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Quantitative analyses of interactions among symptom scores, quality of life score, voiding data and urodynamic findings

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Symptoms and Diagnostics in Clinical BPH

Quantitative analyses of interactions among symptom scores, quality of life score, voiding data and urodynamic findings

Symptomen en Diagnostiek in Klinische BPH

Kwantitatieve analyses van interacties tussen symptoom scores, kwaliteit van leven score, mictiegegevens en urodynamische bevindingen

(met een samenvatting in het Nederlands)

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Contents

Abbreviations

AG number	Abrams-Griffiths number
AUA	American Urological Association
BII	BPH Impact Index
BOO	Bladder Outlet Obstruction
BOON	Bladder Outlet Obstruction Number
BPE	Benign Prostatic Enlargement
BPH	Benign Prostatic Hyperplasia
BPO	Benign Prostatic Obstruction
C_{eff}	effective capacity
CLIPS	CLInical Prostate Score
DRE	Digital Rectal Examination
ICS	International Continence Society
I-PSS	International Prostate Symptom Score
linPURR	linear Passive Urethral Resistance Relation
LUTS	Lower Urinary Tract Symptoms
N_{diuria}	mean diuria
$N_{nocturia}$	mean nocturia
P_{det}	detrusor pressure
$P_{det.Qmax}$	detrusor pressure at maximum flow rate
PSA	Prostate Specific Antigen
PURR	Passive Urethral Resistance Relation
Q	flow rate
Q_{max}	maximum urinary flow rate
$Q_{max.free}$	maximum free urinary flow rate
QoL	Quality of Life
SD	Standard Deviation
Sdiuria	diuria score
Snoct	nocturia score
SPI	Symptom Problem Index
TRUS	TransRectal UltraSonography
TURP	TransUrethral Resection of the Prostate
URA	group-specific Urethral Resistance Algorithm
$V_{intake,day}$	mean fluid intake in the daytime
$V_{intake,night}$	mean fluid intake at night
V_{max}	maximum voided volume
V_{mean}	mean voided volume
$V_{mean,day}$	mean voided volume in the daytime
$V_{mean,night}$	mean voided volume at night
V_{min}	minimum voided volume
$V_{total,day}$	mean total urine production in the daytime
$V_{total,night}$	mean total urine production at night
WHO	World Health Organization

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CHAPTER 1

Introduction

The impact of BPH on health care

Benign prostatic hyperplasia (BPH) is a common disease of men beyond middle age. BPH leads to morphological and functional changes in the urinary tract[1], manifested clinically by lower urinary tract symptoms (LUTS).
The relation between age and prostate volume has been quantified by autopsy studies[2]. After puberty, the prostate measures about 15 ml in volume, but during life it may increase in volume up to 100 ml or even more. No men younger than 30 years had BPH, and the prevalence of BPH rose with age, peaking at 88% in men over 80 years.
BPH is usually a slowly progressive condition. Longitudinal population-based studies have shown an average increase in prostate volume of 1 to 2 ml per year[3]. In a randomly selected cohort of 350 men a prostate volume increase of 1.4% per year[4] was found. Analyses of prostate growth in 164 men (mean age 63±6 years) during 4 years have shown that mean prostate volumes (55±26 ml) changed by -9 to + 30 ml[5].
As the prevalence of BPH and LUTS increases with age, the absolute number of patients affected, is rising worldwide due to ageing populations[6]. Today life expectancy even approaches 80 years in most developed countries[7].
Surgical treatment for BPH is one of the most frequent operations performed in the modern western world. The lifetime probability of surgical treatment of men for BPH is estimated to be 30%[8-10].

> In the Netherlands, in 1999 the transurethral resection of the prostate (TURP) was the second most performed surgery on men above 50 years of age. The TURP took up 5.2% of all operations performed compared to 5.5% for the most performed surgery, the aortocoronary bypass. In the Netherlands, in 1999 about 10,000 TURPs were performed. The total number of days of hospitalisation for the TURP was about 64,000 in 1999 in the Netherlands (Prismant). Taking into account about 450 Euro per day for hospitalisation, and about 270 Euro per TURP, the total cost of performing TURPs in 1999 in the Netherlands was about 32 million Euro.

The chance of undergoing surgical treatment increases with age. Keeping in mind the ageing population, the proportion of men with LUTS caused by BPH will increase considerably in the near future and thus diagnostics and treatment of BPH will make increasing demands on health care facilities. Besides, the probability of treatment for BPH is likely to increase as more men may seek newly available medical therapy for their symptoms in order to avoid surgical management.

Natural history of BPH

The prostate gland is separated into three zones: the transition zone, the central zone and the peripheral zone[11]. Carcinoma occurs mainly in the peripheral zone. The transition zone, which surrounds the urethra, commonly gives rise to BPH. The prostate gland is androgen dependent and testosterone is necessary for the development, growth, differentiation and function of the gland[12]. In the normal prostate, cell formation is balanced by programmed cell death. BPH develops when excessive cell division is promoted or the rate of cell death is reduced[3]. As BPH progresses, the normal prostatic tissue changes into hyperplastic tissue and compresses the prostatic urethra, resulting in progressive obstruction of urinary flow during voiding. The detrusor muscle responds to this obstruction by smooth muscle hypertrophy. Possible consequences are increased voiding pressure, increased bladder stiffness (decreased bladder compliance) and/or troublesome involuntary bladder contractions (detrusor instability), sometimes with urinary incontinence. Detrusor instability may even occur as a result of obstruction-induced changes to the bladder nervous system[3].
BPH is nowadays rarely a life-threatening disease. The worsening of symptoms is usually slow[3], but a serious outcome such as urinary retention is rather common. In 2,000 community-men, an incidence of acute urinary retention of 7 per 1000 persons per year was found[13]. Kidney stones have been detected with similar frequency, but hydronephrosis, acute renal failure and urethral strictures were much less common[13]. Besides, patients may present with symptoms related to complications secondary to BPH, such as urinary tract infection, hematuria, bladder stones, and renal insufficiency[14].

Risk factors for the development of BPH

The aetiology of BPH is undoubtedly multifactorial, but still poorly understood[7]. The only clearly defined risk factors for the development of BPH are age[2,15] and the presence of androgens secreted by functioning testes[3,7]. Men who are castrated before puberty do not develop BPH[16].
Different studies on the risk of family history and BPH show a 1.3 to 4.4 fold increase in risk for men with one or more first-degree relatives with BPH compared to men without such family members[17-19]. The increase in risk was greatest amongst men with

relatives diagnosed with BPH before the age of 60 years[17]. A shortcoming of these studies is, however, the self-reported family history of disease[7].
Clinical BPH might be more common in black races than in white races, and in their turn more common than in Asian races, but further studies are needed to confirm this[7].
Until now, no firm evidence on the impact of lifestyle factors as determinants of the risk of developing BPH has come forth[20,21]. The hormonal influences on the prostate lead to the idea that mechanisms, which can alter the concentration of sex-hormones or the interaction with their environment, may contribute to the aetiology of BPH.
Alcohol consumption may decrease testosterone production, and increases testosterone clearance in humans[7]. Reduced age-adjusted relative risks for alcohol consumption and obesity have been reported, although confidence intervals were wide[22]. Taking BPH surgery as the outcome, a decreased risk of alcohol consumption and BPH could be demonstrated[23,24]. However, the association could be due in part to the poorer surgical risk of heavier drinkers[7].
Androgen and oestrogen levels seem to increase as an effect of smoking cigarettes due to their nicotine content. There is, however, little evidence of an increased risk of BPH for smokers compared to non-smokers[7].
A positive correlation between the incidence of hypertension and symptoms associated with BPH has been reported[25].
BPH has been reported to be less common in men who eat large amounts of vegetables. It has been suggested that certain vegetables protect against BPH because they contain phyto-oestrogens, which have antiandrogenic effects on the prostate[7].
In conclusion, age, the presence of functioning testes and positive family history of BPH are the only proven risk factors for the development of BPH. More research is necessary to give recommendations concerning life-style factors for the prevention of BPH.

Definitions associated with BPH

Historically, hyperplasia of the prostate, prostate enlargement, bladder outlet obstruction and lower urinary tract symptoms were considered to be almost synonymous. Today there is increasing awareness that some men have hyperplasia with or without enlargement of the prostate, some have symptoms, and others bladder outlet obstruction with overlap of these conditions to varying degrees. Histological BPH does not necessarily cause prostatic enlargement and men with enlargement do not necessarily

have bladder outlet obstruction[7].
Abrams[26] pleaded for a more meaningful use of the term "BPH", pointing out that BPH is a histological diagnosis and should be reserved only for this purpose. When either digital rectal examination or transrectal ultrasound has shown gland enlargement, the preferred term is benign prostatic enlargement: "BPE". Bosch et al.[27] and Abrams[28] favour a cut-off point of 30 ml for BPE. When urodynamic studies have demonstrated bladder outlet obstruction (BOO) secondary to BPE, only then should the term benign prostatic obstruction ("BPO") be used. The use of the abbreviations BPH, BPE, BPO and BOO and their definitions are generally accepted nowadays[29]. The still quite current term BPH has to be discussed in terms of BPE, BOO and/or BPO[30]. Lower urinary tract symptoms (LUTS) suggestive of BPH should be interpreted as LUTS suggestive of BPH, BPE and/or BPO.

Symptoms associated with BPH and their bothersomeness

BPH is characterised by a spectrum of symptoms, nowadays often referred to as lower urinary tract symptoms (LUTS)[26]. Previously, LUTS in elderly men were referred to as "prostatism". This term implies that the symptoms have a prostatic origin. However, these symptoms are not gender-specific. Age-matched women have similar symptoms and equal severity of symptoms[31-33]. Even in elderly men the symptoms may be not from prostatic origin but caused by detrusor instability, bladder hypersensitivity and/or possible bladder/urethral denervation with age[14,28] and may occur in men with urinary tract infection, carcinoma *in situ*, bladder stones or other disorders[3,34]. Besides, symptoms can be elevated by life-style factors such as diet, fluid intake, alcohol intake, and anticholinergic effects of commonly used non-prescription medications[7]. It is for these reasons that the International Scientific Committee[29] has recommended the term lower urinary tract symptoms (LUTS) instead of "prostatism". More investigation is needed to establish whether LUTS in an elderly man is associated with BPH.
Traditionally, "prostatism" symptoms (nowadays LUTS suggestive of BPH) have been divided into obstructive and irritative symptoms. As there is only a poor association between "obstructive symptoms" and bladder outlet obstruction (BOO), and because detrusor function impairment also causes "obstructive symptoms", the use of this term is confusing and should be avoided. Voiding symptoms is a more accurate term[28]. "Irritative symptoms" carries the connotation with inflammation that in most men is not the case. Therefore, storage symptoms should be used as a more accurate term

Table 1.1 Lower urinary tract symptoms associated with BPH.

Voiding symptoms	Storage symptoms
Weak urinary stream	Frequency and repeated urination
Abdominal straining	Nocturia
Hesitancy	Urgency
Intermittency	Incontinence
Incomplete bladder emptying	Bladder pain
Terminal and postmicturitional dribble	
Dysuria	

instead of "irritative symptoms"[28]. Typical voiding symptoms and typical storage symptoms associated with BPH are listed in Table 1.1[3].

In addition to the usual factors believed to lead to prostate-induced LUTS, age-related changes can also give rise to symptoms usually interpreted as symptoms associated with BPH[14]. Age-related changes are for example the decrease of bladder capacity[35], the decrease of detrusor contractility, the increase of the incidence of detrusor instability[14,36] and increase of the stiffness of the prostate gland[37,38]. Increase of bladder instability with age probably has a greater impact on symptoms than do changes in other parameters such as impaired urinary stream during voiding.
Of the greatest consequences to the patient are the worry, bothersomeness, and embarrassment from voiding and storage symptoms, all parameters that heavily influence the individual quality of life[14]. Storage symptoms appear to be more bothersome than voiding symptoms[39].
While BPH is relatively common among older men, perceptions about the bothersomeness of the symptoms might vary between individuals and with cultural differences[40]. Consequently, most patients are actually treated not because there is an unequivocal indication for treatment but rather because they consider that their LUTS are seriously deteriorating their quality of life[41].

Diagnostics in BPH

Patronised by the World Health Organisation (WHO), the International Scientific Committee of the International Consultation on BPH attained an increased, but not yet total agreement as to the extent of pre-treatment investigation necessary in men with LUTS suggestive of BPH[29]. This Committee defines four classes of diagnostic tests in men with LUTS suggestive of BPH:

Highly recommended tests are tests that should be done on every patient.

Recommended tests are tests of proven value in the evaluation of most patients and their use is strongly encouraged during initial evaluation.

Optional tests are tests of proven value in the evaluation of selected patients; their use is left to the clinical judgement of the physician.

Not recommended tests are tests of no proven value in the evaluation of most patients. However, such tests may be helpful in selected patients who do not fulfil the criteria for the standard (usual) patients.

Highly recommended tests:

Medical history:

Adequate medical history should be focusing on the nature and the duration of genito-urinary tract symptoms, previous surgical procedures, general health issues, current medication and the patient's fitness for possible surgical procedures.

Physical examination:

Physical examination should include investigation of the suprapubic area for possible bladder distension and neurological examination to exclude a neurogenic bladder. In addition, digital rectal examination (DRE) should be performed to evaluate the prostate gland with regard to size, consistency, shape, and abnormalities suggestive of prostate cancer.

> DRE also provides an estimation of prostate volume and is generally sufficient for selecting the most appropriate treatment when size is a determining factor[14]. However, the correlation between estimated prostate volume by DRE and true prostate volume is low[42,43]. Prostate volume tends to be underestimated by DRE[44].

Urinalysis:

The urine should be analysed to determine possible pathology, such as urinary tract infection or hematuria.

Quantification of symptoms:

Symptom prevalence from the patient's perspective should be objectively documented using the seven questions of the International Prostate Symptom Score (I-PSS) and the question concerning the quality of life (QoL), developed by the Measurement Committee of the American Urological Association[45]. The seven questions, covering incomplete emptying, frequency, intermittency, urgency, weak urinary stream, hesitancy and nocturia, can be answered on a scale of 0 to 5 (ranging from "not at all" to "almost always"). The I-PSS is the sum of the seven scores and, therefore, ranges from 0 to 35. Because the symptoms in an individual can vary on a day-to-day basis, symptom questions have been worded by asking the respondent to integrate his impression of the frequency or severity of those symptoms during a one-month period. Men with an I-PSS of 7 or under more commonly rate the urinary condition as not at all as opposed to a little bothersome. These men might be considered the mild symptom group. Men with an I-PSS of 8 to 19 generally gave intermediate ratings of bother, and can be defined as the group with moderate symptoms. Men with an I-PSS of 20 or above are generally bothered some or a lot by the symptoms, and could be considered the group with severe symptoms[45]. The quality of life question ("If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?") may be answered (QoL score) on a scale of 0 ("delighted") to 6 ("terrible").

There is variation in the extent to which patients with similar symptom scores are bothered by their symptoms[30]. Many patients wish first to be reassured that they do not have cancer. They are then largely concerned with the relief of symptoms and improvement in quality of life. There are indexes to measure the bothersomeness of symptoms. The AUA Measurement Committee developed and validated a Symptom Problem Index (SPI) with 7 bother questions, each corresponding to a symptom question of the AUA Symptom Index[46]. They also developed and validated a BPH Impact Index (BII) which measures how much the urinary problems affect various domains of health.

> The assessment of lower urinary tract symptoms (LUTS) is an essential component of the evaluation of men with BPH in clinical practice and research. Symptom evaluation is necessary for the assessment of outcome in individuals and the evaluation of the effectiveness of treatments in randomised controlled trials[47-49].
>
> The experience of illness from a patient's perspective, which tends to be dominated by symptoms, worry, and functional limitation, is not so easy to measure. To some clinicians, measurements of these phenomena with questionnaires are inherently subjective and 'soft'[50]. However, a number of instruments have been developed and used to quantify the severity of LUTS among men with BPH[45,49]. The resulting measurements, such as validated question-

naires, can result in 'objective' measurements of inherently 'subjective' patient characteristics[50].

Several questionnaires that are self-completed by patients have been developed to assess LUTS, of which some have been shown to be valid and reliable in a number of settings[45,51-55]. The indices are reproducible, internally consistent, and sensitive to changes in symptoms. The specificity is lower because of the nonspecificity of LUTS[32,33], and the indices are not designed as screening instruments[56].

Studies have revealed regional and international differences in symptoms and bothersomeness[57-60], and symptom prevalence varies spontaneously over time[61]. Comparisons between studies have in the past been compromised by the difficulties of defining each of these various aspects and by the use of a wide range of validated and unvalidated questionnaires[62]. Recognising the limitations of previously published indices, a measurement committee appointed by the American Urological Association (AUA), developed and validated the AUA Symptom Index[45]. The primary purpose of the AUA Symptom Index was evaluative. The Index was to be used as an outcome measure in a study of different treatment strategies for BPH. However, implicit in the development and validation of the AUA Symptom Index was a discriminative purpose: to distinguish between men more or less bothered by their urinary condition. The AUA Symptom Index was not developed to distinguish between men with urinary symptoms due to different pathophysiologic processes, to discriminate between men with or without physiologic evidence of bladder outlet obstruction, or to serve as a general measure of urinary symptom severity amongst patients (including women) with various causes of lower urinary dysfunction[50].

The validity and test-retest reliability of the AUA Index has been proven[45]. In a study by Plante et al.[63] in which 64 patients completed two AUA symptom questionnaires during the same office visit, one self-administered and the other by physician interview, mean total AUA Symptom Scores by physician-versus patient-administered questionnaires were similar, irrespective of the order of administration. The index could discriminate between BPH and control subjects and was sensitive to change.

The questionnaire developed by the AUA, with an additional question regarding the impact of BPH on quality of life, was subsequently adopted by the WHO and is known as the International Prostate Symptom Score (I-PSS)[53].

Increasingly, researchers are including the I-PSS in their studies[62]. Because these questionnaires contain identical symptom questions, and because the I-PSS has been translated into a wide variety of languages, this will permit more direct comparisons. However, comparisons between studies in different countries are often difficult because of the finding of different levels of symptoms in different societies, probably because of cultural factors[49].

The I-PSS is considered to be easy for patients to complete[49]. Barry et al.[45] reported no reading difficulties, but MacDiarmid et al.[64] found 15% of 202 patients were unable to read it or unable to understand it. The authors cautioned that this might introduce bias into studies.

Five percent of men in their twenties, and 15% of men in their forties have moderate-to-severe LUTS (IPSS ≥ 8)[65]. Population-based studies all over the world have shown percent prevalence of moderate-to-severe urinary symptoms of about 25%, 33% to 40% for 50-59, 60-69 and 70-79 years, respectively[66-70]. In a community-based study of more than 1,100 men aged 40 years and older in Spain[71], one-quarter were found to have moderate-to-severe symptoms (I-PSS score ≥ 8), which increased in prevalence with increasing age. In a community-based study of 514 men aged 50 years and over, 23% of Korean men reported moderate-to-severe symptoms[72]. The proportions of those severely symptomatic approximately doubled with each decade of age. Reports on longitudinal changes in LUTS-severity in the Olmsted County cohort revealed an average increase in I-PSS of approximately 0.2 points per year of follow-up[73].

It is generally found that men in the community tend to tolerate LUTS, with only a proportion seeking medical attention[74-76]. This finding has been confirmed by a study in Spain of 2,000 community-based men aged 50 years or older[77], in which 38% had sought medical advice for their LUTS. Younger men with moderate symptoms reported a worse quality of life than older men[71].

Relationships between the severity of LUTS and either bothersomeness or impact on quality of life have been investigated in many studies and in many countries, but a consistent pattern has not emerged[49]. Subjective symptoms (LUTS), bothersomeness, and negative impact on the quality of life are the main reasons for the patient to seek treatment for BPH. From the patients' perspective, symptoms and the effect of these symptoms on their state of mind and daily activities are the principal causes of morbidity[50]. Therefore, the improvement of this subjective discomfort ought to be an important treatment goal and criterion of evaluation.

Because surgery is intended to reduce bladder outlet obstruction, it seems inappropriate to submit symptomatic patients who have no obstruction to such treatment. Currently, however, the decision for surgery is usually based on the severity of the symptoms and the impact on quality of life[1]. The management of BPH, although based on the best available evidence, should be individualised to patients' circumstances and personal choices. There is a clear trend to make the patient an active part of this decision process[78]. Nevertheless, the opinion of the treating physician still seems to take an overwhelming impact on the patients' choice[79].

Recommended tests:

Renal function assessment:

Renal function should be investigated for instance by serum creatinine.

Serum prostate specific antigen (PSA):

Serum PSA measurement is recommended in the initial evaluation of patients with an anticipated life expectancy of over 10 years, and in whom the diagnosis of prostate cancer once established would change the treatment plan.

PSA levels are influenced by the amount of benign prostatic enlargement tissue. As a consequence, development of BPH increases the PSA serum level.

A high percentage of patients with BPH has an elevated level of PSA[80] that is variable over time[81,82]. The significant overlap between PSA values in BPH and prostate cancer complicates the distinction between these two diseases. The general consensus is that prostate cancer and BPH cannot reliably be distinguished by PSA alone. Prostate biopsy remains the cornerstone if DRE is unconclusive[14].

Flow rate recording:

Flowmetry is a method of objectively assessing the voiding process. It is non-invasive, simple, and relatively inexpensive. Uroflowmetry measures a number of parameters of micturition, of which the most important is the maximum urinary free flow rate ($Q_{max.free}$)[3]. Because of the great intra-individual variability[81,83-85] and the volume dependency[86-88] of the $Q_{max.free}$, if possible, at least two flow rates, both with a volume ideally of >150 ml voided volume, should be obtained.

From the beginning of the 20th century it has been obvious that bladder outlet obstruction, due to an enlarged prostate, affects the urine flow rate. Many methods have been used to measure the flow rate, but it was not until the end of the 1950's that reliable electronic equipment was developed, by von Garrelts[89]. Uroflowmetry should be performed with the patient in a normal voiding position, in private, and when the patient feels the urge to void[14]. Uroflowmetry is commonly used to identify patients with abnormal voiding physiology and to monitor changes in voiding dynamics over time in watchful waiting programmes and follow-up of therapies[90]. Uroflowmetry confirms that obstruction is or is not likely[14].

Several authors have studied free urinary flow rates in asymptomatic populations and have demonstrated the diminishing of flow variables with advancing age[86-88]. The maximum flow rate decreases with age, ranging from more than 25 ml/s in young men to less than 10 ml/s in 80-year-old men[88]. A decrease of maximum free flow rate from a median of 18.5 ml/s at the age of 50 to 6.5 ml/s at the age of 80 was found in 93 community men, who had no subjective voiding problems[87]. In the latter study, 62% of the men had a maximum free flow rate less than 15 ml/s and 29% had a maximum free flow rate less than 10 ml/s, but 30% voided less than 150 ml.

Uroflow studies are not without problems, such as within-person variability in maximum flow rate over repeated tests. A mean variation has been described of 0.1±3.2 ml/s for maximum flow rate with a variation range from -15 to +14 ml/s[81]. There is evidence that repeated uroflow studies result in increasing maximum flow rate[85]. Several causes contribute to the described variability, such as patients' learning effect, variability related to circadian rhythm[81,84], abdominal straining[91], artefacts from weight or stationary system used to measure flow[92] and dependence of flow rate on voided volume[86-88]. Interestingly, the variability of uroflow studies is higher in the BPH population than in healthy men, suggesting that this variability is related to the disease rather than to the test itself[30]. The exclusion of low voided volumes, below 150 ml[29] is recommended.

Another reason for controversy of the usefulness of peak flow rates in clinical practice and urological research is that uroflowmetry cannot distinguish between obstruction and impaired detrusor function as the cause of a low flow rate[93-95]. Uroflowmetry fails to detect patients with a high-flow/high-pressure BOO or patients with a low-flow/low-pressure without BOO[14]. The prognostic value of maximum flow rate versus the diagnosis of BOO is known to be in the range of 90, 67 and 30% for maximum flow rate values of less than 10 ml/s, 10-15 ml/s and greater than 15 ml/s, respectively[90].

Home uroflowmetry has been proposed as an alternative way to minimise the learning curve effect and to provide a more 'normal' environment for the patient[92,96,97]. Dedicated portable systems have been developed over the years; they are generally easy to operate and can store several flow tracings that can be downloaded and analysed[98] at a later date.

Residual urine:

The measurement of residual urine volume adds important information to the assessment of the severity of BPH[99]. Because of the marked intra-individual variability of residual urine volume, the International Scientific Committee recommends to repeat the test to improve precision, if the first residual urine volume is significant.

Voiding diaries (Frequency-Volume charts):

The International Scientific Committee recommends a voiding diary filled out over several 24-hour periods when nocturia is the dominant symptom. The reason for this recommendation was that voiding diaries would help to identify patients with nocturnal polyuria or excessive fluid intake, which are supposed to be common in the ageing male.

