22)The implication of the finding suggests that men with LUTS and high transition zone index would respond better to therapies designed to reduce TZ volume medically or surgically.

Table-22

TZ index	**No. of pt**	**With BOO**	**No BOO**	**Sensitivity**	**Specificity**	**PPV**
>0.3	48	22	26	100%	7%	45 %
>0.4	35	22	13	100%	50%	60 %
>0.45	29	22	7	100%	75%	76 %
>0.5	24	19	5	83%	84%	80 %

CONCLUSION

- This study demonstrates that transition zone index is significantly correlated with symptom scores, PVR, uroflowmetry, pressure flow studies.
- Therefore transition zone index is a good non invasive tool to assess bladder outlet obstruction in men with BPH.
- Using a Transition Zone index cut off of > 0.45, can identify obstruction with 100% sensitivity, 75% specificity and 76% positive predictive value.

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APPENDIX-1 INFORMED CONSENT FORM

Title of the study:ROLE OF TRANSITION ZONE INDEX IN ASSESSING BLADDER OUTFLOW OBSTRUCTION DUE BENIGN PROSTATIC HYPERPLASIA

Name of the Participant:

Name of the Principal Investigator: Dr.ARUN KUMAR. K

Name of the Institution:

Madras Medical College and Rajiv Gandhi Government Hospital, Chennai- 3

Name and address of the sponsor / agency: Nil

Documentation of the informed consent

I have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in "**ROLE OF TRANSITION ZONE INDEX IN ASSESSING BLADDER OUTFLOW OBSTRUCTION DUE TO BENIGN PROSTATIC HYPERPLASIA**"

1. I have read and understood this consent form and the information provided to me.

2. I have had the consent document explained to me.

3. I have been explained about the nature of the study.

4. I have been explained about my rights and responsibilities by the investigator.

5. I have been informed the investigator of all the treatments I am taking or have taken in the past ____ months including any native (alternative) treatment.

6. I have been advised about the risks associated with my participation in this study.

7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.

8. I have not participated in any research study within the past _____month(s).

9. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.

10. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent.

11. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the sponsors, regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.

12. I have understood that my identity will be kept confidential if my data are publicly presented

13. I have had my questions answered to my satisfaction.

14. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

For adult participants:

Name and signature / thumb impression of the participant (or legal representative if participant incompetent)

Name _____ Signature_____

Date_____

Name and Signature of impartial witness (required for illiterate patients):

Name _____ Signature_____

Date_____

Address and contact number of the impartial witness:

Name and Signature of the investigator or his representative obtaining consent:

Name _____ Signature_____

Date_____

For Children being enrolled in research:

Whether child's assent was asked: Yes / No (Tick one)

[If the answer to be above question is yes, write the following phrase:

You agree with the manner in which assent was asked for from your child and given by your child. You agree to have your child take part in this study].

[If answer to be above question No, give reason (s) :_____.

Although your child did not or could not give his or her assent, you agree to your child's participation in this study.

Name and Signature of / thumb impression of the participant's parent(s) (or legal representative)

Name _____ Signature_____

Date_____

Name _____ Signature_____

Date_____

Name and Signature of impartial witness (required for parents of participant child illiterate):

Name _____ Signature_____

Date_____

Address and contact number of the impartial witness: _____

Name and Signature of the investigator or his representative obtaining consent :

Name _____ Signature_____

Date_____

NOTE

For observational studied in nature or those in which only patient's tissue, body fluids are collected for any kind of analysis, the following elements in the patient information leaflet will need be included – background of the study: the purpose for which the sample will be used: confidentially of data are right to refuse to give specimens should be included.

Points 6, 7,8,9,10,11 of consent document may be excluded in such cases.

Appendix -1-informed consent form

ஆராய்ச்சி ஒப்புதல் கடிதம்

சிறுநீர் பாதை அடைப்பின் காரணங்கள் குறித்த விவரங்களை சேகரிக்கும் ஆராய்ச்சி

பெயர் :
வயது :
பால் :

தேதி:
உள்நோயாளி எண்:
ஆராய்ச்சி சேர்க்கை எண்:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கம் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்து கொண்டு எனது சம்மதத்தை தெரிவிக்கிறேன்.

எனது சிறுநீர் பாதை அடைப்பின் காரணங்களையும் மற்றும் ஆராய்ச்சிக்கு தேவையான அனைத்து விவரங்களையும் தெரியப்படுத்துவதற்கு முழு சம்மதம் தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில்தான் பங்குபெறுகிறேன் மற்றும் இந்த ஆராய்ச்சியில் இருந்து எந்நேரமும் பின் வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்து கொண்டேன்.

சிறுநீர் பாதை அடைப்பின் காரணங்கள் குறித்த இந்த ஆராய்ச்சியின் விவரங்களைக் கொண்ட தகவல்தாளை பெற்றுக்கொண்டேன்.

நான் என்னுடைய சுய நினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதிக்கிறேன்.

இந்த ஆராய்ச்சியின் தகவல்களையும் முடிவுகளையும் அறிவியல் நோக்கத்திற்காக பயன்படுத்துவதற்கு நான் அனுமதிக்கிறேன். நான் இந்த ஆராய்ச்சியில் பங்குபெற சம்மதிக்கிறேன்.

பங்கேற்பவரின் பெயர்

பங்கேற்பவரின் கையொப்பம்
(அல்லது) கட்டைவிரல் ரேகை

ஆய்வாளரின் பெயர்

ஆய்வாளரின் கையொப்பம்

இடம்:

தேதி:

Appendix-2 Patient Information sheet

ஆராய்ச்சி தகவல் தாள்

சிறுநீர் பாதை அடைப்பின் காரணங்கள் குறித்த விவரங்களை சேகரிக்கும் ஆராய்ச்சி

தங்களது சிறுநீர் பாதை அடைப்பின் காரணங்கள் குறித்த விவரங்கள் பெற்றுக்கொள்ளப்பட்டது.

ராஜீவ் காந்தி அரசு பொது மருத்துவனைக்கு வரும் சிறுநீர் பாதை அடைப்பு நோயாளிகள் பற்றிய ஒரு ஆராய்ச்சி நடைபெற்று வருகிறது.

சிறுநீர் பாதை அடைப்பு, பிராஸ்டேட் சுரப்பி வீக்கத்தின் காரணமாக வரும் விளைவுகள் குறித்த விபரங்களை சேகரிப்பது இந்த ஆராய்ச்சியின் நோக்கமாகும்.

நீங்கள் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். இந்த ஆராய்ச்சியில் உங்களிடம் கேள்விகள் கேட்கப்பட்டு அதன் தகவல்களை ஆராய்வோம். அதனால் தங்களது சிகிச்சைக்கு எந்த பாதிப்பும் ஏற்படாது என்பதை தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியின் முடிவுகளை அல்லது கருத்துகளை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின் வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி

APPENDIX -3 Patient Proforma

Patient proforma

Name : age: i.p.no: UNIT:

HISTORY:-
Frequency- urgency - urge incontinence-
Hematuria - Dysuria-
Obstructive LUTS-
IPSS SCORE :
Fever - Loin pain-
Duration of symptoms-
Gen.examination-
BP- / mmHg PR- /min Temperature-
Pallor - Pedal edema-
Examination –
P/A-
E/G: Penis Meatus
SCROTUM TESTES
DRE- Prostate size- gr 1/2/3 firm/hard smooth/nodular tender/non tender
Tone-
Rectal mucosa –
Investigations :
Urine routine- C/S-