In the evaluation of patients with lower urinary tract symptoms, the frequency-volume chart is an important and inexpensive investigative tool[100]. This chart gives information about frequencies and voided volumes during daytime and at night. It can also provide information about fluid intake if this is registered, although the value of this is sometimes disputed[101]. It is known that the usual history taking is liable to subjective interpretation by both patient and physician and that there is a discrepancy between patient questionnaires and frequency-volume charts[102]. Frequency-volume charts give a more objective indication of the patients' voiding pattern. It has been demonstrated that recordings on frequency-volume charts are valid by comparing self-reported voided volumes with collected 24 h voided output in 18 patients[103].

The frequency-volume chart offers physicians a useful instrument, for example to evaluate therapeutic results. At the same time it encourages patients to participate in management of their own problem and increases a more objective awareness of their voiding and drinking habits. However, frequency-volume charts in LUTS are not suitable as a differential tool[101,104]. Although frequency-volume charts are widely used by urologists, little research has been done to examine how many data are sufficient to gain insight into the patients' voiding pattern. In many clinics patients report 24 h voiding patterns for 2 to 7 days. If the requirement could be reduced to 24 h, this would be of interest for both patient and physician. It has been demonstrated that in patients with interstitial cystitis[105] and in women with objective urinary motor urge incontinence[106], the use of one 24 h frequency-volume chart was sufficient to gain insight into the voiding patterns of such a patient.

Optional diagnostic tests:

Pressure-flow studies:

The only reliable method for directly diagnosing bladder outlet obstruction is simultaneous measurement of the driving pressure and the resulting flow rate: pressure-flow studies. If outflow resistance is increased, driving pressure will increase and flow rate will decrease[107]. Pressure-flow measurements involve introducing a small catheter to measure pressure within the bladder (and to fill the bladder). Detrusor pressure measurement during filling the bladder (filling cystometry) provides information about bladder capacity, compliance, and detrusor stability. Detrusor pressure measurement with simultaneous flow rate measurement (pressure-flow study) provides information about the strength of the detrusor muscle and the resistance of the urethra to urine flow.

The rationale for using pressure-flow studies in the evaluation of patients with LUTS (possibly due to BPE) derives from the lack of correlation between symptoms of the lower urinary tract and the presence of an enlarged prostate or BOO. The relationships among symptoms, urodynamics, pathology and pathophysiology of BPH are complex[98]. Pressure-flow studies are widely accepted as the method to separate men with a low urinary flow rate due to an impaired detrusor contractility from those with infravesical obstruction. They are recommended in all patients if invasive treatment is being considered, particularly in patients with maximum flow rates <10 ml/s and whenever the patient's history does not agree with clinical findings.

As the classical surgical treatments of LUTS intend to relieve BOO and relieve the patient of bothersome symptoms, a careful distinction between the presence and absence of BOO seems important. For this purpose urodynamic examination has been advocated as part of the routine evaluation before surgery[108-110].

Originally, prostatectomy has been performed for complications of infravesical obstruction. Today, 70% is performed because of lower urinary tract symptoms which might be due to obstructive BPH, but also might be a consequence of detrusor weakness or other age-related functional changes in the lower urinary tract[110]. The value of pressure-flow studies included in the preoperative evaluation has been studied and different studies have found an increase in success rate if the decision to treat has been based on objective demonstration of obstruction[110-113]. Although the prediction of relief of BOO is good, the findings were found to be only slightly better than free uroflowmetry in predicting the improvement of symptoms and bother[113,114]. A valuable use of pressure-flow studies could be in younger patients in whom BOO is less likely[14].

Pressure-flow studies have been performed for many decades, and even though the method has gained increasing attention, the technique of examination has changed little[115]. In 1997 a subcommittee of the International Continence Society (ICS)[116] published a manuscript about the standardisation of terminology of lower urinary tract function. The paper deals with standardisation of pressure-flow studies, and evaluation of urethral resistance, BOO and detrusor contractility. It also standardises the electronic format in which the information obtained from pressure-flow studies is stored.

The interpretation of results, however, has been altered notably since the early works by von Garrelts[89]. Several methods to analyse and interpret the pressure-flow data have been developed. Some of these are simple, easily interpreted nomograms intended to distinguish obstruction from non-obstruction, while others are complicated computer-based manipulations of data intended to allow grading of obstruction[115]. The oldest of the nomograms, by Abrams and Griffiths[111], simply divides the area of a pressure-flow plot into regions of obstruction, non-obstruction and equivocal. However, there is still controversy among urologists about where on the nomogram to place the borders delineating obstruction, equivocal zone, and no obstruction. Controversy among the experts about what constitutes obstruction is one of the problems with having pressure-flow studies as the basis for treatment[30].

In 168 patients[90] and 105 patients[117] the test-retest variability of pressure-flow studies has been investigated. Overall, 16% and 12% of patients changed diagnostic category according to the provisional International Continence Society (ICS) or the Abrams-Griffiths nomogram after the second or the third test. The observed differences in maximum urine flow rate and detrusor pressure at maximum flow rate values were statistically significant, but of little clinical relevance and showed the presence of a systematic change towards a less obstructed voiding with repeated measures over a short term. The presence of detrusor instability did not affect the test-retest variability[117].

Artificial filling cystometry has been the standard method of investigating lower urinary tract function. However, various factors impose restrictions on the reliability of the data. These include non-physiological rates of bladder filling, short duration of the test, urethral catheterisation, the clinical setting, and the degree of immobility imposed by the investigation[118]. A method aimed at obtaining natural measurements in a more comfortable environment has been ambulatory monitoring with portable data storage devices[119,120].

A promising development to diagnose bladder outlet obstruction noninvasively, is the use of the variable outflow resistance catheter[121]. This catheter is used to measure isovolumetric bladder pressure noninvasively. It has been shown that the combination of this pressure and a separately measured maximum flow rate may be used to diagnose bladder outlet obstruction.

Transrectal ultrasonography (TRUS):

Ultrasonographic imaging of the prostate is mainly used to exclude the presence of a malignant process or other pathology in the prostate[41,99] or when more precise estimations of prostate size and shape are required[122].

TRUS is indicated when DRE findings and/or PSA values suggest the presence of prostate cancer, and it also serves to guide the automatic prostate biopsy needle[3]. TRUS is non-invasive, easy to use, and has good reproducibility[123]. Because the development of BPH is reflected by a change in shape from the usual triangular-shaped appearance to a more rounded appearance on ultrasound, the shape of the prostate on ultrasound might assist in the diagnosis of BPH[99].

TRUS provides the most accurate method for determining the prostate size[124] and is far more precise for determining prostate volume than DRE[122] is. Apart from diagnostic applications, determination of prostate volume may have a rôle in treatment recommendations in patients with LUTS, because prostate volume may predict the outcome of treatment[30,99]. TRUS can guide and evaluate treatment of patients with LUTS[99].

Prostate volume appeared to be poorly correlated to LUTS and urodynamic parameters[112,125,126]. Although there is a weak correlation between prostate volume and symptoms for a large population of patients, this does not imply correlation for the individual patient[30].

Imaging of the upper urinary tract:

Ultrasonography of the upper urinary tract or intravenous urography is recommended for patients in whom there is suspicion of upper urinary tract pathology.

Endoscopy:

Endoscopy of the lower urinary tract is only recommended when success or failure of treatment alternatives depend on the anatomical configuration of the prostate.

Not recommended tests:

Tests, which do not provide useful information in the assessment of patients with LUTS suggestive of BPH, are:

Retrograde urethrography.

Urethral pressure profilometry.

Voiding cystourethrography.
Electromyography of the external urinary sphincter.
Filling cystometry.

Aims of the dissertation and justification of the studies

As men age and the availability and variety of treatments for BPH increase, more and more men receive treatment. BPH is creating an increasing demand on the health care system[21], so total expenses for the management of BPH are expected to increase dramatically[127]. Because appropriate treatment should attack the actual cause of the problem, accurate diagnosis of BPH and patient classification should result in improvements in treatment for this disease[99].

Today, treatment of BPH is no longer reserved for preventing possible severe complications, but is now also used to relieve bothersomeness and to improve quality of life. This has resulted in a more heterogeneous group of patients presenting with LUTS to the urologist. Detrusor instability or hypocontractility, instead of BPO[128] hampers an increasing number of these patients. The distinction between these disorders cannot be made accurately by means of conventional diagnostic tools, such as uroflowmetry and prostatic volume measurement[129,130]. Pressure-flow studies represent the gold standard to establish the presence of obstruction[131]. The inclusion of pressure-flow data in the pre-treatment evaluation and patient selection for interventional therapies improve the overall clinical results[110,112,113]. Therefore it is important that the patients are defined according to their symptom status (LUTS), their prostate status (BPE) and their voiding characteristics (BOO) [28]. The correlation between symptoms and objective measures of outlet obstruction is important[41]. Relationships between reported LUTS and clinical measures such as prostate size, uroflowmetry and urodynamic studies have been found to be weak among men attending urology clinics[7,112,125,126]. In general community populations however, correlations between urological measures have been found to be somewhat stronger than the correlations seen in urology clinic patients[69,131,133]. The selection process that leads to referral to a specialist is complex and may vary from one primary care practice to the next.

The aims of this thesis are:

1. **To evaluate different diagnostic methods and their associations in well-defined groups of men with LUTS suggestive of BPH;**

2. **To estimate the prevalence and bothersomeness of LUTS and their impact on well-being, and**
3. **To quantify the diagnostic value and overlap of the different diagnostic investigation methods and combination of methods.**

What makes our population and data different from those in other studies?
In our studies we investigated a well-defined group of 565 men with LUTS suggestive of BPH, who visited the outpatient department Urology of the University Medical Center in Utrecht from October 1993 until January 2000. The highly recommended and the recommended tests were performed, conforming to the recommendations of the International Consensus Committee on BPH of 1993[53]. Men were included if they were over the age of 50 years, without any of the other specified exclusion criteria of the Committee (prostate cancer, neurological disease, previous prostate surgery, or taking medication active on the urinary tract), they voided >150 ml during uroflowmetry studies, residual urine was estimated and prostate size was determined by transrectal ultrasound. The International Prostate Symptom Score and Quality of life score were collected. We added to these questions also the Symptom Problem Index (SPI) and the BPH Impact Index (BII)[46]. If the men could be included, they were evaluated urodynamically by filling cystometry and by pressure-flow studies.
The reported lack of associations between LUTS and clinical measures in BPH in the literature may be due to the way the men were included in the studies. Our group is different from those used in the reported studies because our men all met the inclusion criteria of the Committee and because we included only men who were able to void a volume of at least 150 ml during free uroflowmetry. The number of patients who had to be excluded for this reason strongly depends on the efforts made to obtain a reliable flow registration. In our urology department, the number of excluded patients for this reason could be reduced to 5%. Men who needed a catheter due to severe retention were excluded anyhow. Excluding men with a voided volume of less than 150 ml and/or with severe retention will lead to an exclusion of those men with (starting) decompensation of the bladder with changes of bladder properties. With our strict selection, we hoped to reduce aetiology to the patients' complaints to a minimum of variables. We judge our included men to be a reasonable representative sample of the population with LUTS who attend a urologic clinic, and for whom there is suspicion of BPH.
Apart from this strict selection of men we tried to estimate parameters as reliably as possible. Free uroflowmetries were performed with the patient private and when the patient feels the urge to void. It was always checked whether the patient had produced a voiding as he would do at home. If not, the flowmetry was repeated. In all patients residual urine was estimated during one of the visits to the outpatient department by

transabdominal ultrasonography. If residual volume was significant, this test was repeated. The urodynamic investigation always started with uroflowmetry and determination of the residual volume by catheterisation. Some men were not able to arrive with a full bladder and sometimes were not able to produce a flow curve. At the end of the urodynamic investigation the bladder of these patients was refilled and after removal of the catheters uroflowmetry was performed. If these patients were known to have significant residual volume, catheterisation was performed once more.

In our urodynamic investigation room, measures are taken to guarantee the privacy of the patients. Telephone calls are not allowed, personnel are not allowed to enter the room during the investigation, and buzzers are forbidden. The number of investigators is restricted to a minimum. During voiding the investigators withdraw to a room with a second display showing the actual pressure and flow curves. It is always verified whether the patient has voided as he would do at home. If not, the study is not suitable for analysis and a new attempt is made to obtain a reliable measurement. Patients who met all inclusion criteria, but were not able to produce a reliable pressure-flow study, were exceptional. We have computerised systems to abstract data from the curves during the filling cystometry, pressure-flow studies and free uroflowmetry. Nevertheless, it is always checked whether these data are correct by visual inspection of the curves and if necessary, data were adjusted.

As transrectal ultrasound is more precise for determining prostate volume than digital rectal examination[122], all patients underwent transrectal ultrasound investigation.

Reliability of data from voiding diaries and their relation to symptoms

In 1997 the International Scientific Committee[29] recommended frequency-volume charts in the initial diagnostic evaluation of men with LUTS suggestive of BPH when nocturia is the dominant symptom.

As data from frequency-volume charts are reflections of the (dys)functions of the lower urinary tract, it is logical to attach more importance to the frequency-volume charts in the diagnostic work-up of men with LUTS suggestive of BPH, than only to identify patients with nocturnal polyuria or excessive fluid intake. Because hardly any study has been performed concerning the diagnostic contribution of frequency-volume charts in men with LUTS suggestive of BPH and the relations of data from these charts with other diagnostic findings, we studied in a sub-population of 160 men frequency-volume charts comprehensively.

In chapter 2 the reliability of frequency-volume charts in men with LUTS suggestive of BPH is studied. In chapter 3 the relations between reported data on these frequency-volume charts and symptoms and quality of life were investigated.

Symptoms, bothersomeness, age, prostate volume and urodynamics

The relationships between reported LUTS and clinical measures such as prostate size, uroflowmetry and urodynamic studies have been found to be weak in men attending urology clinics[7,125,126]. We hoped to reduce aetiology to the patients' complaints to a minimum of parameters and thus to increase possible associations between LUTS and clinical measures.

In chapter 4 associations of symptoms and quality of life with age, prostate volume and urodynamic parameters were estimated.

Up to now, decision making in the treatment of LUTS suggestive of BPH was mainly based on symptoms and the degree of bladder outlet obstruction[53]. However, nowadays the opinion prevails more and more that the degree of bother reported by the patient is not the same as the presence and frequency of their symptoms[39,96,134,135]. Nevertheless, bothersomeness of symptoms and their negative impact on the quality of life are the main reasons for the patient to seek treatment for BPH[96,135,136].

In chapter 5 the prevalence and bothersomeness of symptoms were analysed. Additionally, the impact of each symptom and its specific bother on various domains of health and overall quality of life were studied.

Bladder outlet obstruction

Urodynamics offer an objective tool for the assessment of bladder outlet obstruction (BOO) in BPH. Different methods of analysing pressure-flow plots, to quantify bladder outlet resistance and to classify whether or not a patient is obstructed, have been developed in the past[116]. These different approaches are based on similar theoretical principles, but are different in detail and objectives. **In chapter 6 the extent of (dis)agreement among different methods of analysing pressure-flow plots to define bladder outlet obstruction was quantified.**

Prostate volume, urethral resistance, bladder outlet obstruction, and filling cystometric estimated parameters

In recent years it has become clear that the interrelationships between BPH, prostatic enlargement, LUTS and bladder outlet obstruction are not simple[107]. Prostatic obstruction, impaired detrusor contractility, decreased bladder compliance, reduced bladder capacity, residual volume and/or detrusor instability all play a rôle in the genesis of symptoms as well as in the severity of BPH. These pathophysiological elements are all common in the elderly man and may be present alone or in all possible combinations, each giving rise to specific complaints. When evaluating these characteristics in men with BPH, it is not fair to compare men with recent onset of BPH with those who have severe and prolonged obstruction. In the latter group, the long term effects of obstruction may result in detrusor decompensation or other changes. **In chapter 7 the characteristics of our well-defined group of men with LUTS suggestive of BPH are described. Further, the interactions between prostate volume and different urodynamic parameters were investigated.**

Pressure-flow studies have been widely adopted in the evaluation of patients suspected of having obstruction, as well as in scientific studies, but the method suffers from a lack of validation from urodynamic studies in the normal population[108,137]. However, to decide what is pathological, it seems mandatory to agree on what can be considered normal in elderly men. Objective parameters obtained from urodynamic tests on which functional diagnoses are based should be related to normal standardised reference values.

In chapter 8 the characteristics of healthy elderly volunteers without and of volunteers with LUTS suggestive of BPH were established. Additionally, we compared these characteristics with those in our patient group.

Data from frequency-volume charts versus urodynamic data

The International Scientific Committee on BPH[29] classified filling cystometry as a not recommended test. The dominant reason for this classification was that findings during filling cystometry may not be representative of bladder behaviour during natural bladder filling at home. If this statement is true, one would expect a lack of associations between data obtained during filling cystometry and those obtained from frequency-volume charts. **The relations between data on frequency-volume charts and properties during the bladder-filling phase at urodynamic evaluations were studied in chapter 9.**

In chapter 10 associations of data from frequency-volume charts with bladder-emptying properties were studied. Additionally, the impact of the amount of fluid intake on voiding frequency was investigated.

Bladder outlet obstruction number (BOON)

Different studies have found an increase in success rate if the decision to treat has been based on objective demonstration of obstruction[110-113]. However, pressure-flow studies are often considered too invasive, time-consuming and expensive to be routinely utilized[138,139]. The method is invasive which by its nature may obstruct or irritate the detrusor or urethra[118], and can cause discomfort to the patient. Our experience, however, agrees more with the findings of Kortmann et al. [140] that urodynamic investigation was associated with low objective and subjective morbidity. World wide, this means that some men will undergo urodynamics while other men, with equal medical history and diagnostics, will not, depending on the consent of the investigator. Because we investigated associations of bladder outlet obstruction with diverse other non-invasively obtained parameters (Chapters 4,7,8,10), we wondered whether it was possible to classify men as obstructed, equivocal or unobstructed using a combination of non-invasively estimated parameters. In that way urodynamic investigations may be restricted to a selected group of men. **In chapter 11 possible combinations of non-invasive obtained parameters to discriminate men who are obstructed from those who are not, are developed and validated.**

Finally, in chapter 12 the results are discussed and general conclusions are formulated.

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CHAPTER 2

Analysis and Reliability of Data from 24-Hour Frequency-Volume Charts in Men with Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia

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Abstract

Objectives: The aims of this study were to analyse the data from frequency-volume charts and to study the reliability of these charts in men with lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH).

Methods: Men with LUTS suggestive of BPH were consecutively included in the study if they met the criteria of the International Consensus Committee on BPH, voided more than 150 ml during uroflowmetry, residual volume and prostate size were estimated and frequency-volume charts were completed correctly. From the frequency-volume charts, voiding habits and fluid intake were evaluated.

Results: 160 patients could be included. Another 28 patients who met all other criteria did not complete the frequency-volume charts correctly. Agreement exists between reported voided volumes in the literature and those found by us. We found a significant correlation ($p<0.001$) between nocturia and score on symptom question 7, and between diuria and score on symptom question 2 of the AUA symptom index. The difference between results obtained from frequency-volume charts completed during 24 h and those obtained from charts completed during three or more 24-hour periods was negligible with respect to the variation of data at an individual level.

Conclusions: Frequency-volume charts are reliable in the investigation of patients with LUTS suggestive of BPH. Reporting on frequency-volume charts during just 24 h is sufficient to gain insight into their voiding habits during normal daily life.

Introduction

Frequency-volume charts are important in the investigation of people with voiding disorders and give the urologist information about frequency in the daytime and at night together with the voided volumes[1]. Hansen and Klarskov[2] reported that recordings on frequency-volume charts are valid. McCormack et al.[3] assessed the agreement between patient questionnaire and frequency-volume charts. They reported a poor agreement between patient questionnaire- and chart-determined urinary frequency, suggesting that a frequency-volume chart show a more valid indication of urinary habits, than the patient questionnaire itself. Other authors[4-9] also found the frequency-volume chart to be a basic tool in lower urinary tract symptoms (LUTS), although not suitable for young children or as a differential tool. Most of these studies[6-10] focus on frequency and incontinence, whereas the composition of the patient groups was quite diverse concerning age, sex and symptoms.

Voiding dysfunction in the elderly is a common problem with far-reaching implications. In the past, extensive scientific and clinical considerations have led to an international consensus[11] about the diagnostic work-up of men presenting with LUTS suggestive of benign prostatic hyperplasia (BPH). Nevertheless, hardly any study has been performed concerning the diagnostic contribution of frequency-volume charts in these men and the relation of data from these charts with other diagnostic findings. The American Urological Association (AUA) symptom index and quality of life question[12] are accepted as mandatory tools in the clinical evaluation of these patients[11]. The AUA symptom index consists of seven questions concerning voiding habits. As from frequency-volume charts a lot of information is available concerning voiding habits, it seems logical to investigate whether data on frequency-volume charts can contribute to the diagnosis in BPH.

As a first step in such an extensive investigation, this paper deals with the analysis of data from frequency-volume charts and with the reliability of these data in a well-defined group of men with LUTS suggestive of BPH. Moreover, it is examined whether reporting during 24 h is as sufficient as reporting during three or more periods of 24 h to gain insight into the voiding habits of these patients.

Materials and Methods

In men with LUTS consecutively presenting to our outpatient department of urology, basic standard evaluation (history, quantification of symptoms by the seven questions and quality of life question proposed by the AUA[12], physical examination and digital rectal examination, urinalysis and renal function assessment) and recommended tests (uroflowmetry and residual urine estimation) conforming to the recommendations[13] of the International Consensus Committee on BPH were performed. We introduced an additional question 8 to the AUA symptom index concerning frequency of voiding in the daytime. Patients could score on question 8: score 0: 1-3 times, score 1: 4-5 times, score 2: 6-7 times, score 3: 8-9 times, and score 4: 10 times or more. Patients were requested to report on frequency-volume charts for 3 periods of 24 h during normal daily activity. Patients with LUTS were included if they were over the age of 50 years without any of the specified exclusion criteria of the International Consensus Committee on BPH[13], if they voided a sufficient volume (>150 ml) during one or more free uroflowmetry studies, residual volume was estimated reliably, prostate size was determined by transrectal ultrasound and if frequency-volume charts were available showing voiding and drinking habits during at least one 24 hour period.

From the frequency-volume charts, the minimum voided volume (V_{min}), the maximum voided volume (V_{max}), mean diuria (N_{diuria}) and mean voided volume in the daytime ($V_{mean,day}$), mean nocturia ($N_{nocturia}$) and mean voided volume at night ($V_{mean,night}$) were estimated. Nighttime was defined as the period between 23:00 h and 07:00 h. Voiding volumes on the frequency-volume charts when the patient did not indicate a desire to void were excluded from these analyses, but were included for estimation of mean total urine production in the daytime ($V_{total,day}$) and of mean total urine production at night ($V_{total,night}$). Mean fluid intake in the daytime ($V_{intake,day}$) and mean fluid intake at night ($V_{intake,night}$) were calculated as well. Calculations were repeated after changing the definition of nighttime to the period between 24:00 h and 06:00 h.

Ninety-one men reported on their voiding and drinking habits for three or more nights and 109 men reported on three or more daytime periods. Data from all nights were compared to those of the first night and data from all daytime periods to those of the first daytime period.

Symptom question 7 ("over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?") allows the patient to score between 0 and 5. In order to be able to compare nocturia from frequency-volume charts with symptom question 7 scores, a nocturia score (Snoct) was defined: Snoct=5 for mean nocturia>4, Snoct=4 for 3<mean nocturia≤ 4, Snoct=3 for 2<mean nocturia≤ 3, Snoct=2 for 1<mean nocturia≤ 2, Snoct=1 for 0<mean nocturia≤ 1 and Snoct=0 for mean nocturia=0. In the same way, in order to compare diuria from frequency-volume charts with the score of question 8, a diuria score, Sdiuria, was introduced: Sdiuria=4 for

mean diuria>9, Sdiuria=3 for 7<mean diuria≤ 9, Sdiuria=2 for 5<mean diuria≤ 7, Sdiuria=1 for 3<mean diuria≤ 5, and Sdiuria=0 for mean diuria≤ 3.

The 24-hour day was divided in five time periods: 23:00 h-07:00 h, 07:00 h-11:00 h, 11:00 h-15:00 h, 15:00 h-19:00 h, and finally 19:00 h-23:00 h. For each patient we estimated the period during which the lowest volume was voided and the period during which the largest volume was voided.

Since a normal distribution of some measured parameters is not to be expected, we present means and standard deviations together with the ranges of the parameters. Statistical analyses were done with the distribution free Kendall and Gibbons rank correlation method[14]. The significance level was set at $p<0.05$.