Hb /PCV- BLUREA- S.Cr- RBS- Na/K-

S.PSA- ng/ml
USG KUB-

DWT- mm IPP-

TRUS-

TZ INDEX-

UROFLOWMETRY-

PRESSURE FLOW STUDIES-

APPENDIX 3-IPSS SCORECARD

International prostate symptom score (IPSS)

Name: Date:

	Not at all	Less than 1 time in 5	Less than half the	About half the time	More than half the	Almost always	Your score
Incomplete emptying Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5	
Frequency Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
Intermittency Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
Urgency Over the last month, how difficult have you found it to postpone urination?	0	1	2	3	4	5	
Weak stream Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
Straining Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	

	None	1 time	2 times	3 times	4 times	5 times or more	Your score
Nocturia Over the past month, many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning?	0	1	2	3	4	5	

Total IPSS score	

Quality of life due to urinary symptoms	Delighted	Pleased	Mostly satisfied	Mixed – about equally satisfied and dissatisfied	Mostly dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?	0	1	2	3	4	5	6

Total score: 0-7 Mildly symptomatic; 8-19 moderately symptomatic; 20-35 severely symptomatic.

APPENDIX-3 IPSS SCORE- TAMIL

60-வது நாளில் அறிகுறிகளின் ஸ்கோர்கார்டு

விடையளிக்க வேண்டிய வினாக்கள் :	இல்லவே யில்லை	5-ல் ஒரு தடவைக்கு குறைவாக	பாதி நேரத்துக்கும் குறைவாக	சுமார் பாதி நேரம்	பாதி நேரத்துக்கும் மேலாக	ஏறக்குறைய எப்போதும்	
1. கடந்த மாதத்தில் நீங்கள் சிறுநீர் கழிப்பதை முடித்தபிறகு சிறுநீரப்பையை முழுவதுமாகக் காலி செய்யவில்லை என்று எத்தனை முறை உணர்ந்திருக்கிறீர்கள்?	0	1	2	3	4	5	
2. கடந்த மாதத்தில் நீங்கள் சிறுநீர் கழித்து முடித்தபிறகு 2 மணி நேரத்துக்கும் குறைவாக மீண்டும் எத்தனை முறை சிறுநீர் கழிக்க நேரந்தது?	0	1	2	3	4	5	
3. கடந்த மாதத்தில் நீங்கள் சிறுநீர் கழித்தபோது எத்தனை முறை பாதியில் நிறுத்திப் பல தடவைகள் துவங்கியதாக உணர்ந்தீர்கள்?	0	1	2	3	4	5	
4. கடந்த மாதத்தில் சிறுநீர் கழிப்பதை ஒத்திப்போடுவது கிரமம் என்று எத்தனைமுறை உணர்ந்திருக்கிறீர்கள்?	0	1	2	3	4	5	
5. கடந்த மாதத்தில் எத்தனை முறை உங்களுக்குப் பலவீனமான சிறுநீரோட்டம் இருந்தது?	0	1	2	3	4	5	
6. கடந்த மாதத்தில் எத்தனை முறை நீங்கள் சிறுநீர் கழிக்கத் துவங்க முக்கவோ முனகவோ வேண்டியிருந்தது?	0	1	2	3	4	5	
	ஒன்று மில்லை	1 தடவை	2 தடவைகள்	3 தடவைகள்	4 தடவைகள்	5 அல்லது அதற்கு மேற்பட்ட தடவைகள்	
7. கடந்த மாதத்தில் நீங்கள் இரவில் படுக்கப்போன நேரத்திலிருந்து காலையில் நீங்கள் எழுந்திருந்த நேரம் வரை எத்தனை முறை பெரும்பாலும் சிறுநீர் கழிக்கவென்றே எழுந்திருந்தீர்கள்?	0	1	2	3	4	5	
					மொத்த மதிப்பெண்கள்		
	மகிழ்ச்சி	இதமான உணர்வு	பெரும்பாலும் திருப்தி	கலப்புணர்வு	பெரும்பாலும் அதிருப்தி	மகிழ்ச்சியின்மை	பயங்கரம்
சிறுநீர் சம்பந்தப்பட்ட அறிகுறிகளால் வாழ்க்கைத் தரத்தில் இப்போதுள்ள சிறுநீர் சம்பந்தப்பட்ட நிலையிலேயே நீங்கள் உங்கள் எஞ்சிய வாழ்க்கையைக் கழிக்க நேர்ந்தால் அதுபற்றி நீங்கள் என்ன உணர்வீர்கள்?	0	1	2	3	4	5	6