Results

From 188 men who met all other inclusion criteria, 28 (15%) did not complete the frequency-volume charts correctly during at least 24 h (they reported accumulated volumes, they reported only during parts of days, or they were not willing to complete the charts). The included 160 men (age 64.9±8.3 years, range 50-89) had an average symptom score of 16.9±6.5 (range 3-32) and a quality of life score of 3.8±1.5 (range 1-6). Mean prostate size was 44±21 cm^3 (range 13-155). Mean maximum flow at free uroflowmetry was 12.9±5.4 ml/s (range 3.5-33) and mean residual volume was 51±78 ml (range 0-400).

Figure 2.1A shows the number of men in relation to the number of days they reported on their voiding habits, figure 2.1B shows the number of men in relation to the number of nights they reported on their voiding habits.

Mean $N_{nocturia}$ was 2.1±1.4 (range 0-7), mean $V_{mean,night}$ was 222±101 ml (range 55-660), mean N_{diuria} was 6.7±2.7 (range 1-15), and $V_{mean,day}$ was 188±77 ml (range 65-565). Mean voided volume during 24 h was 195±74 ml (range 65-495). Mean lowest voided volume (V_{min}) was 95±58 ml (range 10-350), and mean largest voided volume (V_{max}) was 351±142 ml (range 100-850).

In figure 2.2A, the relation between symptom question 7 (nocturia) and Snoct, calculated from the frequency-volume charts is given (correlation coefficient 0.44, $p<0.001$). In figure 2.2B, the relation between question 8 (diuria) and Sdiuria, calculated from the frequency-volume charts, is given (correlation coefficient 0.44, $p<0.001$). In figure 2.2C, the relation between diuria calculated from the frequency-volume chart and the score on question 2 (“over the past month, how often you have had to urinate again

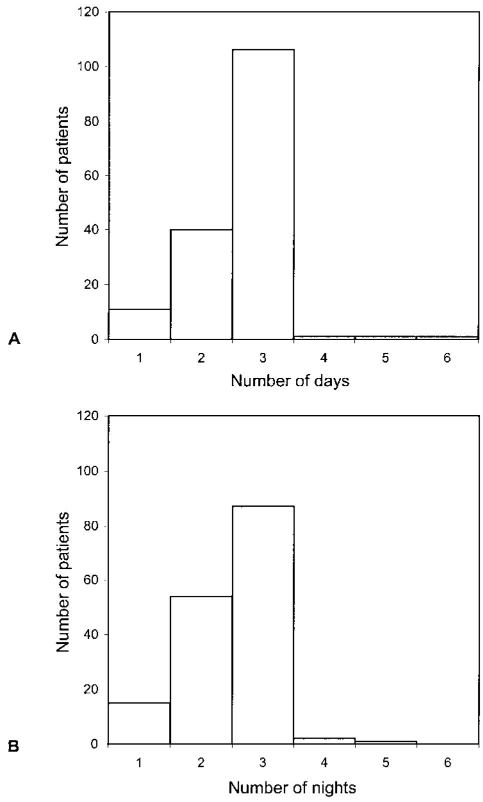


Figure 2.1 A. Number of patients in relation to the number of daytime periods, **B.** number of patients in relation to the number of nights they completed the frequency-volume charts.

less than 2 h after you finished urinating?") of the AUA symptom index is plotted (correlation coefficient 0.38, $p<0.001$).
In figure 2.3A, the number of patients is given in relation to the time period during which the maximum volume (V_{max}) is voided. In figure 2.3B, the number of patients is given in relation to the time period during which the minimum volume (V_{min}) is voided. Ninety-one patients (57%) reported on their voiding and drinking habits for three or more nights. In table 2.1, data from all nights were compared to those of the first night. One hundred and nine patients (68%) reported on three or more daytime periods. In table 2.2, data from all daytime reports were compared to those of the first daytime report.

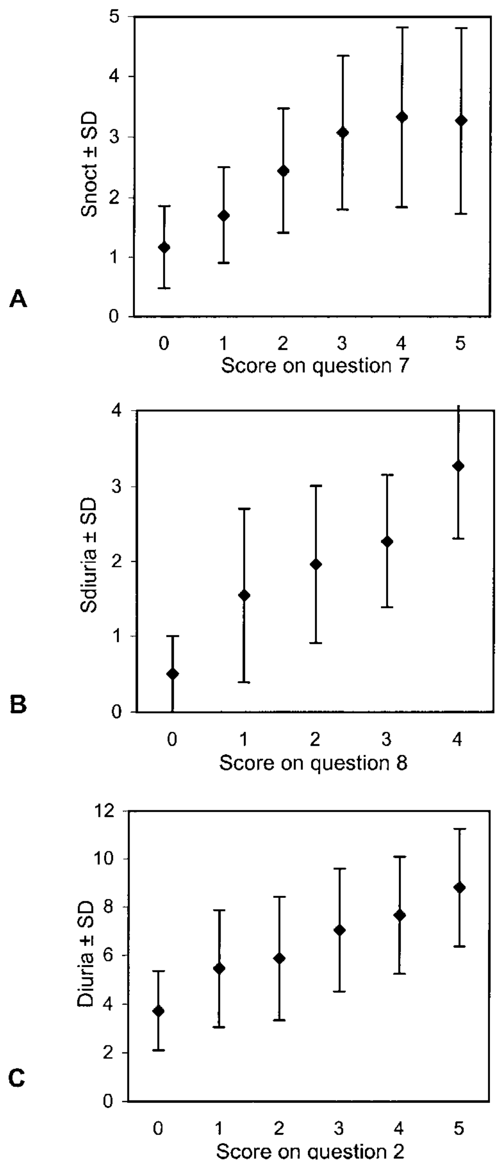
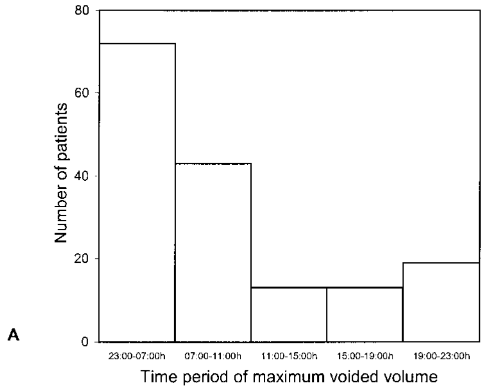


Figure 2.2 A. Scores for nocturia (Snoct) with standard deviation (SD) as calculated from the frequency-volume charts versus score on question 7 from the AUA symptom index. **B.** Scores for diuria (Sdiuria) with SD as calculated from the charts versus score on question 8. **C.** Mean number of diurnal voidings versus score on question 2 of the AUA symptom index.



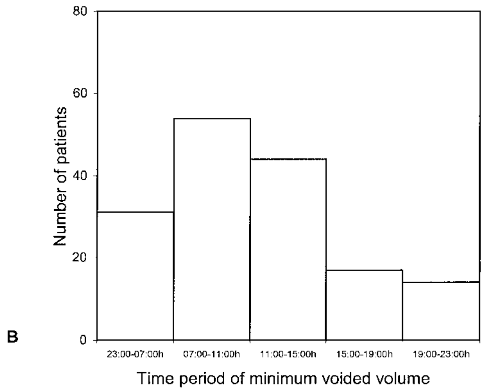


Figure 2.3 A. Number of patients versus time period in which maximum volume is voided. **B.** Number of patients versus time period in which minimum volume is voided.

Table 2.1 Data (mean±SD) from three or more nights (91 patients) compared to those of the first night.

	≥ 3 Nights	First night	Correlation coefficient	Significance	Regression coefficient
Nocturia	2.09±1.22	2.05±1.36	0.79	<0.001	0.96
$V_{mean,night}$ (ml)	208±110	204±152	0.67	<0.001	0.95
$V_{total,night}$ (ml)	433±236	437±359	0.59	<0.001	0.84

Table 2.2: Data (mean±SD) from three or more daytime periods (109 patients) compared to those of the first daytime period.

	≥ 3 Days	First day	Correlation coefficient	Significance	Regression coefficient
Diuria	6.74±2.56	6.65±2.76	0.74	<0.001	0.98
$V_{mean,day}$ (ml)	185±73	190±79	0.75	<0.001	0.99
$V_{total,day}$ (ml)	1250±459	1261±525	0.65	<0.001	0.98

Figure 2.4 compares the mean voided volume during three or more daytime periods with the mean voided volume during the first daytime period.

Figure 2.5A shows the percentage of patients in whom the proportional difference between mean voided volume V_1 during one daytime period and the mean voided volume V_3 during 3 or more daytime periods is lower than the cut-off point, or mathemati-

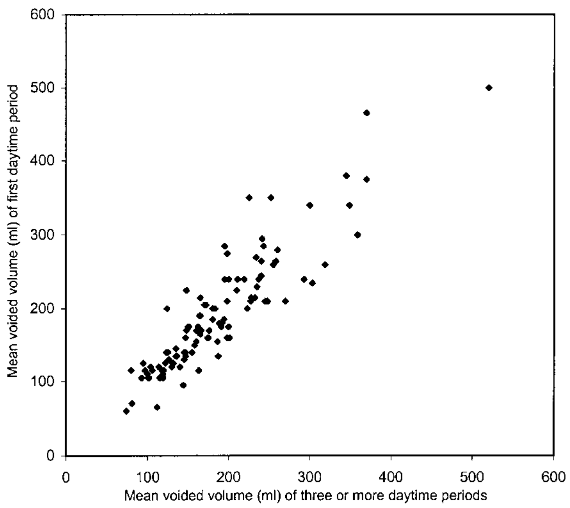


Figure 2.4 Mean voided volume during the first daytime period versus mean voided volume during three or more daytime periods.

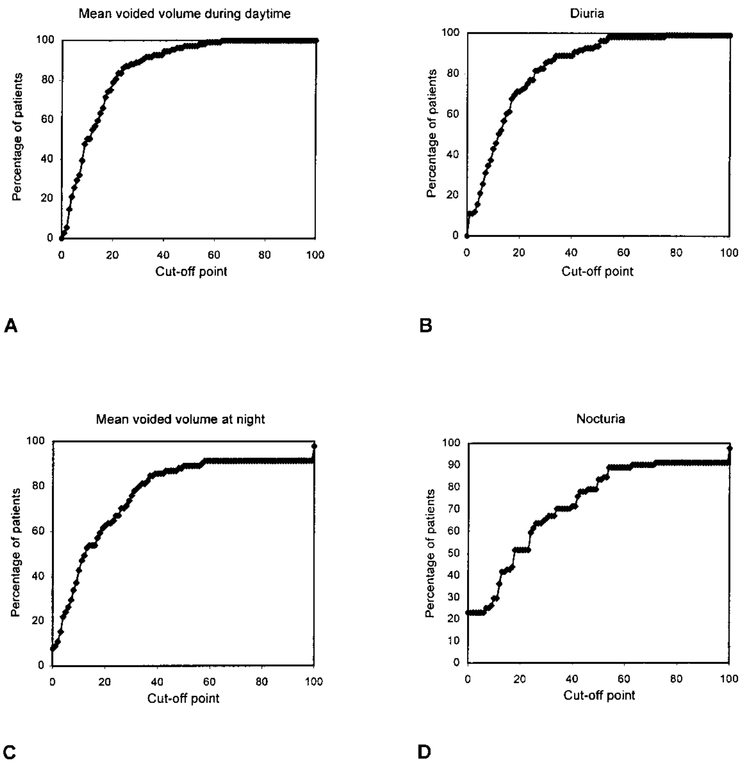


Figure 2.5 Percentage of patients in whom the proportional difference of the value of a parameter calculated from one 24-hour period with respect to that calculated from three or more 24-hour periods is less than the cut-off point. **A.** Mean voided volume in the daytime. **B.** Diuria. **C.** Mean voided volume at night. **D.** Nocturia.

cally formulated: figure 2.5A shows the percentage of men in whom absolute value of $[\{V_1-V_3\}/V_3] * 100\% <$ cut-off point. Figure 2.5B-D shows these percentages for diuria, mean voided volume at night and nocturia, respectively.

Table 2.3 illustrates the effects by changing the definition of nighttime from 23:00 h-07:00 h to 24:00 h-06:00 h.

Table 2.3 Mean values calculated from frequency-volume charts after defining the period of nighttime by the period between 23:00 h and 07:00 h and after defining this period by the period between 24:00 h and 06:00 h.

	23:00 h–07:00 h	24:00 h– 06:00 h
$N_{nocturia}$	2.1±1.4	1.5±1.0
$V_{mean,night}$ (ml)	222±101	231±102
N_{diuria}	6.7±2.7	7.3±2.8
$V_{mean,day}$ (ml)	188±77	190±75

Discussion

The inclusion criteria we used are recommended by the International Consensus Committee on BPH[13]. We consider it not reasonable to change any of these criteria because of the extensive scientific and clinical considerations, which led to the recommendations of the Committee. Nevertheless, we realise that our inclusion criteria, especially the condition that free flowmetry was performed with a voided volume of more than 150 ml, will lead to an exclusion of those men with (starting) decompensation of the bladder. Thus it is reasonable to assume that we selected men in whom obstruction is developing or who are in the early phase of obstruction, i.e. in whom bladders are still able to compensate for impaired outflow condition.

According to Abrams[15] frequency-volume charts are essential in the investigation of the function of the male and female lower urinary tract and they are completed with enthusiasm and accuracy.

From a study in which patients during three consecutive days recorded their fluid intake and voided volume beside collecting 24-hour urinary output, Hansen and Klarskov[2] concluded that recordings on frequency-volume charts are valid and useful in the investigation of patients with voiding symptoms. The mean voided volume in their 18 patients (16 men and 2 women, median age 63 years, range 20-80) was 179 ml (versus 195 ml in our group). The mean lowest voided volume was 73 ml (in our group: 95 ml) and the mean largest volume was 421 ml (in our group: 351 ml). In 95 older people (age 72±5.3 years) Asplund and Åberg[10] found a mean voided volume at night of 256±113 ml (versus 222±101 ml in our group) and a mean voided volume in the daytime of 188±86 ml (versus 188±77 ml in our group). McCormack et al.[3] assessed the agreement between patient questionnaire and frequency-volume charts in 88 patients. They found a mean diurnal voided volume of 176±64 ml and a mean voided volume at night of 233±130 ml. They reported a poor agreement between patient questionnaire- and chart-determined urinary frequency, suggesting that the frequency-volume chart shows a more valid indication of urinary habits than the patient questionnaire. Other authors[4-9] also found the frequency-volume chart to be a basic tool in LUTS, although not suitable for young children or as a differential diagnostic tool.

Despite the fact that the compositions of the reported groups are quite different from the composition of our group and we excluded voidings when patients did not indicate a desire to void, agreement exists between the reported volumes and ours. Agreement also exists (fig. 2.2A-C) between patient questionnaire scores concerning frequency, nocturia and diuria, and the data calculated from the frequency-volume charts.

The mean lowest voided volume was 95 ml and the mean largest voided volume was 351 ml in our group, demonstrating the well-known large variation at an individual level. However, a large variation at an individual level and as a consequence a large variability in voiding parameters does not mean that the frequency-volume charts are completed unreliably. In a patient reporting ten voidings with a volume of 200 ml each the variability in voiding volume is 0 ml, but one may have serious doubts about the reliability of these data. Variability is not caused by measurement errors but by the nature of the parameter: No one has a unique functional capacity! As a consequence, studying variability or calculation of the average within-subject variation is not appropriate to judge the reliability of data on frequency-voiding charts. To judge reliability, we calculated average voided volumes and the minimum and maximum voided volumes and compared their means and standard deviations to data published in validated studies. Moreover, we compared nocturia and diuria calculated from frequency-volume charts with scores on the I-PSS questionnaire. Keeping in mind the large variation at an individual level, we conclude from the agreement between our data and those reported in validated studies and from the agreement between data and scores on questionnaires that our 160 men completed their records reliably.

We excluded volumes when patients did not indicate a desire to void. These voidings may be prophylactic, for instance before going out, and are likely to have no relation to LUTS.

Of our consecutively included patients, 15% were not able or were not willing to complete the frequency-volume charts correctly at all. Despite the fact that all included 160 men were requested to complete charts during three 24-hour periods, 32% reported only during one or two daytime periods (fig. 2.1A) and 43% only during one or two nights (fig. 2.1B). Some of these men may start reporting in the morning of the first day and may finish before going to bed on the second or third day.

At a group level, the number of voidings and volumes and their variability are hardly influenced by the number of 24-hour periods (tables 2.1, 2.2). By including the measurements of the first day in the mean of three or more days as well, the agreements are influenced in a positive way. However, we just wanted to establish whether reporting during one day is as sufficient as reporting during three or more days. Figure 2.5A-D illustrates the reproducibility of some parameters on an individual level. From figure 2.5A, it appears that in more than 80% of the men, the mean voided volume during the first daytime period did not differ more than 20% from the mean voided volume calculated from three or more daytime periods. Compared to the difference between the mean lowest voided volume (95 ml) and the mean largest voided volume (351 ml), this difference of 20% is negligible. This fact and the data of the figure 2.5B-D strongly suggest that reporting on frequency-volume charts during 24 h is sufficient to get an impression of the voiding habits during normal daily life. It may even be better to report for only one 24-hour period, as the less the patient is asked to do so, the more eager he will be to perform the task accurately. We want to emphasise that these conclusions are formulated for our well-defined group of men with LUTS suggestive of BPH.

Because most patients were treated for their symptoms shortly after the examinations, it was not possible to repeat the reporting after some period in order to study the variability as a function of time.

Asplund and Åberg[10] reported that the time going to bed at night and getting up in the morning varied considerably among elderly. Therefore, we decided to use the 8-hour period between 23:00 h and 07:00 h instead of true nocturia. Shortening of this time period to 24:00 h-06:00 h only results in a proportional reduction of mean nocturia and a proportional increase of mean diuria (table 2.3).

The average number of nightly voidings made 24% of the 24-hour frequency. The average urine volume at night was 27% of the total 24-hour urine production. In our group, 16 patients (10%) had a 24-hour urine production of more than 2.5 litres; however, their fluid intake was also more than 2.5 litres. Of all men, only 4 (2.5%) had more than half of their diuresis during nighttime. According to Abrams[15], this shows that nocturia is unlikely to be due to nightly polyuria in our group of men.

Figure 2.2A shows agreement between scores for nocturia and scores between 0 and 3 on symptom question 7. Keeping in mind the rather high standard deviation, a flattening of the curve towards symptom score 4 and 5 is observed. If we change the definition of nighttime to the period of 24:00 h-06:00 h this flattening would even be more pronounced. We assume that as the number of times at which a patient has to get up to urinate increases, he may increasingly overstate this number on the AUA symptom index. Patients may simply be bothered by a nocturia frequency of more than 2 or 3. In

figure 2.2B and 2.2C such a flattening is not observed. Agreement also exists between frequency calculated from the patient questionnaire and diuria calculated from frequency-volume charts. Despite the fact that the correlation coefficients in figure 2.2A-C are highly significant, we have to keep in mind the rather high standard deviation of the data in the figures. Information from a questionnaire may be rather unprecise as regards the number of voidings in the daytime and at night.
The largest volume is voided in most cases at night or in the morning (fig. 2.3A), possibly due to a delay in sensation of a full bladder during sleep. The smallest volume is voided in most cases in the morning or early afternoon (fig. 2.3B).

Conclusions

Frequency-volume charts completed by patients with LUTS suggestive of BPH are reliable. Reporting correctly on frequency-volume charts during just 24 h is sufficient to gain insight into the voiding habits of patients during normal daily life.

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CHAPTER 3

Data from Frequency-Volume Charts Versus Symptom Scores and Quality of Life Score in Men with Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia

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Abstract

Objective: The aim is to study the relations between reported data on frequency-volume charts and the American Urological Association (AUA) symptom scores and quality of life score.

Methods: Men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia (BPH), were consecutively included in the study if they met the criteria of the International Consensus Committee on BPH, they voided >150 ml during uroflowmetry, residual volume and prostate size were estimated and frequency-volume charts were completed correctly. From the frequency-volume charts, voiding habits and fluid intake in the daytime and at night were evaluated.

Results: In the included 160 men no correlation was found between total urine production at night or in the daytime and symptom index or quality of life score. Nocturia was correlated with symptom index, but surprisingly not with quality of life score. Small voided volumes at night and in daytime are attended by high symptom index and high quality of life score (= low quality of life). Diuria has a high impact on symptom index and quality of life score. Men who completed frequency-volume charts during 3 or more daytime periods (68%) had a significantly higher symptom index than those who completed only 1 or 2 daytime periods (32%).

Conclusions: High diuria, and small voided volumes at night and in daytime contribute significantly to high symptoms and low quality of life. Nocturia correlated with AUA symptom index but surprisingly not with quality of life score.

Introduction

The American Urological Association (AUA) symptom index and quality of life question[1] are accepted by the World Health Organisation as mandatory tools in the clinical evaluation of men with lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH)[2]. The AUA symptom index consists of seven questions concerning voiding habits: incomplete emptying (question 1), frequency (question 2), intermittency (question 3), urgency (question 4), weak urinary stream (question 5), hesitancy (question 6), and nocturia (question 7). Symptom index (0-35) is calculated by summing the scores (0-5) on the seven questions. A survey of Gee et al. [3] revealed that 99% of respondents of a random sample of 514 American urologists were aware of and used the AUA symptom index. Even 21% of these respondents had altered their diagnosis and management strategies because of its existence. Many attempts have been made to explain symptoms from prostate size, urinary flow rate, residual urine and pressure-flow studies. However, symptom index hardly correlates with prostate size[4-6], urinary flow rate[5,6], residual volume[5,6], and obstruction grade[4,5,7,8]. Quality of life increases with increasing maximal flow rate during free flowmetry and with decreasing residual volumes[5]. However, quality of life does not correlate with prostate volume and obstruction grade[5].

Frequency-volume charts are an important tool in the investigation of men with voiding disorders and give the urologist information about frequency in daytime and at night together with the voided volumes[9]. The reliability of the data on frequency-volume charts completed by a well-defined group of men with LUTS suggestive of BPH was discussed in a previous paper[10]. It was concluded that frequency-volume charts completed during one period of 24 h are reliable and sufficient to gain insight into the voiding habits of these men.

The relations between reported data on the frequency-volume chart, symptom scores, and quality of life score in men with LUTS suggestive of BPH hardly have been studied. Our aim is to study these relations in a well-defined group of men with LUTS suggestive of BPH.

Materials and Methods

Methods, definitions and units conform to the standards proposed by the International Continence Society (ICS) except when specifically noted.

In men with LUTS consecutively presenting to our outpatient department of urology, basic standard evaluation (history, quantification of symptoms by the seven questions, calculation of the symptom index and quantification of quality of life as proposed by the AUA[1], physical examination and digital rectal examination, urinalysis and renal function assessment) and recommended tests (uroflowmetry and residual urine estimation) conforming to the recommendations[2] of the International Consensus Committee on BPH were performed. Men with LUTS were included if they were older than 50 years without any of the specified exclusion criteria of the International Consensus Committee on BPH[11], they voided a sufficient volume ($>$150 ml) during one or more free uroflowmetry studies, residual volume was estimated reliably, prostate size was determined by transrectal ultrasound and frequency-volume charts were available showing voiding and drinking habits during at least one normal 24-hour period. From the frequency-volume charts, the minimum voided volume (V_{min}), the maximum voided volume (V_{max}), mean diuria (N_{diuria}) and mean voided volume in the daytime ($V_{mean,day}$), mean nocturia ($N_{nocturia}$) and mean voided volume at night ($V_{mean,night}$) were estimated. Nighttime was defined as the period between 23:00 h and 07:00 h. Voided volumes on the frequency-volume charts when the patient did not indicate a desire to void were excluded from these analyses, but were included for estimation of mean total urine production in daytime ($V_{total,day}$) and of mean total urine production at night ($V_{total,night}$). Mean fluid intake in daytime ($V_{intake,day}$) and mean fluid intake at night ($V_{intake,night}$) were calculated as well. Parameters and correlation coefficients were recalculated after changing the definition of nighttime into the period between 24:00 h and 06:00 h.

Statistical analyses were done with Kendall and Gibbons distribution free rank correlation method[12] and Student's t-test. The Kolmogorov-Smirnov goodness of fit test[13] was used to examine whether a distribution of a parameter resembled the normal distribution. Significance (two-tailed) was set at $p<0.05$.

Results

The included 160 men (age 64.9±8.3 years, range 50-89) had an average symptom score of 16.9±6.5 (range 3-32) and quality of life score of 3.8±1.5 (range 1-6). Mean prostate size was 44±21 cm^3 (range 13-155). Mean maximum flow at free uroflowmetry was 12.9±5.4 ml/s (range 3.5-33) and mean residual volume was 51±78 ml (range 0-400). The distributions of the scores on the seven questions, of the symptom index and of the quality of life score are given in figure 3.1. Only the distribution of the symptom index appeared to be normal (Kolmogorov-Smirnov test).

Table 3.1A shows the symptom index and quality of life of the 160 men in relation to the number of daytime periods and table 3.1B in relation to the number of nights they completed the frequency-volume charts correctly.

The mean AUA symptom index in men who completed the charts during 3 or more daytime periods (68%) was significantly higher than in those who completed the charts during only 1 or 2 daytime periods.

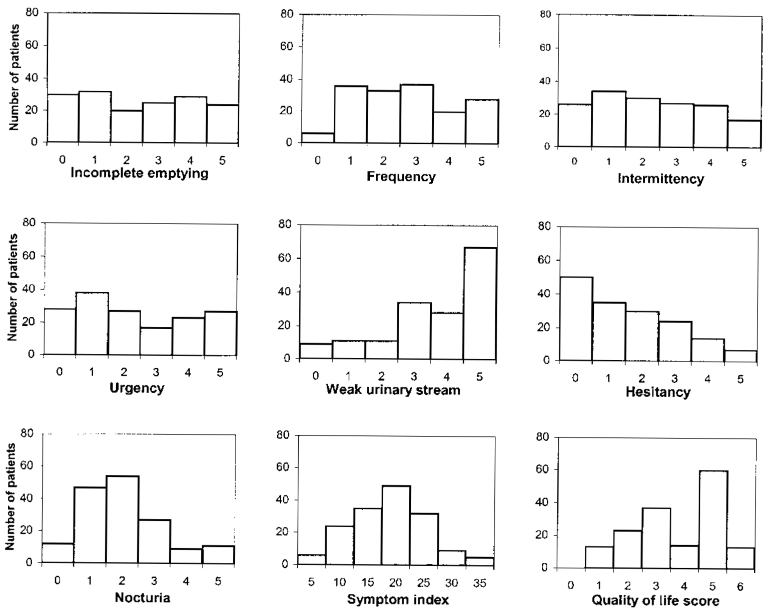

Figure 3.1 Distributions of symptom scores, symptom index and quality of life score.

Table 3.1 AUA symptom index and quality of life score in relation to the number of daytime (A) and nighttime (B) periods the patients reported.

A.

	1 or 2 daytime periods (51 men)	3 or more daytime periods (109 men)	p
Symptom index	15.4±6.3	17.6±6.5	0.045
Quality of life score	3.6±1.5	3.9±1.5	0.24

B.

	1 or 2 nighttime periods (69 men)	3 or more nighttime periods (91 men)	p
Symptom index	16.6±6.8	17.1±6.3	0.63
Quality of life score	3.7±1.4	3.9±1.5	0.38

In table 3.2 correlation coefficients are listed between scores and data calculated from the frequency-volume charts.
A significant correlation was found between minimum voided volume (V_{min}) and the score on question 2 (frequency): correlation coefficient -0.22 ($p<0.01$), resulting in a correlation coefficient between symptom index and V_{min} of -0.17 ($p<0.01$). However, no significant correlation existed between V_{min} and quality of life score (table 3.2).
Eighty men had a residual volume equal or higher than 10% of the mean voided volume in daytime. The score on symptom question 1 (incomplete emptying) was 2.54±1.73 in these men. In the others the score was 2.25±1.74. This difference is not significant ($p=0.15$).
Of the 160 men, 25 (15.6%) noted sometimes voidings at night without desire to void. By taking into account these voidings, average nocturia in this group of 25 men increased from 1.6 to 2.3. Recalculations of the correlation coefficients between scores and nocturia (including voidings without desire to void) for all 160 men, resulted in minor differences with respect to the values listed in table 3.2.
Fifty-six men (35.0%) sometimes voided in daytime without desire to void. In this group diuria increased from 5.5 to 7.4 by including these voidings in the calculations. Taking into account these voidings did not result in significant changes in the correlation coefficients between scores and diuria listed in table 3.2.

Table 3.2 Kendall and Gibbons correlation coefficients between scores and parameters calculated from frequency-volume charts (correlation coefficients without significance are not shown).

Symptom	$N_{nocturia}$	$V_{mean,night}$	$V_{total,night}$	N_{diuria}	$V_{mean,day}$	$V_{total,day}$	V_{min}	V_{max}
Incomplete emptying		-0.18**		0.19**	-0.16**		-0.15*	-0.12*
Frequency	0.14*	-0.26**		0.37**	-0.22**	0.12*	-0.22**	
Intermittency	0.13*			0.14*				
Urgency				0.28**	-0.13*	0.13*		-0.14*
Weak stream					-0.13*		-0.13*	-0.12*
Hesitancy		-0.14*						-0.14*
Nocturia	0.46**	-0.19**	0.21**	0.21**	-0.21**			-0.27**
Symptom index	0.21**	-0.20**		0.31**	-0.21**		-0.17**	-0.17**
Quality of life score		-0.22**		0.18**	-0.12*			-0.14*

* Correlation is significant at the 0.05 level
** Correlation is significant at the 0.01 level

In table 3.3 the correlation coefficients are listed between the scores on the different questions and the quality of life score.

In table 3.4 the relation between nocturia and quality of life score is given. This relation is hardly affected by taking into account the voidings without desire to void.

In table 3.5 urinary symptoms are listed in decreasing order of score, and listed in decreasing order of correlation with quality of life.
Changing the definition of nighttime into the period between 24:00 h and 06:00 h resulted in minimal changes in the correlation coefficients listed in table 3.2 for diuria, mean voided volume in daytime and total urine production in daytime. For nocturia, mean voided volume at night and total urine production at night, the correlation coefficients slightly decreased.

Table 3.4 Relation between nocturia and quality of life score.

	Number of men	Quality of life score ± SD
0≤ nocturia<1	17	4.2±1.3
1≤ nocturia<2	54	3.6±1.6
2≤ nocturia<3	50	3.6±1.5
3≤ nocturia<4	22	4.1±1.2
4≤ nocturia	17	4.4±1.3

Table 3.5 Urinary symptoms listed in decreasing order of score, and listed in decreasing order of correlation with quality of life.

Decreasing order of score	Decreasing order of correlation with quality of life
Weak urinary stream	Frequency
Frequency	Incomplete emptying
Incomplete emptying	Urgency
Urgency	Intermittency
Intermittency	Weak urinary stream
Nocturia	Hesitancy
Hesitancy	Nocturia

Table 3.3 Kendall and Gibbons correlation coefficients between scores (correlation coefficients without significance are not shown).

Symptom	Incomplete emptying	Frequency	Intermittency	Urgency	Weak stream	Hesitancy	Nocturia	Symptom index
Incomplete emptying	-	-	-	-	-	-	-	-
Frequency	0.39**	-	-	-	-	-	-	-
Intermittency	0.21**	0.19**	-	-	-	-	-	-
Urgency	0.21**	0.42**		-	-	-	-	-
Weak stream	0.22**		0.27**		-	-	-	-
Hesitancy	0.24**	0.16*	0.46**		0.21**	-	-	-
Nocturia		0.18**	0.14*	0.22**			-	-
Symptom index	0.50**	0.52**	0.48**	0.44**	0.44**	0.41**	0.32**	-
Quality of life score	0.30**	0.35**	0.22**	0.30**	0.20**	0.20**	0.16*	0.40**

* Correlation is significant at the 0.05 level
** Correlation is significant at the 0.01 level

Discussion

The inclusion criteria and the reliability of the frequency-volume charts are discussed in a previous paper[10]. It was concluded that reporting correctly on frequency-volume charts during 24 h is sufficient to gain insight into the voiding habits of patients during normal daily life.

The distributions of the scores on the seven symptom questions and the score for quality of life do not resemble normal curves. Only the distribution of the symptom index is normal (fig. 3.1). Kendall and Gibbons rank correlation method is a distribution-free test and thus suited for our purposes.

As reported in our previous paper[10] there is an overstatement of score on question 7 (nocturia) compared to the reported nocturia on the frequency-volume charts. Although this overstatement suggests that nocturia is experienced as uncomfortable, surprisingly no relation was found between nocturia calculated from frequency-volume charts, and quality of life score (table 3.4). From the seven questions, even question 7 (nocturia) has the lowest impact on quality of life (tables 3.3, 3.5). Saito et al.[14] studied frequency in elderly (age >65 years) and adults (age <65 years). They found no difference between the two groups in sleeping hours: 8.64±0.96 h for the elderly (n=85) and 8.46±1.09 h for the adults (n=130), Nevertheless, some elderly patients may have very short sleeping times and may void because they wake up and not because they are waken up by the desire to void. These patients may include these voidings in their score on question 7 (nocturia). In our group 15.6% of the men noted some voidings at nighttime without desire to void on their micturition dairy. Including these voidings in the analysis did not change the reported overstatement on question 7 (nocturia) compared to the reported nocturia on the frequency-volume chart.

A reasonable number of men scored 5 (“unhappy”) for quality of life. If all patients with quality of life score 5 are excluded and Kendall and Gibbons correlation method is applied to the remaining patients, again no correlation was found between nocturia and quality of life. Thus the high incidence of score 5 for quality of life does not mask a correlation between nocturia and quality of life. In contrast with nocturia, decreasing voided volumes at night result significantly in a decreasing quality of life (table 3.2).

There is a fair correlation between mean diuria and score on symptom question 2 (frequency). Patients do not overstate diuria[10]. Nevertheless, diuria has an important impact on AUA symptom index and quality of life (table 3.2), which may be due to the interference of diuria with social life. This assumption seems to be justified by the correlation of frequency (symptom question 2) and urgency (symptom question 4) with quality of life score (tables 3.3, 3.5): frequency and urgency have a high impact on quality of life. Correlations of symptom scores and quality of life with nocturia or diuria were hardly affected by including voidings without desire at night or during daytime.

The feeling of incomplete emptying (symptom question 1) is associated with a decrease in quality of life as well. High diuria and small voided volumes correlate significantly with score on symptom question 1 (table 3.2). Nevertheless, the score on question 1 is hardly influenced by the presence or absence of residual volume. Possibly frequent voiding of small volumes may be interpreted by the patient as caused by inability to empty the bladder completely. Anyhow a significant correlation exists between score on question 1 (incomplete emptying) and question 2 (frequency) (table 3.3) and a significant negative correlation between minimum voided volume and score on question 2 (table 3.2). As expected, scores on symptom questions 3 (intermittency), 5 (weak urinary stream) and 6 (hesitancy) are hardly affected by data from frequency-volume charts.

Total urine productions at night and in daytime have no influence on AUA symptom index and quality of life. Changing the definition of nighttime into the period between 24:00 h and 06:00 h appears to have no implications for our conclusions.

Some source of bias may arise from voidings without desire to void, as the next desired voiding will be delayed by the voiding without desire. This will affect frequency and urgency. However, in our opinion these voidings are part of a patient's habits. We assume that these voidings are prophylactic and will not contribute to symptoms and quality of life. Therefore we considered it not reasonable to include these voidings in the calculations of voided volumes.

The ICS "benign prostatic hyperplasia" study group reported on the bothersomeness of urinary symptoms in BPH[15]. They found a higher order for the score on nocturia than for the score on frequency. We included only men who were able to void at least 150 ml during uroflowmetry. In this way men may be excluded with a high score on nocturia. Nevertheless, the ICS study group also reported a higher bothersomeness for frequency (times/day) than for nocturia. In their men the high prevalence of a weak urinary stream also did not have an impact on bothersomeness.

Conclusions

Diuria has a much higher impact on symptom index and quality of life than nocturia has. High diuria, and small mean voided volumes at night and at daytime contribute significantly to high symptom scores and high quality of life score (= low quality of life). Total urine productions during nighttime and during daytime do not influence symptom index and quality of life score.

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CHAPTER 4

Symptoms and Quality of Life Versus Age, Prostate Volume, and Urodynamic Parameters in 565 Strictly Selected Men with Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia

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Abstract

Objectives: To investigate the associations of symptoms and quality of life with age, prostate volume, and urodynamic parameters in a large group of strictly selected men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia.
Methods: The 565 consecutive men met all the criteria of the International Consensus Committee on benign prostatic hyperplasia, and voided more than 150 ml during uroflowmetry. The residual volumes and prostate sizes were estimated. The International Prostate Symptom Score (I-PSS) and quality of life score were collected, and urodynamic evaluations performed.
Results: The prostate volume and obstruction grade were not, but low detrusor contractility and low bladder capacity were significantly associated with symptoms. Except for nocturia, older men presented with lower voiding scores on the I-PSS. The presence of a residual urine volume hardly influenced patients' symptoms and quality of life. Men with an unstable bladder scored higher on frequency, urgency, and nocturia on the I-PSS but the symptom index or quality of life score were not affected by the presence of an unstable bladder. Because of the high variability and subjective interpretation of symptoms and the opposite implication from the urodynamic evaluation on symptoms, associations were still weak.
Conclusions: Except for nocturia, older men had higher voiding scores on the I-PSS. Prostate volume and obstruction grade were not, but low detrusor contractility and low capacities were, associated with the symptom index. The presence of an unstable bladder and/or residual volume was hardly associated with the symptom index or quality of life score. Although we used a large group of strictly selected men, the associations were still weak.

Introduction

The International Prostate Symptom Score (I-PSS) and quality of life question[1] have been adopted by the World Health Organisation International Consultation on Benign Prostatic Hyperplasia (BPH) as an important part of the evaluation of men with lower urinary tract symptoms (LUTS)[2].

The I-PSS includes seven questions concerning incomplete emptying, frequency, intermittency, urgency, weak urinary stream, hesitancy, and nocturia. Each question can be answered on a scale of 0 to 5 (ranging from "not at all" to "almost always"). The symptom index is the sum of the seven scores and, therefore, ranges from 0 to 35 points. Additionally, one question concerning the patient's quality of life with LUTS may be answered on a scale of 0 ("delighted") to 6 ("terrible").

The symptom index and quality of life score measure the severity of LUTS suggestive of BPH. The urodynamic examination objectively evaluates bladder and urethral behaviour in men with LUTS and allows quantification of the degree of urethral obstruction[3]. Prostate volume estimation and free uroflowmetry are also important in the diagnosis of LUTS due to BPH.

However, according to the results of various studies, symptoms do not appear to correlate with prostate size[4-6], urinary flow rate[4], residual volume[4], and obstruction grade[5,7-9]. Barry et al.[4] only found a weak significant correlation between prostate volume and nocturia. Ezz el Din et al.[6] found weak associations between prostate volume and urgency and weak stream. The lack of distinct correlations may be due to the rather heterogeneous composition of the groups of men in whom the studies were performed. On the other hand, other parameters, such as impaired detrusor contractility, reduced bladder capacity, and the prevalence of detrusor instability, may play a role in the severity of LUTS.

The present study was composed of a large group of men with LUTS in whom it is reasonable to assume that the symptoms were primary due to BPH. Therefore, as recommended by the International Consensus Committee on BPH[10], patients with prior failed invasive treatment for BPH, patients with a possibility of neurological disease, and patients taking drugs affecting lower urinary tract functions were excluded. In addition, we included only patients who were able to void more than 150 ml during free flow recording. Thus patients with severe and prolonged obstruction and with (starting) decompensation of the bladder were excluded. With these restrictions we hoped to reduce the aetiology of the patients' complaints to a minimum number of variables.

The aim of this study was to establish in this large group of strictly selected men with LUTS suggestive of BPH, whether the associations of symptoms and quality of life with age, prostate volume, and urodynamically estimated degrees of obstruction, bladder contractility, residual volume, bladder capacities, and prevalence of detrusor instability are more pronounced.

Materials and Methods

From October 1993 until January 2000, in consecutive men with LUTS who were self-referred or referred by their primary care physician to the outpatient department of urology, basic initial evaluations (history, physical examination, digital rectal examination, urinalysis and renal function assessment) and recommended diagnostic tests (uroflowmetry and residual urine estimation) were performed, conforming to the recommendations of the International Consensus Committee on BPH[2].

Men were included if they were older than 50 years of age, without any of the specified exclusion criteria of the International Consensus Committee on BPH[10], and if they voided a sufficient volume (>150 ml) during one or more free uroflowmetry studies, if the residual urine was estimated reliably and if prostate size was determined by transrectal ultrasound.

The I-PSS[1] were collected for all patients. The symptom index was calculated by summing the 7 scores. Every patient answered the question concerning quality of life[1]. According to the clinical judgement of the urologist, if the results of the evaluation were suggestive of LUTS due to BPH, the patients were also evaluated urodynamically.

Filling cystometric studies were performed with the patient supine and erect. Pressure-flow studies were done twice with the patient erect. Bladder pressure was recorded with a 5F catheter, and rectal pressure was measured with a 14F catheter connected to external pressure transducers. The bladder was filled with saline at 37°C through a second 5F catheter at a constant rate of 50 ml/min. In some men, an 8F double-lumen catheter was used for bladder pressure measurement and bladder filling. Filling was stopped when the patient had a strong desire to void. If two catheters were used, the first pressure-flow study was done with the measuring and filling catheters in the bladder, and the second study was done after removal of the filling catheter. The pressure-flow study with the lowest urethral resistance (usually during voiding with only the measuring catheter in the bladder) was used for additional analysis.

In all patients, the residual urine volume was estimated during one of the visits at the outpatient department by transabdominal ultrasound or catheterisation. If the residual volume was significant, the test was repeated. From the pressure-flow studies, the obstruction grade (0, no obstruction to 6, severe obstruction) and detrusor contractility grade (0, very weak to 5, strong bladder), as proposed by Schäfer[11], were estimated. Men with an obstruction grade of 3 or more were considered to have obstruction. An effective bladder capacity was defined as

the maximum cystometric bladder capacity minus the residual volume.
Statistical analyses were performed with the distribution-free Kendall and Gibbons correlation method and the Mann-Whitney *U* test. The Kolmogorov-Smirnov goodness of fit test was used to analyse the normal distribution of variables[12]. The level of significance (two-tailed) was set at $p<0.05$.

Results

We excluded about 5% of the patients because they did not void more than 150 ml during the free flow recording. Results were obtained from the 565 included men. The mean age of the men was 66±8 years (range 50-90). The mean prostate volume was 38±19 ml (range 10-155), and mean maximum free flow rate was 12±5 ml/s (range 3-35). Except age and symptom index, no parameter was normally distributed (Kolmogorov-Smirnov test).
Figure 4.1 shows the distributions of symptom scores, symptom index, and quality of life score.

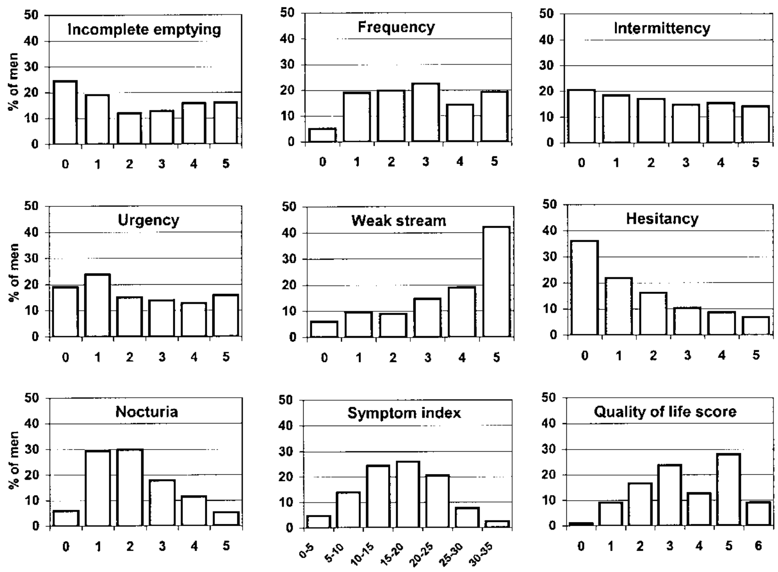

Figure 4.1 Distributions of symptom scores, symptom index, and quality of life score.

According to our definition, 301 men (53%, 66±7 years of age) had obstruction, and 264 men (47%, 66±8 years of age) had no obstruction. Of the 565 men 31 (5%) had a prostate volume of less than 20 ml. Nevertheless, 8 (26%) of the 31 were obstructed.
Correlation coefficients are listed between scores on the symptom questions, symptom index, and quality of life score, and between these variables and age, prostate size, and urodynamic parameters in table 4.1. The correlation coefficient between the symptom index and quality of life score was 0.44 ($p<0.001$).
Of 565 men, 148 patients (26%, 68±7 years of age) had a residual volume more than 20% of cystometric capacity, 199 (35%, 65±8 years of age) had residual volume equal or lower than 20% of cystometric capacity, and 218 (39%, 65±8 years of age) did not have a residual volume. The scores on I-PSS question 1 (incomplete emptying) in these three groups (score 2.4±1.8, 2.2±1.8, and 2.1±1.8, respectively) did not differ significantly.

The presence of residual volume did result in a higher symptom index but this difference was not significant ($p=0.065$). The quality of life score was not affected by residual volume.
Of the 565 men, 259 (46%, 67±7 years of age) had an unstable bladder: 55 only in the supine position, 106 only in the sitting position and 98 in both positions. In 306 men (54%, 64±8 years of age), no instabilities were detected. No significant relation was found between scores and the position in which instability occurred. Scores on frequency, urgency, and nocturia were significantly higher in the men with an unstable bladder than in those with a stable bladder. However, the difference in symptom index was not significant. The patients' quality of life was not affected by the presence of instability during filling cystometry.

Discussion

We excluded men with prior failed invasive treatment for BPH and men with possible neurological diseases because their symptoms are likely not to be associated with BPH. Men taking drugs affecting urinary tract functions were excluded because the severity of their symptoms will depend on the medication. Conforming to the recommendation of the International Consensus Committee on BPH[10], we included men who were able to void a volume more than 150 ml during free uroflowmetry. The number of patients who had to be excluded for this reason strongly depends on the efforts made to obtain a reliable flow registration. At our outpatient department, this number of

Table 4.1 Kendall and Gibbons correlation coefficients among symptom scores, symptom index and quality of life score, and among these scores and age, prostate volume, and urodynamic parameters (only significant correlations are listed).

	Incompl. emptying	Frequency	Intermit-tency	Urgency	Weak stream	Hesitancy	Nocturia	Age (years)	Prostate volume (ml)	Schäfer's grade	Contrac-tility	Cystometric capacity (ml)	Effective capacity (ml)
Incomplete emptying	-	-	-	-	-	-	-	-0.08**			-0.12**		-0.06*
Frequency	0.32**	-	-	-	-	-	-					-0.17**	-0.17**
Intermittency	0.32**	0.20**	-	-	-	-	-				-0.13**		
Urgency	0.14**	0.38**	0.13**	-	-	-	-		0.07*	0.13**	0.12**	-0.16**	-0.16**
Weak stream	0.22**	0.17**	0.31**	0.10**	-	-	-	-0.16**			-0.12**		
Hesitancy	0.29**	0.16**	0.38**	0.07*	0.23**	-	-	-0.10**					
Nocturia	0.13**	0.26**	0.11**	0.23**		0.07*	-	0.10**		0.08*		-0.17**	-0.19**
Symptom index	0.53**	0.53**	0.54**	0.41**	0.42**	0.45**	0.31**	-0.06*			-0.09**	-0.10**	-0.13**
Quality of life score	0.30**	0.33**	0.28**	0.29**	0.25**	0.28**	0.16**	-0.07*				-0.09**	-0.10**

* Correlation significant at 0.05

** Correlation significant at 0.01

patients could be reduced from about 20% in the early 1990s to about 5% during the period of our study. This latter percentage agrees with the 8% reported by Ezz el Din[6]. Excluding men with a voided volume of less than 150 ml leads to the exclusion of those men with (starting) decompensation of the bladder with changes in bladder properties. In a number of these men, a transurethral catheter had to be placed because of severe retention. With our strict selection process, we hoped to reduce the aetiology of the patients' complaints to a minimum of variables. We believe the men we included in our study to be a reasonable representative sample of the population who attend a urologic clinic with LUTS, and for whom there is suspicion of BPH. Regardless, the mean and variability of age, cystometric capacity, residual urine volume, and symptom index in our group were comparable to those reported by Rosier and de la Rosette[5] for a group of 521 men with micturition complaints. In their group the average prostate volume (44.1 cm^3) was higher than in our group (38 cm^3). We found 53% of the men in our study to be obstructed, slightly lower than reported by the International Continence Society on BPH study group (60%)[13]. These differences may be partly due to our condition of a voided volume of more than 150 ml during free uroflowmetry.

The value range of all the parameters was rather wide (fig. 4.1 and Results section). Even though we only included men in whom it was reasonable to assume that their symptoms are associated with BPH, the reported absence of a correlation among prostate volume and symptom index and quality of life score[4-6,9] and among Schäfer's obstruction grade and symptom index and quality of life score[5,7-9] was reconfirmed in our study. Only the scores for urgency (question 4) and nocturia (question 7) correlated significantly but weakly with Schäfer's grade. The replacement of the discrete Schäfer grade by the continuous AG number[14], did not have a significant impact on the results listed in table 4.1.