பதில்களுக்கு மதிப்பெண்ணிடுதல்

1 முதல் 7 வரையான கேள்விகளுக்குரிய உங்கள் விடைகளிலிருந்து எண்களைக் கூட்டுங்கள். அதிகபட்ச இயன்ற மதிப்பெண் 35. கடைசிக் கேள்வி உங்கள் அறிகுறிகள் பற்றி நீங்கள் எப்படி உணர்கிறீர்கள் என்பதை மதிப்பிட உங்களுக்கு உதவும்.

மதிப்பெண்கள் : 0-7 இலேசானது
8-18 நடுத்தரம்
> 18 கடுமை

குறிப்பு : இந்தச் சோதனை உங்கள் அறிகுறிகளின் கடுமையை அளப்பதற்கே. இது நோயறியும் ஒரு சோதனை அல்ல. வேறு வார்த்தைகளில் சொன்னால், உங்களுக்கு BPH இருக்கிறதா இல்லையா என்று இது சொல்லாது. உங்கள் அறிகுறிகள் BPH-னால்தானா என்பதைத் தீர்மானிக்க உங்கள் டாக்டரிடம் பேசுங்கள்.

இந்தத் தகவல் மருத்துவச் சிகிச்சைக்கு ஒரு மாற்று அல்ல.

பார்க்க : BPHக்கு அமெரிக்கன் யூரோலாஜிகல் அசோசியேஷன் (AUA) அறிகுறி கூட்டவனை.