As in the study by Ezz el Din et al.[6], we found a weak correlation between prostate volume and urgency. Impaired bladder outflow because of low detrusor contractility correlated better with symptoms than obstruction grade (table 4.1). Low cystometric and effective capacities resulted in higher scores for frequency, urgency and nocturia and for symptom index and quality of life. These findings agree with the earlier reported significant relation between frequent voiding of small volumes as estimated from frequency-volume charts and symptom index and quality of life score[15]. We advice performing urodynamic evaluations to be aware of a low bladder contractility and/or small bladder capacity without outlet obstruction. It is generally accepted that patients with low flow/low pressure BPH might not realise the same benefit from surgical treatment as do other patients[10]. Surgery in unobstructed men will result in less benefit (symptom index decrease from 19.6 ± 9.4 to 10.1 ± 6.8 and quality of life score decrease from 3.6 ± 1.7 to 2.6 ± 1.7) than in obstructed men (decreases from 19.1 ± 6.6 to 5.4 ± 4.3 and from 3.7±1.3 to 1.3±1.5, respectively)[8]. By performing urodynamic investigations, patient can be informed preoperatively in an optimal manner.

Our study showed a negative correlation between age and symptom index and quality of life score ($p=0.049$ and $p=0.027$, respectively). In most community-based studies, age and symptom scores are correlated positively[16-19]. In our group, this association was reversed. In our population, older patients tended to visit the outpatient department with lower scores than younger ones.

The presence of residual volume resulted in a slight, but not significant, increase of some symptom scores. Even in our group of 565 men this did not result in a significant increase in the symptom index. The quality of life score was not affected by residual volume.

Of the 565 men, 46% had an unstable bladder during filling cystometries. This percentage is lower than the reported preoperative incidence of between 49% and 74% in 12 studies[10]. However, it is unclear whether the latter findings were from patients who were already selected for operation.

In our study, the frequency, urgency, and nocturia scores were significantly higher in patients with an unstable bladder than in those with a stable bladder. In patients with an unstable bladder, these symptoms did not contribute to a significant higher symptom index or higher quality of life score. The position in which the instabilities were detected did not affect the patients' symptoms or quality of life.

Despite the strict selection criteria, the correlations in table 4.1 are still weak. This may be due to a number of factors. The parameters show a high variability and some kind of saturation towards a higher score. Only 6 discrete values are possible as a score on an I-PSS question. This has a negative impact on correlation calculations. The weak association between the urodynamic parameters and symptom index (table 4.1) is also due to the different and sometimes opposite impact of a urodynamic parameter on the symptoms. For instance, a high contractility will result in a low score on question 5 (weak urinary stream) but a high score on question 4 (urgency) (table 4.1). Another important issue is the still subjective nature of some questions. Patients do not have quantitative information of whether their bladder is empty after voiding. No relation was found between the score on question 1 (incomplete emptying) and the actual presence or absence of residual volume. Possibly, the frequent voiding of small volumes may be interpreted by the patient as being caused by the inability to empty the bladder completely, as illustrated by the high correlation between the score on incomplete emptying and the score on frequency (table 4.1). Despite the strict selection of men, strong associations of symptoms and quality of life with the results of urodynamic investigations hardly exist. Symptoms and urodynamic evaluations show different aspects of BPH.

Conclusions

Older men scored significantly higher on the nocturia question but had significantly lower scores for incomplete emptying, weak urinary stream, and hesitancy. They noted less bother than younger patients did. Despite the strict selection of the men, prostate volume and Schäfer's obstruction grade did not correlate with the symptom index or quality of life score. A weakly significant correlation was found between contractility degree and symptom index. Low cystometric and effective bladder capacities resulted in higher scores on the storage symptoms of frequency, urgency, and nocturia, but only in a slightly higher symptom index and higher quality of life score. The presence of residual volume and/or bladder instabilities was hardly associated with symptoms or quality of life.

The lack of, or weak, association of the symptom index and quality of life score with the urodynamic parameters was caused by the high variability and distribution and the sometimes subjective interpretation of symptoms. Moreover, the urodynamic parameters may have opposite implications than symptoms and vice versa, because symptoms and the urodynamic parameters reveal different aspects of BPH.

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CHAPTER 5

Prevalence and Bothersomeness of Lower Urinary Tract Symptoms in Benign Prostatic Hyperplasia and Their Impact on Well-Being

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Abstract

Objective: We established the prevalence and bothersomeness of symptoms and their impact on well-being in a large group of strictly selected men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia (BPH).
Methods: Included in our study were 475 consecutive men who met the criteria of the International Consensus Committee on BPH and voided more than 150 ml during uroflowmetry. International Prostate Symptom Scores and quality of life score were determined. We included the 7 bothersomeness questions of the Symptom Problem Index and the 4 of the BPH Impact Index of the American Urological Association Measurement Committee. These questions refer to the degree of bothersomeness caused by urinary problems and how they affect various health domains.
Results: The symptoms with the highest prevalence based on mean scores were weak urinary stream, frequency, and urgency. Urgency, nocturia, and hesitancy were the most bothersome symptoms. Patients were only discouraged from performing normal daily activity when the symptom index exceeded 20. Incomplete emptying and frequency bothersomeness strongly correlated, and weak urinary stream and hesitancy bothersomeness weakly correlated with all health and quality of life domains.
Conclusions: Weak urinary stream, frequency, and urgency were the most prevalent symptoms, while urgency, nocturia, and hesitancy were the most bothersome symptoms. In contrast to weak urinary stream and hesitancy, the bothersomeness of incomplete emptying and frequency was strongly associated with well-being.

Introduction

The International Prostate Symptom Index and quality of life question were developed and validated by the multidisciplinary measurement committee of the American Urological Association (AUA)[1]. It was adopted by the World Health Organisation International Consensus Committee (ICC) on benign prostatic hyperplasia (BPH) as important aid for diagnosing of lower urinary tract symptoms (LUTS) suggestive of BPH[2].

To date decision making in regard to treatment has mainly been based on symptoms and the degree of bladder outlet obstruction[2]. However, today the opinion is more prevalent that the degree of bothersomeness reported by the patient is not the same as the presence and frequency of their symptoms[3-6]. Symptom bothersomeness and negative impact on quality of life are the main reasons that patients seek treatment for BPH[5-7].

Generally the most frequently reported symptoms have been associated with the voiding phase, such as hesitancy, intermittency, weak urinary stream and incomplete emptying, and the most bothersome have been associated with the storage phase, frequency, urgency and nocturia[4]. This relationship also applies to community men with symptomatic BPH[8,9] and even to those in whom prostatic obstruction has been objectively identified[10].

Bothersomeness appeared to be much less sensitive to international differences than symptom prevalence[11]. Barry[12] assumed that bothersomeness was a common denominator that caused men to present to urologists. His assumption agreed with the finding of Jacobsen et al.[13] that men with greater bothersomeness than expected from symptom frequency were more likely to seek medical care. Baseline bothersomeness has been described as more predictive of outcome after prostatic surgery than symptom score[7,14].

The WHO International Guidelines for BPH treatment emphasised that therapy for BPH must be initiated according to the degree of bothersomeness[2]. BPH management should be individualised according to patient circumstances and personal choice. Therefore, appropriate scores for quantifying the bothersomeness of LUTS are needed to evaluate the need for and outcome of treatment for BPH from the patient perspective[3,5]. The AUA symptom index measures the occurrence of lower urinary tract symptoms. The AUA Measurement Committee developed and validated a symptom problem index (SPI) with 7 bothersomeness questions, of which each corresponds to a symptom question of the AUA symptom index[1,15]. The SPI indicates how bothersome patients consider urinary symptoms. The Measurement Committee also developed and validated the BPH impact index (BII) to measure how much the urinary problems affect various domains of health[15,16]. We combined the AUA symptom index and the quality of life question with the SPI and BII into one questionnaire. We analysed symptom prevalence and bothersomeness in a large group of strictly selected men with LUTS suggestive of BPH. In addition we investigated the impact of each symptom and its specific bothersomeness on various domains of health and on overall quality of life.

Materials and Methods

In accordance with the recommendations of the ICC on BPH[2] from October 1993 onward we performed basic initial evaluations, including history, physical and digital rectal examinations, urinalysis and renal function assessment and recommended diagnostic tests, including uroflowmetry and post-void residual urine estimation, in consecutive men with LUTS who presented to our outpatient department of urology.

Men were included in the study if they were over the age of 50 years and had no other specified exclusion criteria of the ICC on BPH[17], such as prostate cancer, neurological disease, previous prostate surgery or medication that acts on the urinary tract. In addition, they voided a sufficient volume (>150 ml) during one or more free uroflowmetry studies, residual urine was estimated reliably and prostate size was determined by transrectal ultrasound.

The International Prostate Symptom Scores (I-PSS)[1] were determined in all patients, including seven questions on the prevalence of incomplete emptying, frequency, intermittency, urgency, weak urinary stream, hesitancy and nocturia. Each question may be answered on a scale of 0-"not at all" to 5-"almost always". The prostate symptom index is the sum of the seven scores with a range of 0 to 35. In addition, each patient answered the validated[2] question on quality of life (QoL) with lower urinary tract symptoms on a scale of 0-"delighted" to 6-"terrible"[1].

We included the 7 bothersomeness questions of the symptom problem index[1,15], each of which corresponds to a symptom question. Bothersomeness questions were separated from symptom questions on the questionnaire and scored separately. Bothersomeness questions refer to how troubled patients were by urinary symptoms during the last month, for example: "Over the past month, how much has a sensation not emptying your bladder been a problem for you?". Each question may be answered on a scale of 0 to 4 as 0- no, 1- very small, 2- small, 3- medium and 4- big problem. The AUA symptom problem score is the sum of the seven bothersomeness scores with a range of 0 to 28 points. We also included the BII[15,16], consisting of four questions on health-feeling with and social implications of LUTS on a scale with a range of 0 to 13 points:

B1. Over the past month, how much physical discomfort did any urinary problem cause you? (Answers: "none" or "only a little" or "some" or "a lot", range 0 to 3)

B2. Over the past month, how much did you worry about your health because of any urinary problems? (Answers: "none" or "only a little" or "some" or "a lot", range 0 to 3)

B3. Overall, how bothersome has any trouble with urination been during the past month? (Answers: "not at all bothersome" or "bothers me a little" or "bothers me some" or "bothers me a lot", range 0 to 3)

B4. Over the past month, how much of the time has any urinary problem kept you from doing the kinds of things you would usually do? (Answers: "none of the time" or "a little of the time" or "some of the time" or "most of the time" or "all of the time", range 0 to 4)

Patients were excluded from analysis when they did not complete the symptom and bothersomeness questions consistently.

Statistical analysis was performed with the Kendall and Gibbons distribution-free correlation method. The Kolmogorov-Smirnov goodness of fit test was used to analyse whether or not the distribution of a variable was normal[18]. The level of significance (2-tailed) was set at $p<0.05$.

The scores of all patients on a symptom question were plotted versus the corresponding scores on the associated bothersomeness question. Quadratic curve estimation was applied on the seven scatter plots. How the bothering due to each symptom was estimated is explained under RESULTS.

Results

Of the total population of 789 men older than 50 years old in whom basic initial evaluations and recommended tests were performed 565 met all study inclusion criteria. Patients were excluded from analysis for various reasons, but the dominant reason was that they were on medication that acted on the lower urinary tract.

Of the 565 men who met all other inclusion criteria, 90 (16%) completed at least one symptom-bothersomeness combination inconsistently. These excluded patients reported bothersomeness due to the corresponding symptom, while answering "not at all" to that symptom prevalence question.

Thus, our study included 475 men (66±8 years of age, range 50-89) with an average symptom index of 17±7 (range 1-35), average symptom problem index of 13±7 (range 0-28), average BPH impact score of 5.6±3.2 (range 0-13), and average quality of life

score of 3.6±1.5 (range 0-6). Mean prostate size was 39±20 ml (range 10-155). Mean maximum flow on free uroflowmetry was 12±5 ml/s (range 3-34) and mean post-void residual volume was 61±91 ml (range 0-630).
Except for patient age and symptom index, no parameters were normally distributed. In the literature it is not unusual to calculate the mean plus or minus standard deviation, despite nonuniform distributions. Therefore, these values are provided.
Table 5.1 shows a correlation matrix relating each I-PSS symptom score and the I-PSS Index with patient age, its bothersomeness score, SPI, the QoL score, score on each BII question, and BII. Figure 5.1 shows the distributions of the scores per symptom. For each symptom score we plotted the average score of the associated bothersomeness question.

Figure 5.2 shows the results of quadratic curve estimations from the scatter-plots of bothersomeness versus symptom scores per symptom based on all pairs of data.

Symptom bothersomeness was quantified by the area under the curve in figure 5.2 (grey area) and expressed as a percent of the total area of the rectangle with the horizontal and vertical axes as sides.
Table 5.2 lists the average symptom score and bothersomeness of urinary symptoms based on the percent of area under the curve (figure 5.2).

Table 5.2 Symptom scores and bothersomeness of urinary symptoms.

Symptom	Mean score ± SD	Bothersomeness order*	% Area under curve
Weak urinary stream	3.6±1.6	7	32.2
Frequency	2.8±1.5	5	40.9
Urgency	2.4±1.7	1	57.3
Incomplete emptying	2.3±1.8	4	41.7
Intermittency	2.3±1.7	6	37.2
Nocturia	2.2±1.3	2	47.1
Hesitancy	1.6±1.6	3	46.6

* Order 1- most to 7- least bothersome

Table 5.1 Correlation matrix relating each I-PSS symptom score with patient age, bothersomeness, SPI and quality of life score, score on each BII-question and BII.

Symptom score	Age	Bother-someness	Symptom Problem Index (SPI)	Quality of Life score (QoL)	Questions of the BPH Impact Index (No.): Physical discomfort (B1)	Worry about health (B2)	Overall bother with urination trouble (B3)	No normal activity part of time (B4)	BPH Impact (BII)
Incomplete emptying	-0.10**	0.62**	0.44**	0.33**	0.34**	0.25**	0.35**	0.25**	0.34**
Frequency	-0.01	0.45**	0.36**	0.37**	0.33**	0.21**	0.37**	0.33**	0.34**
Intermittency	-0.07*	0.58**	0.38**	0.29**	0.23**	0.15**	0.25**	0.16**	0.22**
Urgency	0.06	0.64**	0.33**	0.31**	0.33**	0.19**	0.34**	0.35**	0.33**
Weak urinary stream	-0.19**	0.32**	0.24**	0.27**	0.15**	0.10**	0.21**	0.07	0.14**
Hesitancy	-0.11**	0.72**	0.45**	0.31**	0.32**	0.25**	0.26**	0.23**	0.30**
Nocturia	0.10**	0.45**	0.26**	0.14**	0.19**	0.12**	0.23**	0.20**	0.21**
I-PSS	-0.07*	-	0.57**	0.45**	0.41**	0.26**	0.44**	0.33**	0.42**

* Correlation significant at 0.05

** Correlation significant at 0.01

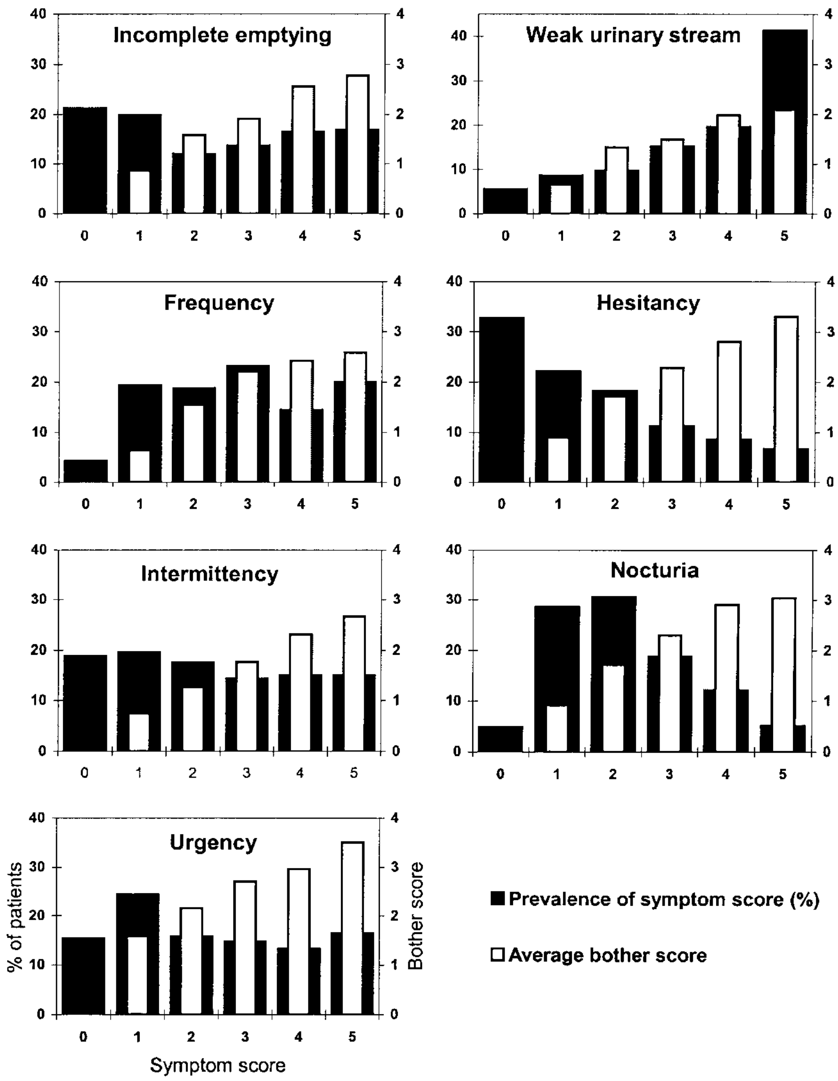

Figure 5.1 Distributions of symptom scores with average associated bothersomeness (bother score) per symptom score.

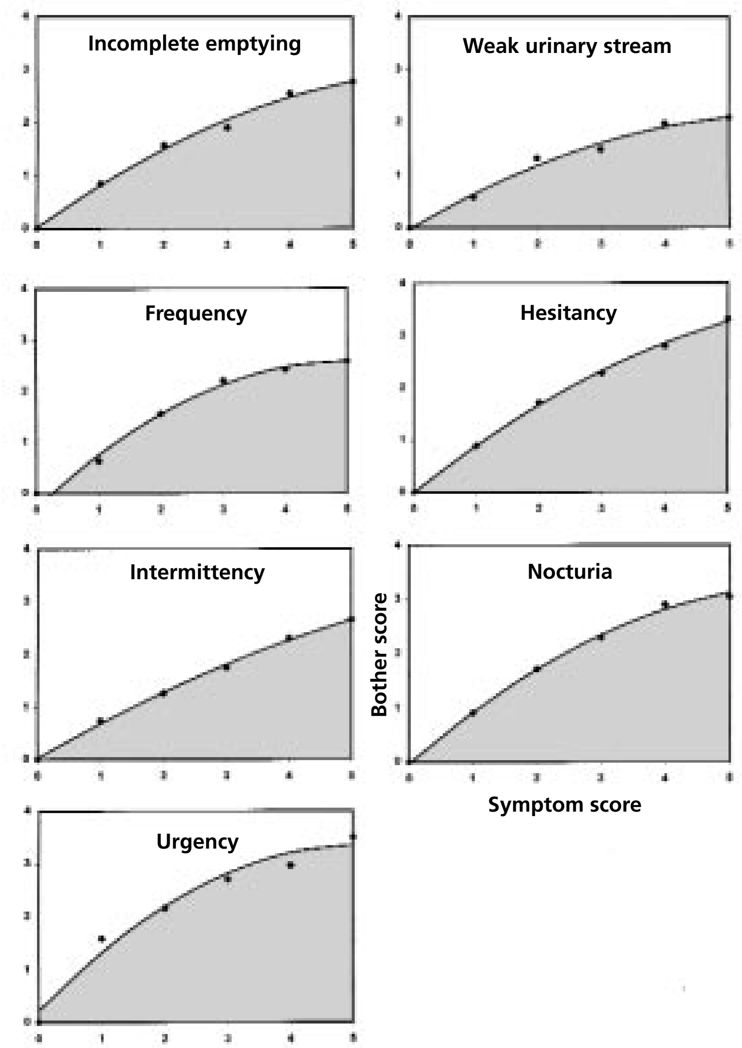

Figure 5.2 Results of quadratic curve estimations from scatter-plots of bothersomeness scores versus symptom scores (◆=average bothersomeness score of corresponding symptom score=top of bars in figure 5.1).

Figure 5.3 shows the results of quadratic curve estimations from scatter-plots of symptom index versus scores on the quality of life question and on the additional bothersomeness questions.

There was little or some physical discomfort due to urination problems in 66% of the men, while 60% and 64% worried about health due to urination problems and about the overall bothersomeness of urination problems, respectively. Urination problems did not at all discourage 54% of the patients from performing normal daily activity, while only 5% discouraged most or all of the time.

Table 5.3 lists the correlations of age with SPI, quality of life, score on each BII question and BII.

Table 5.4 shows correlation matrixes relating each symptom specific bothersomeness score with age, SPI, quality of life score, score on each BII question, and BII. Table 5.5 lists symptom specific bothersomeness correlated with SPI, quality of life score and BII.

Table 5.3 Kendall and Gibbons correlation coefficients of patients age with SPI, quality of life, BII questions, and BII.

Parameter	Age
Symptom Problem Index (SPI)	- 0.08*
Quality of Life (QoL)	- 0.09**
BII-question (No.):	
-Physical discomfort (B1)	- 0.02
-Worry about health (B2)	- 0.05
-Overall bothersomeness of urination problem (B3)	- 0.06
-No normal daily activity part of the time (B4)	0.08*
BPH Impact Index (BII)	-0.02

* Correlation significant at 0.05

**Correlation significant at 0.01

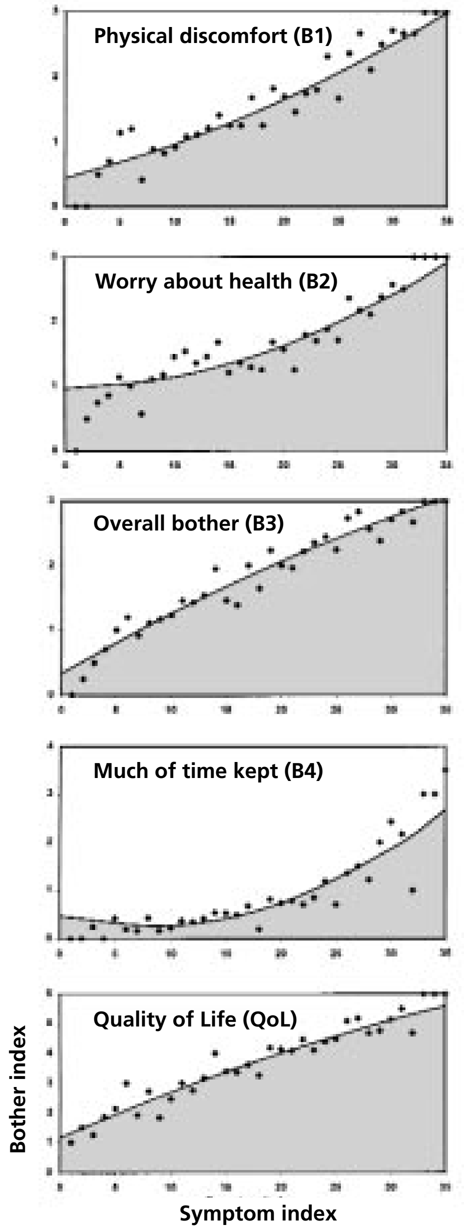

Figure 5.3 Results of quadratic curve estimations from scatter-plots of symptom index versus quality of life and BII (B1 to B4)(◆=average bothersomeness score of corresponding symptom index).

Table 5.4 Correlation matrix relating each symptom specific bothersomeness score with patient age, SPI, quality of life score, score on each BII question, and BII.

Bothersomeness of the symptom:	Age	Symptom Problem Index (SPI)	Quality of Life score (Qol)	Questions of the BPH Impact Index (No.)				BPH Impact Index (BII)
				Physical discomfort (B1)	Worry about health (B2)	Overall brother with urination trouble (B3)	No normal activity part of time (B4)	
Incomplete emptying	-0.10**	0.67**	0.47**	0.50**	0.36**	0.49**	0.37**	0.50**
Frequency	-0.02	0.64**	0.48**	0.54**	0.34**	0.56**	0.49**	0.54**
Intermittency	-0.09 **	0.64 **	0.41**	0.38**	0.31**	0.40**	0.29**	0.40**
Urgency	0.03	0.52**	0.39**	0.42**	0.24**	0.46**	0.44**	0.43**
Weak urinary stream	-0.10**	0.61**	0.39**	0.36**	0.31**	0.40**	0.27**	0.38**
Hesitancy	-0.13**	0.59**	0.35**	0.38**	0.32**	0.35**	0.28**	0.38**
Nocturia	-0.04	0.58**	0.40**	0.41**	0.29**	0.47**	0.36**	0.44**

* Correlation is significant at the 0.05 level.
** Correlation is significant at the 0.01 level.

Table 5.5 Symptom specific bothersomeness correlated with SPI, quality of life and BII.

Correlation order*	SPI	QoL-score	BII
1	Incomplete emptying	Frequency	Frequency
2	Frequency	Incomplete emptying	Incomplete emptying
3	Intermittency	Intermittency	Nocturia
4	Weak urinary stream	Nocturia	Urgency
5	Hesitancy	Urgency	Intermittency
6	Nocturia	Weak urinary stream	Weak urinary stream
7	Urgency	Hesitancy	Hesitancy

* Order 1- most to 7- least correlated

Discussion

The mean AUA symptom index, symptom problem score and BPH impact score were similar to those noted by Barry et al.[15] (17±7, 12±6 and 5.0±3.1, respectively).
The condition that men were included in the study only when they voided at least 150 ml urine during free uroflowmetry may have excluded those with severe and prolonged obstruction. However, in a reasonable number of these excluded patients, bladder properties may have changed, resulting in a partially decompensated bladder. Our inclusion criteria were based on the recommendations of the International Consensus Committee on BPH[2] and we did not consider it reasonable to change any of these recommendations.
Figure 5.1 shows that the most common symptoms were not always the most bothersome symptoms. For example, 41% of our patients reported a weak urinary stream almost always with a mean bothersomeness of 2.1. Only 7% of respondents had hesitancy almost always but that symptom had a mean bothersomeness of 3.3.
The symptoms with the highest prevalence based on average scores were weak urinary stream, frequency and urgency (table 5.2). Hesitancy had the lowest prevalence. Based on the area under the curve in figure 5.2 urgency, nocturia and hesitancy were the most bothersome symptoms in our study (table 5.2). For all symptoms figure 5.2 shows a flattening of the bothersomeness curve toward a higher symptom score. Recalculating the areas using a third degree equation resulted in a minimal difference

of less than 1% with the areas listed in table 5.2. Rank order was not affected.

Our results on the most bothersome symptoms agree with the conclusions of the ICS "BPH" Study[4]. However, in that series rank order was based on decreasing order of the proportion of patients reporting that the symptom was no problem. When we used the category of "no problem" to create a rank order, similar to that of the ICS, urgency, incomplete emptying and hesitancy were the most bothersome symptoms.

A limitation of the analytic approach was that the area under the bothersomeness curve and, therefore, rank order may have been sensitive to the various response frames of the questions. On the I-PSS nocturia has a different response frame from the other questions, which may have changed the relationship of the ordered response categories and bothersomeness ratings. Perhaps this possibility explains why nocturia changed order so much when the ICS ratings of bothersomeness were used in our population.

Urinary problems had the highest impact on overall bothersomeness and the lowest impact on patients not performing normal daily activity part of the time (fig. 5.3). Most patients were not discouraged from normal daily activity until the symptom index was at least about 20 (fig. 5.3).

Tables 5.1 and 5.3 show that in our population generally older patients tended to present with slightly fewer symptoms and less bothersomeness than younger patients.

The bothersomeness of incomplete emptying and frequency was strongly associated with the symptom problem index, quality of life score, score on the BPH impact questions and BII (tables 5.4 and 5.5). In BPH the bothersomeness of incomplete emptying and frequency had a high impact on well-being in contrast to that of weak urinary stream and hesitancy. Also, the prevalence of the symptoms of incomplete emptying and frequency had a strong impact on SPI, quality of life and BII (table 5.1).

Of our 475 patients 290 had post-void residual volume. The mean bothersomeness score for incomplete emptying was 1.53 ± 1.42. No post-void residual volume was evident in 185 men with a mean bothersomeness for incomplete emptying of 1.47 ± 1.43. This finding shows the lack of correlation of incomplete emptying bothersomeness with actual incomplete emptying, suggesting that patients believed that the cause of increased frequency was incomplete emptying.

The ICS "BPH" Study indicated that international differences are relevant when reporting specific lower urinary tract symptoms[11]. Inevitably individual countries have different cultural backgrounds and specific health care delivery systems. Therefore, the results of studies of LUTS in specific countries may not be generally applicable in other countries. An alternative would be to focus on bothersomeness, which appeared to be much less sensitive to international differences[11].

We emphasise that our conclusions were formulated for our group of strictly selected men with LUTS suggestive of BPH.

Conclusions

Based on mean scores, the symptoms with the highest prevalence were weak urinary stream, frequency, and urgency. Hesitancy had the lowest prevalence. Urgency, nocturia, and hesitancy symptoms were the most bothersome in our study.
Of the four BII questions that on overall bothersomeness scored highest. Patients were only discouraged from normal activity when the symptom index exceeded 20. In contrast to weak urinary stream and hesitancy, the bothersomeness of incomplete emptying and frequency were strongly associated with all domains of health and quality of life.

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CHAPTER 6

Urethral Resistance Factor (URA) Versus Schäfer's Obstruction Grade and Abrams-Griffiths (AG) Number in the Diagnosis of Obstructive Benign Prostatic Hyperplasia

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Abstract

Objectives: Different methods of analysing pressure-flow plots to quantify bladder outlet resistance in men with lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) were developed in the past. The aims of this study were to quantify the degree of agreement between the diagnosis of obstruction by the different methods, and to compare the applicability of the different methods in the evaluation of bladder outflow conditions, in a large group of these men.
Methods: In consecutive men with LUTS basic initial evaluations, recommended diagnostic tests and urodynamic investigations were performed. From pressure-flow studies, the group-specific resistance factor (URA), Schäfer's obstruction grade and Abrams-Griffiths (AG) number were estimated. Men with 21 cm $H_2O \leq$ URA$\leq$ 29 cm H_2O and men with Schäfer's grade equal 2 were classified as equivocal. In conformity with the provisional ICS definition, men with 20$\leq$ AG number$\leq$ 40 were classified as equivocal.
Results: In 78% of the 565 included men Schäfer's classification agreed with URA classification. In 82% ICS classification agreed with URA classification. Most agreement (94%) existed between Schäfer's classification and ICS classification. Men with relatively low detrusor pressure at maximum flow and relatively low maximum flow had a high prevalence among those in whom URA and Schäfer's classifications and among those in whom URA and ICS classifications differed.
Conclusions: Differences between URA, Schäfer's and ICS classification were near the points of intersection of the different boundaries, and a decision whether or not to perform surgery is not likely to be influenced by this disagreement.

Introduction

The only reliable method for directly diagnosing bladder outlet obstruction (BOO) is simultaneous measurement of the driving pressure and the resulting flow rate. If outflow resistance is increased, detrusor pressure will increase and flow rate will decrease[1]. Urodynamics offers an objective tool for the assessment of BOO in benign prostatic hyperplasia (BPH). Whether or not to perform surgery on patients with lower urinary tract symptoms (LUTS) suggestive of BPH is partially based on the extent of obstruction derived from pressure-flow relations.
Different methods of analysing pressure-flow plots and to quantify bladder outlet resistance in patients with BPH have been developed in the past[2]. These different approaches are based on similar theoretical principles, but are different in detail and objectives.

Urethral resistance factor (URA)
The concept of the passive urethral resistance relation (PURR) to quantify bladder outflow conditions from the complex pressure-flow relation in a few parameters[3] is generally accepted. Urethral resistance can be quantified using a group-specific resistance factor (URA) that is based empirically on the pressure-flow plots obtained in a large number of voidings of adult patients. Every combination of pressure and corresponding flow occurring during a micturition, can be represented in the figure by a point. The value of the intercept on the pressure axis (at zero flow) for the curve on which the point lies, represents the urethral resistance factor URA[4]. URA can be calculated for any pair of pressure-flow values by solving the following equation for URA (p_{det} is detrusor pressure (in cm H_2O) and Q is the corresponding flow rate (in ml/s)):

$$URA = [(1 + 1.52.10^{-3} * Q^2 * p_{det})^{1/2} - 1] / (7.6.10^{-4} * Q^2)$$

The units of URA are the same as those of pressure, i.e., cm H_2O. In practice, URA is calculated from the maximum flow rate and corresponding detrusor pressure.

Schäfer's obstruction grade
A simplification of the PURR is the linear PURR (linPURR)[5], which allows clear identification of individual outflow conditions with distinction of different obstruction types[6]. Reduction to single-value grading is reached when the linear PURR is plotted in a specific pressure-flow diagram, which is divided in seven areas corresponding to different outflow conditions: Schäfer's obstruction grade (0, no obstruction to 6, severe obstruc-

tion). Classification of what is more or less obstructed is to a minor degree influenced by subjective judgement[7].

AG number

Based upon the Abrams-Griffiths nomogram[8], Lim and Abrams[9] introduced the Abrams-Griffiths (AG) number for quantifying the urethral resistance. Each pressure-flow plot can be represented by an AG number that can be easily calculated by the following equation (where $p_{det.Qmax}$ is detrusor pressure in cm H_2O at maximum flow rate and Q_{max} is maximum flow rate in ml/s):

$$\text{AG number} = p_{det.Qmax} - 2 * Q_{max}$$

Obstructed, unobstructed, equivocal

URA and AG number are continuous variables and Schäfer's grade is a discrete variable, all allowing quantification of urethral resistance. Special values of URA, Schäfer's grade, and AG number offer the possibility to classify men in obstructed, unobstructed, and equivocal categories. Patients with URA>29 cm H_2O were classified as obstructed[10] and those with URA<21 cm H_2O as unobstructed (see results and discussion). The remaining patients were classified as equivocal.

Patients with Schäfer grade 0 or 1 are defined as unobstructed and those with grade 3 or higher as obstructed[5]. We defined men with Schäfer grade 2 as equivocal.

In 1997, the International Continence Society published a provisional nomogram, which is a modification of the Abrams-Griffiths nomogram[8]. Classification is based upon where a plot of (Q_{max}, $p_{det.Qmax}$) is positioned in the nomogram[2]. Because the AG number also originates from the Abrams-Griffiths nomogram, the ICS cut-off values are particular values of the AG number:

If: $(p_{det.Qmax} - 2 * Q_{max}) < 20$: ICS unobstructed
If: $20 \leq (p_{det.Qmax} - 2 * Q_{max}) \leq 40$: ICS equivocal
If: $(p_{det.Qmax} - 2 * Q_{max}) > 40$: ICS obstructed

Aim of study

Our aim is to quantify the extent of (dis)agreement among the different methods of analysing pressure-flow plots to define bladder outlet obstruction in a large group of men with LUTS suggestive of BPH.

Materials and Methods

From October 1993 on, in consecutive men with LUTS basic initial evaluations (history, quantification of symptoms, physical examination and digital rectal examination, urinalysis and renal function assessment) and recommended diagnostic tests (uroflowmetry and residual urine estimation) were performed, conforming to the recommendations of the International Consensus Committee on Benign Prostatic Hyperplasia (BPH) [11].

Men were included if they were over the age of 50 years, without any of the other specified exclusion criteria of the International Consensus Committee on BPH[12], they voided a sufficient volume (>150 ml) during one or more free uroflowmetry studies, residual urine was estimated reliably and prostate size was determined by transrectal ultrasound. International Prostate Symptom Index (S) for BPH and quality of life assessment (L) as developed and validated by the American Urological Association Measurement Committee[13], were used to quantify symptoms. In case the results of these evaluations were suggestive of bladder outflow obstruction, these patients were also evaluated urodynamically by filling cystometry and pressure-flow studies. Filling cystometric studies were performed with the patient supine and erect. Pressure-flow studies were done twice with the patient erect. Bladder pressure was recorded with a 5F catheter and rectal pressure was measured with a 14F catheter connected to external pressure transducers. The bladder was filled with saline at 37°C, through a second 5F catheter, at a constant rate of 50 ml/min. In some men an 8F double lumen catheter was used for bladder pressure measurement and bladder filling. Filling was stopped when the patient had a strong desire to void. The first pressure-flow study was done with measuring and filling catheters in the bladder, and the second study was done after removal of the filling catheter. The pressure-flow study with the lowest urethral resistance (usually during voiding with only the measuring catheter in the bladder) was used for further analysis.

In all patients residual urine was estimated during one of the visits at the outpatient department by transabdominal ultrasound or catheterisation. If residual urine was significant, this test was repeated. The urodynamic investigation always started with uroflowmetry and determination of the residual volume by catheterisation. Some patients were not able to arrive with a full bladder and sometimes were not able to produce a flow curve. At the end of the urodynamic investigation the bladder of these patients was refilled and after removal of the catheters uroflowmetry was performed. If these patients were known to have significant residual volume, catheterisation was performed once more.

From pressure-flow studies, the group-specific resistance factor URA and Schäfer's obstruction grade were estimated and the provisional ICS method for definition of obstruction was applied, using the values of the maximum flow rate and corresponding detrusor pressure.

Patients with URA>29 cm H_2O were classified as obstructed[10]. We defined patients with 21 cm $H_2O \leq$ URA $\leq$ 29 cm H_2O as equivocal and patients with URA<21 cm H_2O as unobstructed

(see results and discussion). Patients with Schäfer grade 0 or 1 were classified as unobstructed, with grade 2 as equivocal and with grade ≥ 3 as obstructed.
Patients with AG number>40 were classified as obstructed, with AG number<20 as unobstructed, and with 20≤ AG number≤ 40 as equivocal.
Descriptive statistics were used, including Spearman's distribution-free correlation coefficient. The Kolmogorov-Smirnov goodness of fit test[14] was used to examine whether or not the distribution of a variable was normal.

Results

Results were obtained from 565 included men. Table 6.1 describes baseline characteristics of the evaluated patients.
A capacity of 1100 ml was found in one patient. The maximum capacity in the other men was 900 ml. In 218 patients (39%) no residual volume was found. In men with a residual volume, this volume was lower than or equal to 50 ml in 131 men (23%), between 50 and 100 ml in 107 men (19%) and higher than 100 ml in 109 men (19%).
From 511 (90%) of our 565 men the pressure-flow point lies in the area enclosed by maximum flow between 0 and 25 ml/s and detrusor pressure between 0 and 100 cm H_2O.

Table 6.1 Mean, standard deviation (SD) and range of different baseline characteristics of the evaluated population (N=565).

	Mean	SD	Range
Age (yrs)	66	8	50-90
Prostate volume (ml)	39	19	10-155
$Q_{max.free}$ (ml/s)	13	5	3-35
Q_{max} (ml/s)	10	5	1-31
$p_{det.Qmax}$ (cm H_2O)	65	26	17-265
Capacity (ml)	416	153	150-1100
Residual volume (ml)	63	92	0-630
Symptom Index (S)	17	7	1-35
Quality of Life (L)	3.6	1.5	0-6

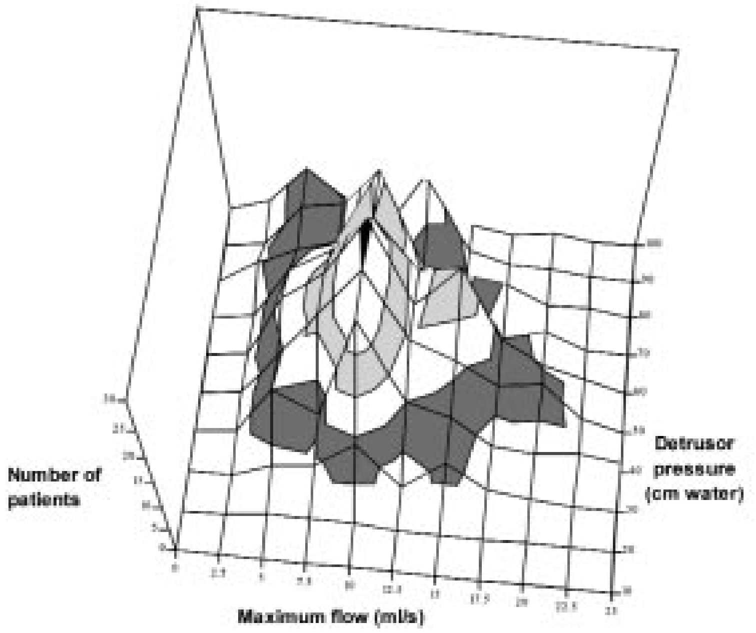

Figure 6.1 Distribution of men with respect to detrusor pressure (cm H_2O) and maximum flow (ml/s). *Note: 54 men are not included (detrusor pressure >100 cm H_2O or maximum flow rate >25 ml/s).*

Figure 6.1 shows the distribution of these 511 men with respect to detrusor pressure (cm H_2O) at maximum flow and with respect to maximum flow (ml/s). The upper boundary values of 25 ml/s and 100 cm H_2O were chosen in order to exclude extreme pressure-flow points.

Figure 6.2 shows frequencies of URA, Schäfer's grade and AG number for all 565 men. Normal curves are displayed. Distributions of all three variables are not normal (Kolmogorov-Smirnov test).

In our group, highest agreement between URA classification and Schäfer's classification of unobstructed and equivocal was reached by choosing URA=21.3 cm H_2O. Highest agreement between URA and ICS classification was obtained by setting URA=21.1 cm H_2O. Therefore, as boundary value between unobstructed and equivocal men URA=21 cm H_2O was chosen.

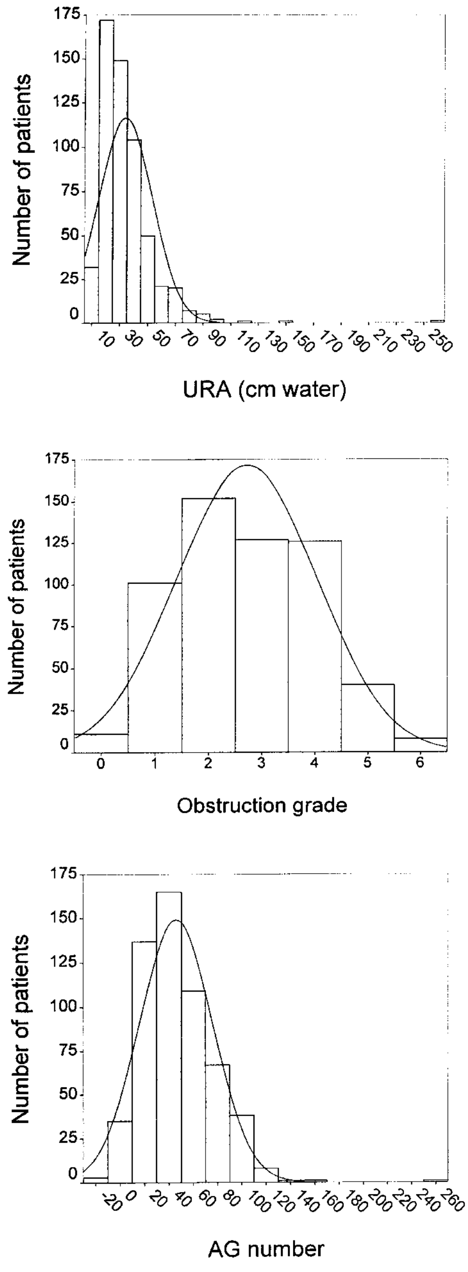

Figure 6.2 Frequencies of URA, Schäfer's grade and AG number. Normal curves are displayed.

Table 6.2 Distribution of 565 patients in unobstructed, equivocal and obstructed, following URA, Schäfer's grade and the definition of the ICS

	Unobstructed	Equivocal	Obstructed
URA	21%	26%	53%
Schäfer's grade	20%	27%	53%
ICS	19%	30%	51%

Although in our study we defined URA=29 cm H_2O as the limit between equivocal and obstructed, in our well-defined group most agreement with Schäfer's classification and with ICS classification was reached when we defined URA>30 cm H_2O as obstructed. In that case, agreement of 7 more patients was reached between URA and Schäfer's classification and between URA and ICS classification.
Table 6.2 shows the distribution of the patients in unobstructed, equivocal, and obstructed, following URA, Schäfer's grade, and the definition of the ICS. According to all three possible classifications, about 50% of our patient group is defined as obstructed and about 20% as unobstructed.

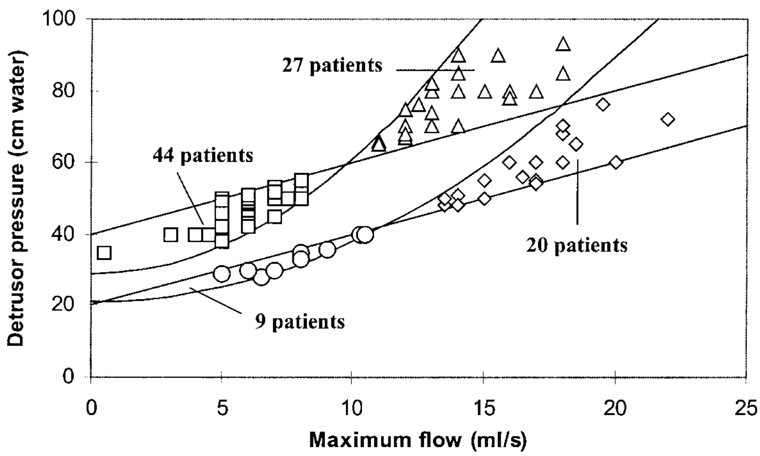

Figure 6.3A Scatterplot of patients where ICS classification differs from URA classification. Borderlines in URA and ICS nomograms are indicated. *Note: Due to overlapping data, the number of points in the figure may be lower than the actual number of men.*

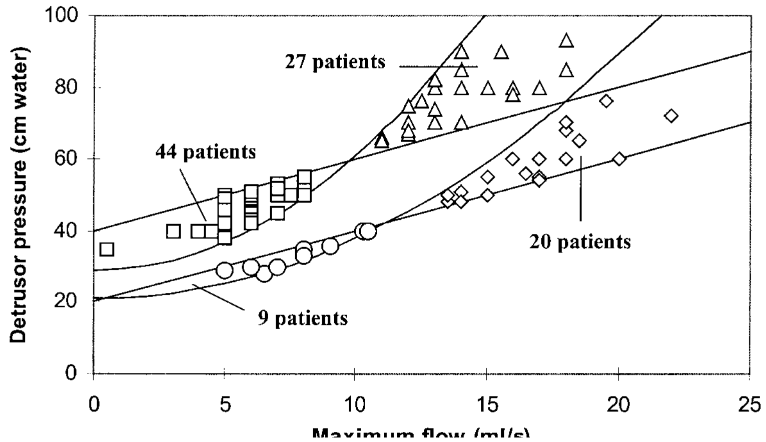

Figure 6.3B Scatterplot of patients where Schäfer's classification differs from URA classification. Borderlines in URA and Schäfer's nomograms are indicated. *See note figure 6.3A. Due to the properties of the printer program, minimal differences may be observed between the positions of common men in the figures 6.3A and 6.3B.*

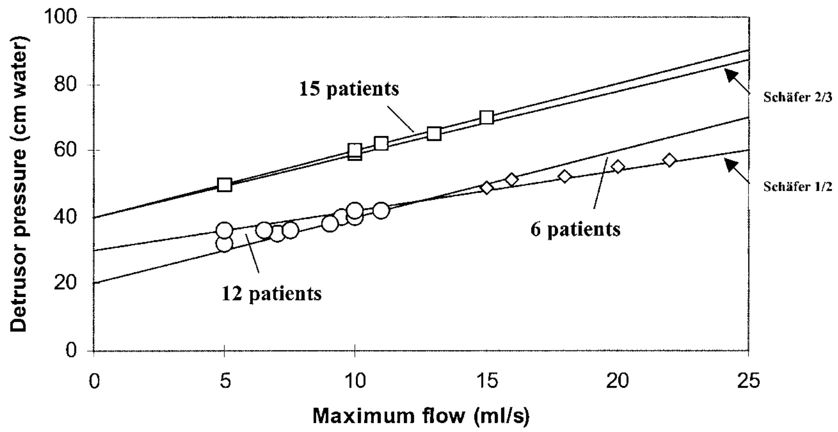

Figure 6.3C Scatterplot of patients where Schäfer's classification differs from ICS classification. Borderlines in Schäfer's and ICS nomograms are indicated. *See note figure 6.3A.*

In figure 6.3A-C patients are shown where the three classification methods differ from each other. Borderlines in URA, ICS, and Schäfer's nomograms are indicated. The area enclosed by maximum flow from 0 to 25 ml/s and detrusor pressure from 0 to 100 cm H_2O is displayed.

Discussion

Extensive scientific and clinical considerations led to the recommendations of the International Consensus Committee on BPH[11]. Our inclusion criteria were based on these recommendations and we considered it not reasonable to change any of these recommendations. However, we realise that the condition that men were included only if they could void a volume of at least 150 ml during free uroflowmetry may have excluded men with severe and prolonged obstruction. In a reasonable number of these excluded men, however, bladder properties may have changed resulting in (partly) decompensated bladders. We assume that our group included men who were able to compensate more or less for the impaired outflow condition. In our group most men (81%) did not have a residual volume, or had a residual volume lower than 100 ml.