Appendix -4 MASTER CHART

name	age	DURATION	obst LUTS	Irrit. LUTS	IPSS	DRE	GR	S.CREAT	S.PSA	PVR	PV -TRUS	TZV-TRUS	TZ index	DWT	IPP	Q max	AG no
ganesan	62	3 months	yes	no	22	1		0.9	2.4	40ml	58.6	35.2	0.6	5mm	0	9ml	42
venkatesan	70	4months	yes	yes	8	1		0.6	2	10ml	20	6.4	0.32	4mm	0	17ml	18
radhakrishnan	72	6 months	yes	yes	17	1		1	1.8	50ml	33.5	20.2	0.6	7mm	4mm	6ml	44
anwar	62	4 months	yes	yes	17	2		1	3.2	60ml	55.2	38.6	0.7	5mm	3mm	7ml	44
idhayan	55	2months	yes	yes	9	1		0.8	0.7	20ml	24.1	9	0.37	3mm	0	14ml	16
pandurangan	56	1 month	no	yes	14	1		1	1.9	5ml	20	8	0.4	2mm	0	18ml	22
vairavan	77	7months	yes	yes	26	2		1.7	3.8	90ml	42.3	26.5	0.63	7mm	6mm	10ml	44
raman	63	12 months	no	yes	15	1		0.6	0.8	30ml	16.3	9.8	0.62	2mm	0	8ml	40
mani	64	4months	no	yes	7	1		0.7	0.9	10ml	22	8	0.36	2mm	0	14ml	16
devaraj	60	8 months	yes	yes	17	1		1.4	0.7	40ml	10	4.4	0.44	5mm	0	10ml	28
sulaiman	62	4months	no	yes	11	1		3.2	2.2	15ml	34	12	0.35	4mm	0	16ml	20
subramani	61	3 months	yes	yes	24	2		0.9	2.8	70ml	55.2	44.1	0.8	4mm	0	9ml	46
jayaraman	60	12months	yes	yes	22	2		1.2	2.5	75ml	30.4	15.3	0.51	6mm	4mm	10ml	40
krishnan	57	12 months	yes	yes	16	1		1.1	1.4	40ml	20.6	10.8	0.54	6mm	0	6ml	48
kribakaran	59	3months	yes	no	10	1		0.8	1	10ml	22	7.1	0.32	3mm	0	25ml	16
kullan	65	2 months	yes	yes	16	1		4.1	1.1	60ml	22.8	10.5	0.46	12mm	5mm	7ml	41
sivamurugan	67	8months	yes	yes	12	1		1.8	0.7	30ml	26	10.4	0.4	3mm	0	10ml	14
arumugam	63	4months	yes	no	19	2		1.2	3.8	50ml	25.6	14.67	0.57	15mm	6mm	4ml	52
viswanathan	52	3months	yes	no	8	1		2.2	0.8	15ml	28	12.6	0.45	2mm	0	13ml	20
krishnan	65	5months	yes	no	18	1		1.2	3.4	80ml	78.3	40.71	0.52	8mm	0	5ml	50
vijayan	63	2 months	yes	yes	7	1		1	0.9	15ml	30	8.8	0.29	3mm	0	16ml	16
subramaniam	65	4 months	yes	yes	17	1		0.9	2.78	40ml	25.9	16.32	0.63	6mm	0	8ml	54
gurumoorthy	64	3 months	yes	yes	7	1		0.8	1.5	10ml	37.5	21	0.56	2mm	0	12ml	14
khader basha	60	3months	yes	yes	12	1		0.9	3.7	30ml	20.5	11.1	0.54	6mm	0	8.4ml	54
ramaswamy	62	3months	yes	yes	22	1		0.8	1.1	60ml	34.7	19.2	0.57	4mm	0	10ml	18
parthasarathy	78	4months	yes	yes	25	1		0.7	1.8	80ml	40.5	28.7	0.71	5mm	0	4ml	56
kothandam	66	5months	yes	yes	10	1		0.8	1.4	30ml	31	10.4	0.33	2mm	0	12ml	18
ramakrishnan	60	8months	yes	yes	21	1		1	1.8	70ml	32	19.8	0.62	8mm	0	6ml	61
umapathy	62	2months	no	yes	24	2		0.8	1.2	60ml	30	17.2	0.56	3mm	0	8ml	54
krishnan	67	12months	yes	yes	14	1		0.6	1.6	30ml	34.4	15.49	0.45	4mm	0	16ml	34
shankar	52	5months	yes	no	8	1		0.7	1	20ml	32	8.9	0.27	2mm	0	16ml	14
munusamy	65	12months	yes	yes	18	2		0.8	4	150m	87.7	47.3	0.54	6mm	7mm	5ml	68
datchinamurthy	62	2months	no	yes	10	1		0.9	3.1	15ml	36	12	0.33	2mm	0	14ml	20