In our urodynamic department measures are taken to guarantee the privacy of the patients. Telephone calls are not allowed, personnel are not allowed to enter the examination room during the investigation, buzzers are forbidden. The number of investigators is restricted to a minimum. During voiding the investigators withdraw in a room with a second display showing the actual pressure and flow curves. It is always verified whether the patient has voided like at home. If not, the study is not suited for analysis and a new attempt is made to obtain a reliable measurement. On an average an examination lasted one hour. Patients who met the inclusion criteria of the consensus committee but were not able to produce a reliable pressure-flow study were exceptional. We have computerised systems to abstract data from the curves. Nevertheless, it is always checked by visual inspection of the curves whether these data are correct and if necessary data are adjusted.

Schäfer[5] defines the line between grade 1 and grade 2 as the upper limit of non-obstruction and the line between grade 2 and 3 as the lower limit of real obstruction. The authors of the provisional ICS definition[2] recommend among others the use of an equivocal zone. Schäfer[5] has objections against the use of the term equivocal. In men who are urodynamically clearly unobstructed or who are urodynamically clearly obstructed this finding will play a prominent role, but not the only one, in the decision whether or not to perform surgery. In patients falling in the equivocal zone other clinical findings will dominate that decision. Based on the knowledge we have now, this is our interpretation of the term equivocal. Strictly speaking, urodynamic findings can not be equivocal but a classification can. Whether Schäfer's grade 2 or the ICS zone should be taken as equivocal zone is a question we can not (yet) answer; nevertheless the equivocal zone of the provisional method of the ICS is similar, but not identical, to the region defining Schäfer's grade 2.

According to Rollema et al.[10] patients with URA>29 cm H_2O were classified as obstructed. No URA value was defined to discriminate between unobstructed and equivocal. We calculated the values of URA with the best agreement between classification by Schäfer's grade and by URA of equivocal and unobstructed men (URA=21.3 cm H_2O) and between classification by ICS and by URA of these men (URA=21.1 cm H_2O). For reasons of simplicity we finally took URA=21 cm H_2O as the cut-off point. In order to be able to compare the consequences of the use of the ICS classification with those of the URA classification, we recommend definition of the zone 21 cm $H_2O \leq$ URA $\leq$ 29 cm H_2O as equivocal. Despite the fact that the URA equivocal zone is based on ICS equivocal zone, still 20 men are classified as unobstructed by URA and equivocal by ICS and nine more are classified as equivocal by URA and unobstructed by ICS (see figure 6.3A).

In our group of 565 men with LUTS suggestive of BPH, in 127 men (22%) classification according to Schäfer differs from that by URA. In 100 men (18%) classification by ICS differs from that by URA.

Using URA=30 cm H_2O as boundary between equivocal and obstructed increased the agreement between classification by URA on the one side and classification by Schäfer's grade and ICS on the other side. However, this increase related to 7 men of 127 and 7 men of 100, respectively. In 33 men (6%), Schäfer's grade differs from ICS. No patient was classified more than one class different.

Fifty-four men had a point in the pressure-flow plot outside the area enclosed by maximum flow between 0 and 25 ml/s and detrusor pressure between 0 and 100 cm H_2O. No disagreement among the different methods existed in these patients. Thus all differences between the classifications by URA, Schäfer, and ICS are concentrated near the points of intersection of the different boundaries. The decision whether or not to perform surgery is not likely to change when in these cases another classification is applied. Not only degree of obstruction, but also many more, objective and subjective, variables will lead to this decision.

Lim et al.[15] reviewed urodynamic tracings of 85 patients who had pressure-flow studies before and after prostatectomy. They classified equivocal patients as unobstructed. Like in our study, AG number>40, URA>29 cm H_2O, and Schäfer's grade$\geq$ 3 were considered as obstructed. About 73% of these 85 patients were classified as obstructed. In our study only about 50% of the patients were obstructed. This difference could be expected, because Lim et al.[15], in contrast to our inclusion, studied men who were already selected for surgery.

The classification agreement between URA and Schäfer's grade was 95% (in our study it was 86%, defining only two categories of patients: unobstructed and obstructed). Agreement between URA and ICS was 94% (in our study it was 87%) and between Schäfer's grade and ICS 98% (in our study it was 97%). The higher agreement in the study of Lim et al.[15] may be due to the higher prevalence of men who are obstructed. Defining just two classes of obstruction, unobstructed and obstructed, will increase the agreement between URA, Schäfer's grade and AG number.

In figure 6.1 men are concentrated in the area around a detrusor pressure at maximum flow of about 60 cm H_2O and a maximum flow of about 10 ml/s. In 127 men of our well-defined group of 565 men, classification according to Schäfer's grade differs from that by URA. Of these 127 men, 41 (32%) lie in the area in which URA classified them as obstructed and Schäfer's grade as equivocal. In 100 men of the 565 men ICS-classification differs from that by URA. Of these 100 men 44 (44%) lie in the area in which URA classified them as obstructed and ICS as equivocal. Thus men with relatively low detrusor pressure at maximum flow and relatively low maximum flow have the highest prevalence among those in which URA and Schäfer's grade classifications and among those in which URA and ICS classifications differ.

We want to emphasise that these conclusions are formulated for our well-defined group of men with LUTS suggestive of BPH. However, we assume that the men included in our study form a reasonable representative sample of the population of men who attend a urology clinic, and for whom there is some suspicion of prostatic obstruction.

Conclusions

In our group of 565 included men with LUTS due to BPH, in 438 men (78%) classification according to Schäfer's grade agrees with classification according to URA. In 465 men (82%) agreement exists between classification by URA and ICS. Disagreement between the methods of classification exists only near the points of intersection of the different boundaries, and a decision whether or not to perform surgery is not likely to be influenced by this disagreement.
Men with relatively low detrusor pressure at maximum flow and relatively low maximum flow have a high prevalence among those in which URA and Schäfer's grade classifications and among those in which URA and ICS classifications differ.

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CHAPTER 7

Interactions Between Prostate Volume, Filling Cystometric Estimated Parameters and Data from Pressure-Flow Studies in 565 Men with Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia

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Abstract

Objective: The aim of this study was to establish the characteristics and to investigate the interactions between prostate volume, degree of obstruction, bladder contractility, the prevalence of residual volume, bladder compliance, bladder capacities, and the prevalence of instability in a large, well-defined group of men with lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH).

Methods: The 565 consecutive men included in the study met the criteria of the International Consensus Committee on BPH and voided more than 150 ml during uroflowmetry. Their residual urine volume and prostate size were estimated, and filling cystometry and pressure-flow studies were performed.

Results: Fifty-three percent of the men appeared to have obstruction. We found a positive correlation between prostate volume and Schäfer's obstruction grade, except that mean prostate volume decreased at Schäfer's grades 5 and 6. Significant negative correlations existed between Schäfer's grade and cystometric bladder capacity and effective capacity. Bladder outlet obstruction results in incomplete emptying. Of all men, 26% had a significant residual volume (>20% of cystometric capacity). Thirty-nine percent did not have residual volume. Of the 565 men, 46% had an unstable bladder. In particular, patients with an unstable bladder in the sitting and lying positions had a significantly higher Schäfer's grade and contractility grade and a significantly lower cystometric and effective bladder capacity compared to patients without instability. Patients with a residual volume or instability were significantly older.

Conclusions: We conclude that in men with LUTS suggestive of BPH, abnormalities of bladder and bladder outlet function vary greatly and have complex mutual interactions.

Introduction

In the past, urodynamics in men with lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) focused on distinguishing between prostatic obstruction and impaired detrusor contractility.

If improvement in symptoms and quality of life is considered the primary outcome, the results after laser prostatectomy in men with obstruction appeared to be significantly better than in men without obstruction, but those without obstruction also derived benefit[1]. If improvement of maximum flow rate, average flow rate, and postvoid residual volume is taken into account, even patients with impaired detrusor contractility and minimal obstruction appeared to have a good outcome[2].

In the recent years, it has become clear that the interrelationships between BPH, prostatic enlargement, LUTS, and bladder outlet obstruction are not simple[3]. Even elderly women develop LUTS very similar to LUTS in men[4].

Decreased bladder compliance, reduced bladder capacity, residual urine volume, and/or detrusor instability all play a role in the genesis of symptoms as well as in the severity of BPH. These pathophysiological elements are all common in the elderly man and may be present alone or in all possible combinations, each giving rise to specific complaints[3].

The probability of having an unstable bladder in men with BPH is approximately 60%, decreasing to approximately 25% after surgery[5-7]. Surprisingly, even in a group of 17 healthy older men, the prevalence of detrusor instability was 53%[8]. Thus, the association of detrusor instability and LUTS suggestive of BPH is non-specific.

A decrease in bladder compliance does not appear to be a consistent finding in patients with outlet obstruction, although the proportion of men with low bladder compliance is higher in the group with obstruction and/or detrusor instability than in those with normal urodynamic findings[9].

Residual urine was present in 69% of the obstructed men and in 52% of the unobstructed men as well[10].

When evaluating these characteristics in men with BPH, it is not fair to compare men with recent onset of BPH with those who have severe and prolonged obstruction. In the latter group, the long-term effects of obstruction may result in detrusor decompensation or other changes.

The aim of this study was to establish the characteristics of a large, well-defined group of men with LUTS due to BPH who are able to compensate more or less for the impaired outflow condition. Further, we investigated the interactions between prostate volume, degree of obstruction, bladder contractility, the prevalence of residual volume, bladder compliance, bladder capacities and the prevalence of instability in this large, well-defined group.

Materials and Methods

From October 1993 on, in consecutive men with LUTS presenting to the outpatient urology department, a basic initial evaluation (history, physical examination, digital rectal examination, urinalysis, and renal function assessment) and recommended diagnostic tests (uroflowmetry and residual urine estimation) were performed, conforming to the recommendations of the International Consensus Committee on BPH[11].

Men were included if 1) they were older than 50 years of age, 2) they had no exclusion criteria according to the International Consensus Committee on BPH[11], 3) they voided >150 ml during one or more free uroflowmetry studies, 4) their residual urine was estimated reliably, and 5) their prostate size was determined by transrectal ultrasound. They also underwent filling cystometry and pressure-flow studies.

Cystometric studies were performed with the patient supine and erect. Pressure-flow studies were done twice with the patient erect. Vesical pressure was recorded with a 5F catheter, and rectal pressure was measured with a 14F catheter connected to external pressure transducers. The bladder was filled with saline at 37^0C, through a second 5F catheter, at a constant rate of 50 ml/min. In some men, an 8F double-lumen catheter was used for vesical pressure measurement and bladder filling. Filling was stopped when the patient had a strong desire to void. If two catheters were used, the first pressure-flow study was done with the measuring and filling catheters in the bladder, and the second study was done after removal of the filling catheter. The pressure-flow study with the lowest urethral resistance (usually during voiding with only the measuring catheter in the bladder) was used for further analysis.

Residual urine was estimated during one of the visits at the outpatient department by transabdominal ultrasonography or catheterisation. If residual urine was significant, this test was repeated. The urodynamic investigation always started with a uroflowmetry and determination of the residual volume by catheterisation. Some patients were not able to arrive with a full bladder and sometimes were not able to produce a flow curve. At the end of the urodynamic investigation, the bladder of these patients was refilled, and after removal of the catheter uroflowmetry was performed. If these patients were known to have significant residual volume, catheterisation was performed once more. The smallest residual volume was used for further analysis.

From pressure-flow studies, obstruction grade (range 0 - no obstruction to 6 - severe obstruction) and detrusor contractility grade (range 0 - very weak to 5 - strong bladder) as proposed by Schäfer[12] and the Abrams-Griffiths (AG) number[13] and urethral resistance factor (URA)[14] were estimated, using the values of the maximum flow rate and corresponding detrusor pressure. Men with an obstruction grade of 0 or 1 were considered not to have infravesical obstruction, those with obstruction grade 2 were considered as equivocal, and those with an obstruction grade of 3 or more were considered to have obstruction.

Effective bladder capacity was defined as maximum cystometric bladder capacity minus residual volume.

Statistical analyses were performed with the Kendall and Gibbons distribution-free correlation method and Mann-Whitney test. The Kolmogorov-Smirnov goodness-of-fit test was used to analyse normal distribution of variables[15]. The level of significance (two-tailed) was set at $p<0.05$.

Results

Results were obtained from the 565 included men. Figure 7.1 shows distributions of different parameters for all men.

Table 7.1 Mean, standard deviation (SD), and range of different baseline characteristics of the evaluated population (n=565).

Characteristic	Mean	SD	Range
Age (yr)	66	8	50-90
Prostate volume (ml)	38	19	10-155
Maximum free flow rate (ml/s)	12	5	3-35
Schäfer’s grade	2.7	1.3	0-6
AG number	46	30	–22-264
URA (cm H_2O)	34	19	9-259
Contractility degree	3.0	1.2	0-5
Cystometric capacity (ml)	415	155	150-1100
Effective capacity (ml)	355	140	100-850
Residual volume (ml)	65	90	0-630
Symptom index	17	7	1-35
Quality of life score	3.6	1.5	0-6

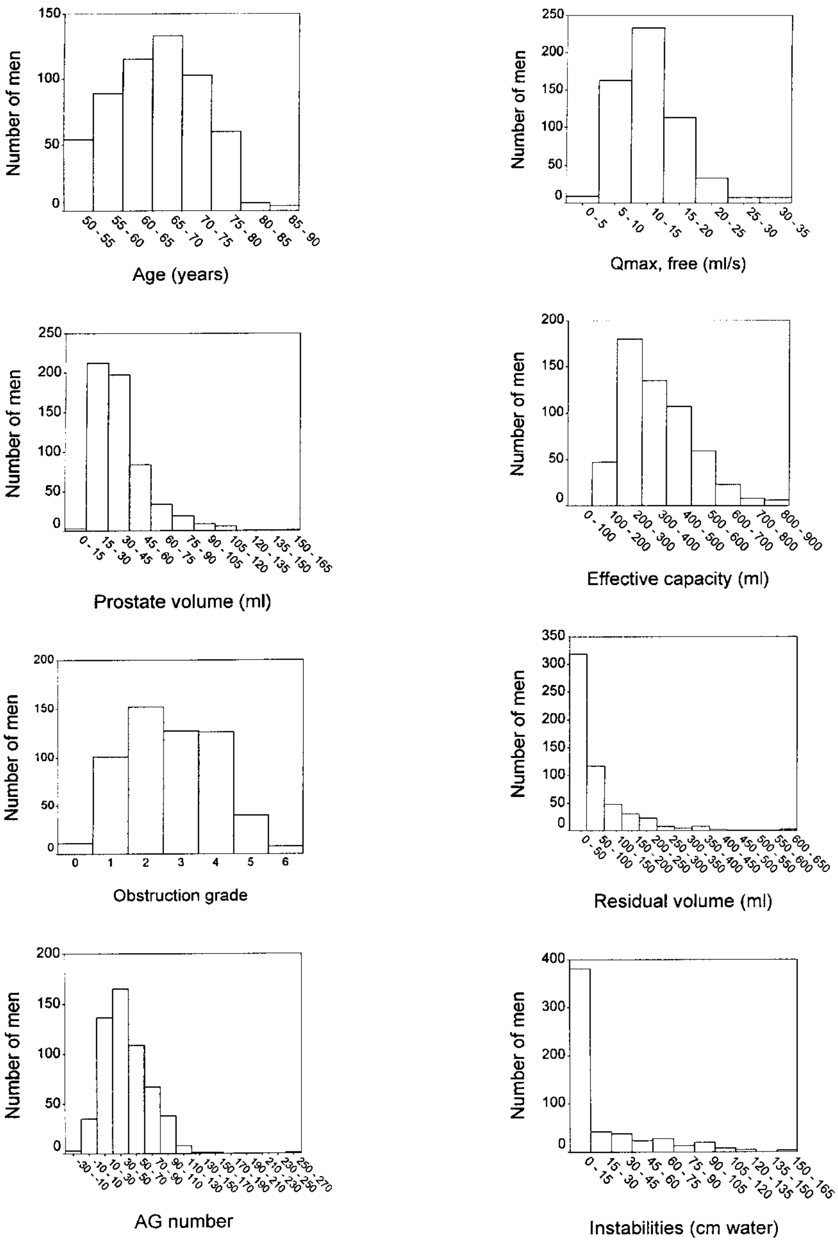

Figure 7.1 Distribution of age, prostate volume, Schäfer's obstruction grade, AG number, maximum free flow rate (Qmax.free), effective capacity, residual volume, and instability.

Except age, no parameter was normally distributed (Kolmogorov-Smirnov test).
Table 7.1 describes baseline characteristics of the evaluated patients. In the literature, it is not unusual to calculate the standard deviation, despite nonuniform distributions. Therefore, these values are listed as well.
According to our definition, 112 of 565 men (20%) appeared not to have obstruction, 152 (27%) were equivocal, and 301 (53%) appeared to have obstruction.
Mean maximum flow during free uroflowmetry ($Q_{max.free}$) was 16±6 ml/s in the non-obstructed group, 13±5 ml/s in the equivocal group, and 11±4 ml/s in the obstructed group. These differences are significant ($p<0.001$). Nevertheless, the maximum flow during uroflowmetry was <15 ml/s in 47% of patients without obstruction and ≥ 15 ml/s in 11% of patients with obstruction.
Correlation coefficients between different urodynamic parameters are listed in table 7.2. Only significant correlations are listed.
One hundred forty-eight patients (26%) had a residual volume of >20% of cystometric capacity, 199 (35%) had residual volume ≤ 20% of cystometric capacity, and 218 (39%) did not have residual volume. Table 7.3 shows urodynamic parameters in these three groups. Patients with a significant residual volume (>20% of cystometric capacity) are older and have slightly larger prostates and more obstruction than patients without residual volume. Their cystometric capacity is higher and their effective capacity is lower.

Table 7.3 Mean±SD of age, prostate size, and urodynamic parameters in patients with and without residual volume (p value obtained with Mann-Whitney test; n.s. = not significant).

	Residual volume			
	0 (n=218)	0< and ≤ 20 % of cystometric capacity (n=199)	>20 % of cystometric capacity (n=148)	Significance (no residual against >20 %) (p value)
Age (yr)	65±8	65±8	68±7	<0.001
Prostate volume (ml)	37±16	39±21	41±20	<0.05
Schäfer's grade	2.4±1.2	2.7±1.3	3.2±1.4	<0.001
Contractility	3.0±1.1	3.0±1.0	2.8±1.2	n.s.
Cystometric capacity (ml)	385±140	425±155	450±160	<0.001
Effective capacity (ml)	385±140	375±140	275±105	<0.001
$Q_{max.free}$ (ml/s)	14±5	13±5	11±4	<0.001

Table 7.2 Kendall's correlation coefficients between age, prostate size, and urodynamic parameters. Only significant correlations are listed.

	Age (yr)	Prostate volume (ml)	Schäfer's grade	Contractility	Cystometric capacity (ml)	Effective capacity (ml)
Prostate volume (ml)	0.08**	-	-	-	-	-
Schäfer's grade		0.28**	-	-	-	-
Contractility		0.12**	0.31**	-	-	-
Cystometric capacity (ml)			-0.19**	-0.12**	-	-
Effective capacity (ml)	-0.07*	-0.08**	-0.28**	-0.07*	0.68**	-
Qmax.free (ml/s)		-0.12**	-0.34**	0.13**	0.15**	0.24**

* Correlation is significant at the 0.05 level.

** Correlation is significant at the 0.01 level.

Table 7.4 Mean±SD of age, prostate size, and urodynamic parameters in patients with a stable and an unstable bladder.

	Men with instabilities (n=259)			Bladder		
	Only in supine position (n=55)	Only in erect position (n=106)	In supine and in erect positions (n=98)	Unstable (n=259)	Unstable (>15 cm H_2O) (n=170)	Stable (n=306)
Prostate volume (ml)	39±17	39±18	42±22	40±19	41±19	37±19
$Q_{max.free}$ (ml/s)	12±5	13±6	12±4	12±5	13±5	12±5
Schäfer's grade	3.0±1.3	2.7±1.2	3.2±1.3	3.0±1.3	3.0±1.3	2.5±1.3
Contractility	3.3±1.0	3.1±1.1	3.4±1.1	3.3±1.1	3.4±1.1	2.7±1.1
Cystometric capacity (ml)	415±195	390±105	355±130	380±140	370±135	445±155
Effective capacity (ml)	330±150	335±105	284±105	315±120	305±120	385±150
Age (yr)	67±8	67±8	68±7	67±7	68±7	64±8

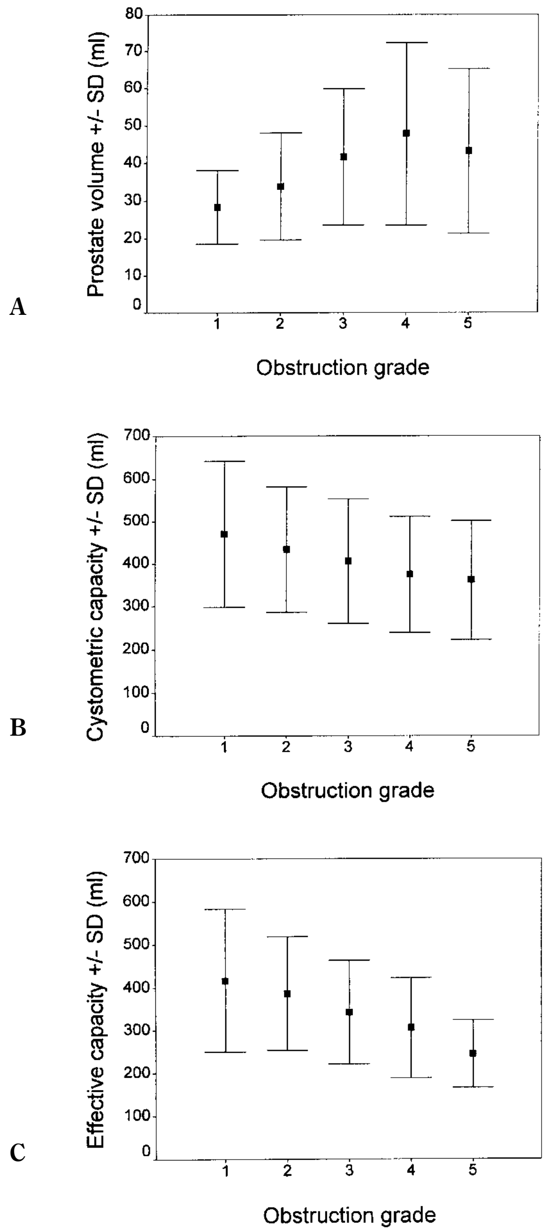

Figure 7.2 Prostate volume (**A**), cystometric capacity (**B**) and effective capacity (**C**) (mean ± SD) plotted against Schäfer's obstruction grade. *Note: Schäfer's obstruction grades 0 and 1, and 5 and 6 were united.*

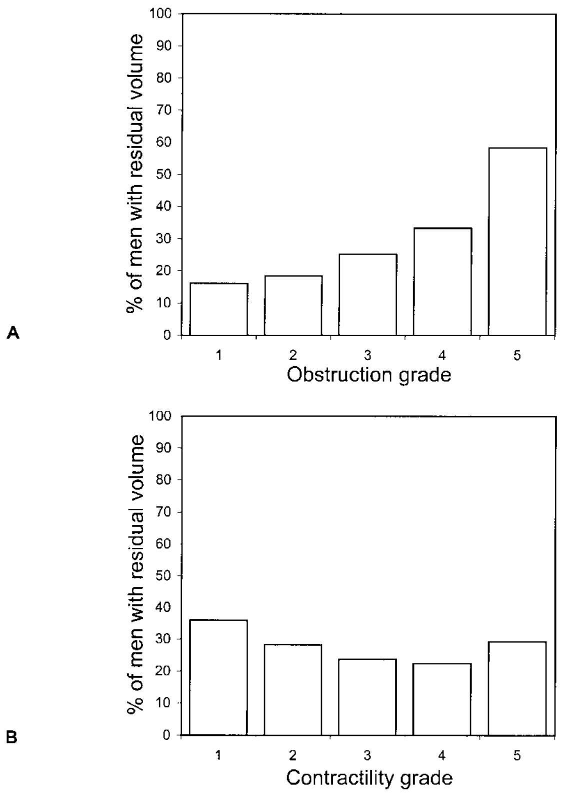

Figure 7.3 Prevalence of residual volume (%) plotted against Schäfer's obstruction grade (**A**) and Schäfer's contractility grade (**B**). *Note: Schäfer's obstruction grade 0 and 1, and grade 5 and 6 were united and Schäfer's contractility grades 0 and 1 were united.*

Of the men, 259 (46%) had an unstable bladder; in 55 of whom it occurred only in the supine position, in 106 only in the erect position, and in 98 in both positions. Table 7.4 shows urodynamic parameters in patients with and without detrusor instability. No significant differences appeared to exist between men with instability only in the supine position and those with instability only in the erect position.