APPENDIX-4 MASTER CHART

satyamurthy	75	6months	yes	yes	17	2	1.2	2.4	80ml	71.62	37.2	0.52	10mm	6mm	6ml	52
srinivasan	54	3months	yes	yes	10	1	1.1	0.3	25ml	32.1	9.4	0.34	2mm	0	16ml	16
malakondaya	65	3months	yes	yes	17	2	0.9	3.7	80ml	111	59	0.53	8mm	9mm	4ml	56
rajamanikam	70	4months	no	yes	6	1	0.6	1.4	20ml	24	10.2	0.42	3mm	0	15ml	16
papannan	63	6months	yes	yes	12	2	1.3	2.2	40ml	21	9.2	0.44	4mm	0	7ml	40
muniratnam	69	4 months	yes	no	10	1	1.3	1.7	30ml	36	14	0.38	3mm	0	25ml	28
gopal	65	2months	yes	yes	25	2	0.8	2.8	60ml	48.6	23.3	0.48	4mm	3mm	3ml	42
gangadaran	78	1month	yes	yes	20	2	1.6	3.2	80ml	28	12.8	0.46	6mm	0	8ml	44
rathnam	65	4months	yes	yes	16	1	2.1	0.9	40ml	38.2	20.6	0.66	8mm	0	11ml	42
kanniappan	58	6months	yes	yes	16	2	1.2	1.4	100m	34.1	17.9	0.52	3mm	0	12ml	40
ranganathan	60	12 months	yes	no	12	1	0.9	1.2	30ml	40.2	18.1	0.45	3mm	0	12ml	14
ibrahim	63	3months	yes	yes	7	1	0.8	2.7	30ml	30	12	0.4	2mm	0	14ml	18
yelumalai	62	2months	yes	no	10	1	1.9	0.5	40ml	36	12	0.33	4mm	0	13ml	20
munnusamy	61	10months	yes	yes	24	2	1.1	2.2	100m	42	23.9	0.57	3mm	0	9ml	44
rangasamy	65	24 months	yes	yes	23	1	0.7	1.9	25ml	32	22.4	0.7	4mm	0	5ml	50
periasamy	70	1month	no	yes	6	1	1.2	0.4	20ml	18	6.4	0.3	2mm	0	12ml	18
munusamy	68	7months	yes	no	15	1	0.8	2.4	100m	34	19.7	0.58	3mm	0	12ml	40

APPENDIX-5 ETHICAL COMMITTEE APPROVAL

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

Telephone No: 04425305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. K. Arunkumar
PG in MCH Urology
Madras Medical College, Chennai -3.

Dear Dr. K. Arunkumar

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the propoal entitled "Role of transition zone index in assessing baldder outflow obstruction due to benign prostatic hyperplasia " No. 01072011.

The following members of Ethics Committee were present in the meeting held on 21.07.2011 conducted at Madras Medical College, Chennai -3.

1.	Prof. S.K. Rajan, MD	-- Chairperson
2.	Prof. V. Kanagasabai, MD Dean, Madras Medical College, Chennai-3,	-- Deputy Chairman
3.	Prof. A. Sundaram, MD Vice Principal , Madras Medical College, Chennai -3	-- Member Secretary
4.	Prof R. Sathianathan , MD	-- Member
5.	Prof R. Nandhini, MD Director, Institute of Pharmacology, MMC, Ch-3	-- Member
6.	Prof. Geetha Subramanian MD. DM Prof & Head , Dept. of Cardiology, MMC, Ch-3	-- Member
7.	Prof. Pregna B. Dolia, MD Director , Institute of Biochemistry, MMC, Ch-3	-- Member
8.	Prof. C. Rajendiran, MD Director , Institute of Internal Medicine, MMC, Ch-3	-- Member
9.	Thiru. A. Ulaganathan Administrative Officer, MMC, Chennai -3	-- Layperson
10.	Thiru. S. Govindasamy , BA.BL	-- Lawyer
11.	Tmt. Arnold Soulina MA	-- Social Scientist

We approve the proposal to be conducted in its presented form

Sd /. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee

APPENDIX-6 LIST OF ABBRIEVIATIONS

BPH	-	Benign prostatic hyperplasia
BOO	-	Bladder outflow obstruction
PV	-	prostate volume
TZV	-	Transition zone volume
TZI	-	Transition zone index
TRUS	-	Transrectalultrasonogram
PVR	-	Post void residual urine
LUTS	-	lower urinary tract symptoms
AG number	-	Abrams-Griffith number
PSA	-	Prostate Specific antigen
Q max	-	Peak flow rate
DWT	-	Detrusor wall thickness
IPP	-	IntravesicalProtrusion of prostate
IPSS	-	International Prostate symptom score
DRE	-	Digital Rectal Examination