Because of the relatively large number of men in both groups, significant differences appeared to exist between the men with instability only in the erect position and those with instability in the supine and erect positions with respect to obstruction grade ($p<0.01$), contractility ($p=0.03$), cystometric capacity ($p<0.01$), and effective capacity ($p<0.01$).

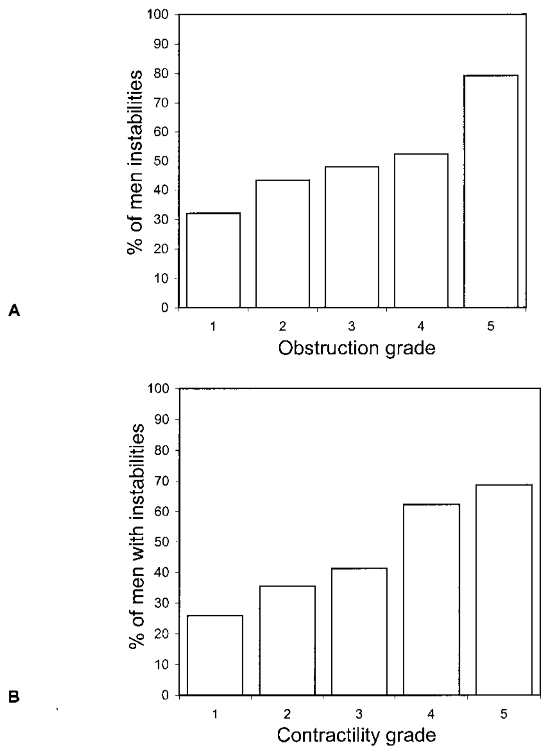

Figure 7.4 Prevalence of instabilities (%) plotted against Schäfer's obstruction grade (**A**) and Schäfer's contractility grade (**B**). *See note figure 7.3.*

A significant negative correlation was found in the unstable group between highest magnitude of instability and cystometric bladder capacity (correlation coefficient -0.11, $p=0.02$), and effective bladder capacity (correlation coefficient -0.16, $p<0.001$).
Figure 7.2 shows prostate size, cystometric bladder capacity, and effective bladder capacity plotted against Schäfer's obstruction grade. Due to the fact that just a small number of patients had Schäfer's grade 0 (11 patients) and Schäfer's grade 6 (8 patients), grades 0 and 1, and grades 5 and 6 were combined.
In figure 7.3, prevalence of residual volume is plotted against Schäfer's obstruction grade and Schäfer's detrusor contractility grade. Because only 5 patients had contractility grade 0, contractility grades 0 and 1 were combined.
Prevalence of instability is plotted against Schäfer's obstruction grade and contractility grade in figure 7.4 .

Discussion

Age, cystometric capacity, residual urine, and symptom index (table 7.1) in our group were comparable with those reported by Rosier and de la Rosette[16] for a group of 521 men with LUTS. Nevertheless, in their group, prostate volume (44.1 cm^3) and URA (37.6 cm H_2O) were higher than in our group (38 cm^3 and 34 cm H_2O, respectively). In contrast to Madersbacher et al.[17], the detection of a significantly low (<40 ml/cm H_2O) bladder compliance was exceptional in our group. However, in their group, mean prostate volume was 47 cm^3. We found 53% of the men to be obstructed, which is slightly lower than reported by the ICS-BPH study group (60%)[18]. These differences may be due to different inclusion criteria. Our criterion that men were included only if they could void a volume of more than 150 ml during free uroflowmetry may have excluded men with severe and prolonged obstruction. In a reasonable number of these excluded men, however, bladder properties may have been changed, resulting in a lower compliance and/or (partly) decompensated bladders. Mean prostate volume and obstruction grade in these excluded men will be greater than in the included men, explaining the above mentioned differences in prostate volume and obstruction grade. Our inclusion criteria were based on the recommendations of the International Consensus Committee on BPH[11].

Conforming to the findings of Rosier and de la Rosette[16], prostate volume was significantly positively correlated with Schäfer's obstruction grade ($p<0.001$), although mean prostate volume slightly decreased at Schäfer's grade 5 and 6 (fig. 7.2A).

Although maximum free flow rate in men without obstruction differs significantly from that in men with obstruction, 47% of the former patients have a low maximum free flow rate (<15 ml/s).

Significant negative correlations existed between Schäfer's grade and cystometric bladder capacity and effective capacity (table 7.2, fig. 7.2B,C). Increasing Schäfer's obstruction grade leads logically to an increase in detrusor contractility. Maximum free flow rate is negatively correlated with Schäfer's grade and prostate volume but of course positively correlated with contractility (table 7.2). Such a compensatory response to obstruction was previously demonstrated[9].

Patients with increased residual urine volume or detrusor instability were significantly older (tables 7.3, 7.4). Older patients have a significantly greater prostate volume, but age does not correlate with Schäfer's obstruction grade (table 7.2).

Bladder outlet obstruction results in incomplete emptying. Patients with a significant residual volume have a higher prostate volume and higher Schäfer's grade but no significantly lower contractility grade (table 7.3). These associations also can be seen in figure 7.3A,B. Despite the increase in cystometric capacity of approximately 65 ml, residual volume results in a significantly lower effective bladder capacity of approximately 90 ml (table 7.3).

Having a significant residual volume leads to a significantly lower maximum free flow rate despite the unchanged contractility grade. This can be explained by the significant positive correlation between residual volume and Schäfer's grade and by the significant negative correlation between residual volume and effective capacity in that group (correlation coefficient -0.19, $p<0.001$), leading to lower maximum flow rates[19].

Of the 565 men, 46% had an unstable bladder as estimated by our filling cystometries. This percentage is lower than the reported preoperative incidence between 49% and 74% in 12 clinical studies[20]. However, it is unclear whether these reports are based on patients with BPH who were already selected for operation.

No significant differences appeared to exist between men with detrusor instability in the supine position compared with those with instability only in the erect position. Patients with an unstable bladder in the erect and supine positions have a significantly higher Schäfer's grade and contractility grade and a significantly lower cystometric and effective bladder capacity, compared with patients without instability (table 7.4, fig. 7.4A,B).

Conclusions

In our group of 565 men with LUTS due to BPH, we found 53% to be obstructed.

We found a significant increase in prostate volume from unobstructed to obstructed men, although mean prostate volume decreased at Schäfer's obstruction grades 5 and 6.

Significant negative correlations existed between Schäfer's grade and cystometric and effective bladder capacity and maximum free flow rate.

Patients with increased residual urine volume or detrusor instability were significantly older. Patients with a significant residual volume have a greater prostate volume and higher Schäfer's grade but not a lower contractility grade.

Forty-six percent of the men had an unstable bladder during filling cystometries. Patients with an unstable bladder had a significantly higher Schäfer's obstruction and contractility grade and significantly lower bladder capacities.

We conclude that in men with LUTS suggestive of BPH, abnormalities of bladder and bladder outlet function vary greatly and have complex mutual interactions.

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CHAPTER 8

Symptoms, Prostate Volume and Urodynamics in Elderly Male Volunteers without and Elderly Male Volunteers with Lower Urinary Tract Symptoms (LUTS), and in Patients with LUTS Suggestive of Benign Prostatic Hyperplasia

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Abstract

Objective: The aim was to estimate differences between symptoms, prostate volume and urodynamic variables of symptom-free elderly volunteers, of volunteers with lower urinary tract symptoms (LUTS), and of urologic patients with LUTS suggestive of benign prostatic hyperplasia (BPH).

Methods: The included 14 male volunteers without LUTS, the 17 male volunteers with LUTS and the 565 urologic patients with LUTS met the criteria of the International Consensus Committee on BPH. They were older than 50 years, they voided more than 150 ml during free uroflowmetry, their residual volume and prostate volume were estimated and AUA symptom scores were collected. All males were evaluated by urodynamics as well.

Results: Prostate volume, residual volume, urethral resistance factor, and symptom scores were significantly lower, and maximum free flow rate and effective capacity significantly higher in symptom-free volunteers than in volunteers and patients with LUTS. Except prostate volume, the variables in volunteers with LUTS closely approximate those of the patients with LUTS. Volunteers with LUTS had a smaller prostate volume than patients with LUTS. Nevertheless, maximum free flow rate, symptoms, degree of obstruction and prevalence of residual volume did not differ between both groups. In all groups, males with an unstable bladder were present.

Conclusions: Symptom-free volunteers have smaller prostate volumes, less residual volume, lower symptom scores, lower urethral resistance factor, higher maximum free flow rate and higher effective capacity than males with LUTS. Except a smaller prostate volume, findings in volunteers with LUTS closely approximate those of urologic patients with LUTS.

Introduction

Urodynamics in patients with lower urinary tract symptoms (LUTS) is used for objective assessment of bladder and bladder outlet behaviour. However, to decide what is pathological it seems mandatory to agree on what can be considered normal[1]. Objective parameters obtained from urodynamic tests on which functional diagnoses are based should be related to normal standardised reference values. Although urodynamics is used frequently to evaluate voiding disorders in elderly men with LUTS suggestive of benign prostatic hyperplasia (BPH)[2], only a few studies have included sufficient age-matched controls.

A number of studies in symptom-free persons have dealt with young men and women (mean age less than 40 years). In the studies of Robertson et al.[3] and Wyndaele et al.[1] of young adults, most urodynamic parameters showed large variations. Different and changing flow patterns, low maximum flow rate, large bladder capacity, bladder overactivity and residual urine, which are all usually considered signs of pathological conditions, were seen.

Considering obstruction, Schäfer et al.[4] found 10% of 30 healthy young male volunteers (mean age 28 years) to be classified in the ICS “equivocal zone”, and Griffiths et al.[5] found 60% of 7 asymptomatic volunteers (all members of the urology department[6] with a mean age of 42 years, range 34-53) to be classified as “equivocal”.

The filling and voiding phase of the bladder in the elderly symptom-free man was studied by urodynamic investigations in 17 men by Andersen et al.[7], in 13 men by Jensen et al.[8], in 25 men by Walker et al.[9], in 29 men by Bøtker-Rasmussen et al.[10] and in 19 men by Diokno et al[11]. Some of these studies show a surprising number of apparently “normal” elderly men to be classified as obstructed on pressure flow study[9-11]. In addition, a large proportion of these men exhibits in some studies detrusor instability on filling cystometry[7,9].

The urodynamic study of Homma et al.[12] involving 65 subjectively symptom-free men aged over 30 (mean age 55 years, range 34-84) indicated that urodynamic variables change with age, even in “normal” subjects. Urodynamics showed reduced urinary flow rate and increased residual urine with advancing age. This warrants a careful interpretation of urodynamic variables in elderly subjects.

Above mentioned studies support the statement of Wyndaele[1] that since normality in urodynamics may include so many different features, the interpretation of urodynamic evaluations should be made with caution. To decide what is pathological, it is important to know what can be considered normal in elderly men. Only by fully understanding the range of values seen in the normal population can we be sure that our observation of

the "abnormal" is genuine and relevant to clinical management[3].
The aims of this study are to describe and to compare symptoms, prostate volume and urodynamic findings in symptom-free elderly community-based male volunteers, in elderly community-based volunteers with LUTS suggestive of BPH and in elderly urologic patients with LUTS suggestive of BPH.

Materials and Methods

For research objectives two groups of elderly volunteers were recruited. The first group was selected from men who responded to an advertisement recruiting healthy men with an age between 45 and 75 years. The second group was selected from men who responded to an advertisement recruiting men with an age between 45 and 75 years, with lower urinary tract symptoms like hesitancy, weak urinary stream, feeling of inability to empty the bladder completely, frequent voiding of small volumes and/or postvoid dribbling. The local ethical committee approved the research program and informed consent was obtained.
The volunteers were examined conform to the recommendations of the International Consensus Committee (ICC) on BPH[13] and were without any of the specified exclusion criteria of the committee (prostate cancer, neurological disease, previous prostate surgery, or taking medication active on the urinary tract). They voided a sufficient volume (>150 ml) during one or more free uroflowmetry studies, their residual urine was estimated reliably, and their prostate size was determined by transrectal ultrasound. A practised urologist examined all men.
The AUA Symptom Index[14] on incomplete emptying, frequency, intermittency, urgency, weak urinary stream, hesitancy and nocturia were collected for all men. Each question could be answered on a scale of 0 (not at all) to 5 (almost always). The AUA Symptom Score (range 0 to 35) was calculated by summing the 7 scores on question 1 through 7.
All volunteers who claimed to be without LUTS were included in the present paper when, conform to the recommendations of the ICC, they were older than 50 years of age and when the practised urologist qualified them as healthy without LUTS. All volunteers who claimed to have LUTS were included when they were older than 50 years and when the urologist qualified them as "men with LUTS suggestive of BPH".
Filling cystometric studies were performed with the volunteer supine or erect. Bladder pressure was recorded with a 10F double lumen catheter and rectal pressure was measured with a 14F catheter connected to external pressure transducers. The bladder was filled with saline at 37^0C, at a constant rate of 50 ml/min. Filling was stopped when the volunteer had a strong desire to void. The pressure-flow study was done with the volunteer erect. When the results

of the pressure-flow study were not reliable, the test was repeated.

From pressure-flow studies, obstruction grade (range 0 - no obstruction to 6 - severe obstruction) and detrusor contractility grade (range 0 - very weak to 5 - strong bladder) as proposed by Schäfer[15], the Abrams-Griffiths (AG) number[16] and urethral resistance factor (URA) [17] were estimated, using the values of the maximum flow rate and the corresponding detrusor pressure. Men with obstruction grade 0 or 1 were considered not to have infravesical obstruction, those with obstruction grade 2 were considered as equivocal. And those with an obstruction grade of 3 or more were considered to have obstruction.

Effective bladder capacity was defined as maximum cystometric bladder capacity minus residual volume.

The findings in the two groups of volunteers were compared with those of a group of 565 consecutive men who presented to our outpatient department of urology with LUTS suggestive of BPH. The patients fulfilled the same criteria and were examined in the same way as the volunteers. Only urodynamic investigations in these patients were performed with one or two F5 bladder catheters or one F8 bladder catheter.

Data of all groups are reported as mean plus or minus standard deviation and range. Statistical analyses were performed with the Fisher-Irwin test for two-by-two tables and the distribution-free Kendall and Gibbons correlation method and Mann-Whitney test. The level of significance was set at $p<0.05$.

Results

Of the 16 male volunteers without LUTS, participating in the research project, 2 were excluded from the present study because they were younger than 50 years. For the same reason 1 of 18 volunteers with LUTS was excluded.

Table 8.1 shows parameters in the 14 volunteers without LUTS, in the 17 volunteers with LUTS suggestive of BPH and in the 565 patients with LUTS suggestive of BPH.

In only one volunteer with LUTS the pressure-flow study had to be done twice because of excessive straining during the first study.

Prostate volume was significantly lower in the volunteers without complaints compared to the prostate volume in volunteers with complaints. The prostate volume in the latter group was in turn significantly lower than prostate volume in the patient group. Maximum free flow rate was significantly higher and residual volume significantly lower in the volunteers without LUTS compared to the volunteers with LUTS. From the variables Schäfer's grade, AG number and URA, only URA was significantly

Table 8.1 Mean, standard deviation and range of age, prostate volume, and urodynamics in elderly volunteers without and with LUTS and in patients with LUTS.

	Volunteers without LUTS (n=14)	p_1=	Volunteers with LUTS (n=17)	p_2=	Patients with LUTS (n=565)
Age (yrs)	62 ± 4 (55-68)		65 ± 6 (55-74)		66 ± 8 (50-90)
Prostate volume (ml)	21 ± 4 (14-28)	0.01	29 ± 8 (19-46)	0.02	38 ± 19 (10-155)
Max. free flow (ml/s)	18 ± 3 (13-24)	<0.001	10 ± 2 (7-13)	0.04	12 ± 5 (3-35)
Residual volume (ml)	35 ± 55 (0-140)	0.04	60 ± 45 (0-180)		65 ± 90 (0-630)
Schäfer's grade	2.1 ± 0.8 (1-3)		2.8 ± 1.3 (0-5)		2.7 ± 1.3 (0-6)
AG number	30 ± 18 (6-61)		45 ± 22 (13-94)		46 ± 30 (-22-264)
URA (cm H_2O)	25 ± 8 (15-42)	0.02	35 ± 14 (18-71)		34 ± 19 (9-259)
Contractility degree	2.8 ± 1.1(1-5)		2.4 ± 1.1 (0-4)	0.04	3.0 ± 1.1 (0-5)
Cystometric cap. (ml)	505 ± 150 (200-750)		425 ± 170 (175-750)		415 ± 155 (150-1100)
Effective cap. (ml)	470 ± 140 (200-670)	0.048	365 ± 165 (150-750)		355 ± 140 (100-850)

p_1: significance of difference between volunteers without and volunteers with LUTS
p_2: significance of difference between volunteers with LUTS and patients with LUTS

higher in the volunteers with LUTS compared with those without complaints. Effective capacity in the symptom-free group was significantly higher than in the group with LUTS.

Despite the fact that prostate volume in the volunteers with LUTS was between prostate volume of patients and that of volunteers without LUTS, the other parameters of the volunteers with LUTS in table 8.1 approximate those of the patients with LUTS. In the group volunteers without LUTS, 4 (28%) of 14 men were unobstructed, 5 (36%) were equivocal and 5 (36%) were obstructed. In the volunteers with LUTS 2 (12%) of 17 men were unobstructed, 4 (23%) were equivocal and 11 (65%) were obstructed. In the patient group 112 (20%) of 565 men were unobstructed, 152 (27%) were equivocal and 301 (53%) were obstructed. The distribution of the volunteers with LUTS again approximates that of the patients, however the numbers of volunteers are to small to proof significant differences.

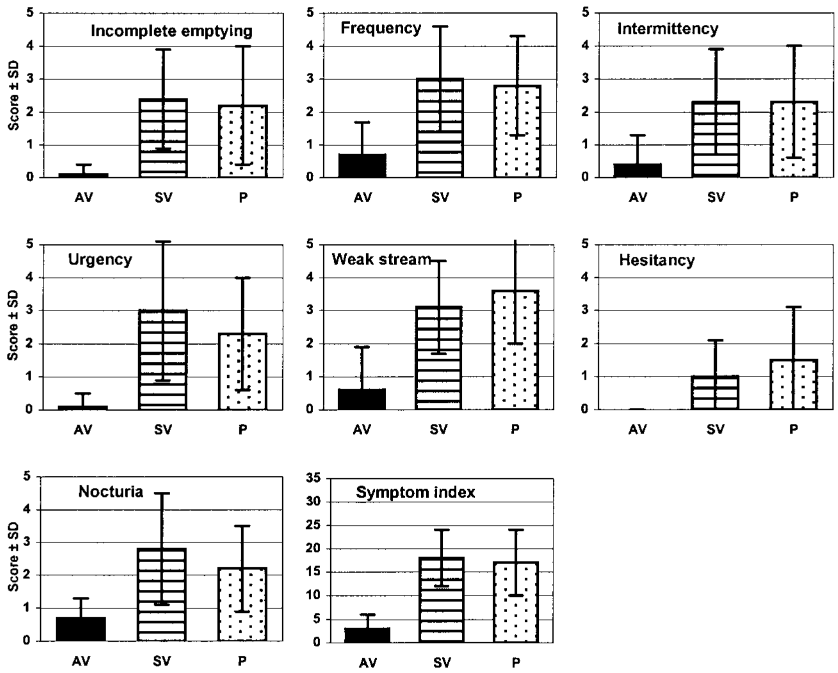

Figure 8.1 Mean scores on each symptom and symptom index together with the standard deviation for asymptomatic volunteers (AV), symptomatic volunteers (SV) and patients with LUTS (P).

After micturition the bladder was empty in 8 (57%) out of 14 volunteers without LUTS. This proportion is significantly greater than 1 (6%) out of 17 volunteers with LUTS ($p<0.01$) and than 220 (39%) out of 565 patients with LUTS. In 29% of the volunteers without LUTS, in 47% of the volunteers with LUTS and in 44% of the patients residual volume was 50 ml or more.
Of the volunteers without LUTS, 6 (43%) out of 14 had an unstable bladder during filling cystometry, with instabilities of 12 to 67 cm H_2O. In the group volunteers with LUTS 5 (29%) out of 17 had an unstable bladder with instabilities of 15 to 85 cm H_2O. In the patient group 259 (46%) out of 565 showed an unstable bladder. Any significant differences between the prevalence of instabilities in the groups could not be proved.
In figure 8.1 scores on the symptom questions are shown for the three groups.
Healthy volunteers had significantly lower symptom scores than volunteers and patients with LUTS ($p<0.01$ for all questions). No significant difference was found between a score in the group volunteers with LUTS and that score in the patient group.

Discussion

In most studies older volunteers were usually patients and were classified as 'normal' because of their history and subjective symptom assessment. We included community men in stead of patients, and compared them with the patient population visiting our outpatient clinic.

Age in our group volunteers without LUTS was similar to other studies[7-10]. Prostate volume in this group was 21±4 ml, and was somewhat lower than in the study of Walker et al.[9] with prostate volumes of 26±13 ml. The AUA symptom index of our healthy volunteers was low (3±3; range 0-8), and agreed with the index reported by Walker et al.[9] (4±5).
Values of maximum free flow rate exceeding 15 ml/s are generally accepted as normal, while values less than 10 ml/s indicate infravesical obstruction, provided detrusor insufficiency is absent[18]. Mean maximum free flow rate in our group healthy volunteers was 18±3 ml/s and similar to the values reported by Walker et al.[9] and Jensen et al.[8] which show a maximum free flow rate of 18±8 and 16 (range 5-33) ml/s, respectively. Andersen et al.[7] and Bøtker-Rasmussen et al.[10] found lower free flow rates (12 ml/s and 13 ml/s, respectively). No healthy volunteer had a maximum free flow rate less than 10 ml/s.
After micturition the bladder was empty in 57% of the elderly volunteers without

LUTS (versus 6% of our volunteers with LUTS and 39% of our patients with LUTS). Mean residual volume in men without LUTS was 35 ml (range 0-140), and somewhat higher than reported residual volumes of 10 to 28 ml (range 0 to 160) in literature[7-10].
Normal bladder capacity can vary widely, although in the literature a range between 300 and 550 ml is accepted as normal[1]. We found a large mean maximum cystometric bladder capacity of 505±150 ml (range 200-750). Also in other studies wider ranges than 300 to 550 ml were found[7,8,10].
Many observers agree that the minimal natural prevalence of detrusor instability is at least 10 percent[19]. It thus becomes questionable whether it is reasonable to regard instability as abnormal. The prevalence of instability appears to be at lowest between about the ages of ten and thirty, probably in the region of 10 percent of the population. By the age of 50, urodynamic clinic studies indicate that the incidence is higher than this and that it rises still further in the elderly[19].
Of our volunteers without LUTS, 43% had an unstable bladder. Andersen et al.[7] found in 53% of 17 healthy elderly men bladder instabilities (with an amplitude >15 cm H_2O), and Jensen et al.[8] found in 25% of 13 elderly asymptomatic men uninhibited detrusor contractions. Thus, detrusor instability seemed to be a common finding in elderly men without LUTS and without signs of neurological disease.
According to Schäfer and according to the AG number, 36% (5 of 14) of our healthy elderly volunteers were obstructed. Walker et al.[9] found 23% of healthy men to be obstructed according to Schäfer, and 17% according to the AG number. Bøtker-Rasmussen et al.[10] found 52% of 29 healthy community-based volunteers to be obstructed, according to AG nomogram. Diokno et al.[11] found 47% of 19 men over 60 years of age to be obstructed, but the criteria for diagnosing obstruction were not well described. Mean URA (25±8) in our healthy men approximated mean URA (22±15) of Walker et al[9]. During the extensive urodynamic examinations of the volunteers, it was required to empty the bladder quickly at regular times. To avoid repeated catheterisations for measurements and bladder emptying, we were restricted to use a double-lumen catheter with a dimension of at least 10F. This could introduce differences between the pressure-flow data of volunteers with LUTS and of patients with LUTS. Nevertheless, such differences were not detected.
Prostate volume, residual volume, URA, every symptom score and AUA symptom index were significantly lower, and maximum free flow rate and effective bladder capacity were significantly higher in the group healthy elderly volunteers compared to the group volunteers with LUTS. However, there was an overlap of values between the two groups. These results were similar to those of a study of Jensen et al.[8], who compared 13 asymptomatic male volunteers to 83 patients who were awaiting transurethral resection of the prostate.

The variables in the volunteers with LUTS, who responded on the advertisement, approximate those of the patients with LUTS, visiting our outpatient department of urology. Only prostate volume was significantly lower in the group volunteers with LUTS, although maximum free flow rate, AUA symptom index and degree of obstruction were comparable to our patients with LUTS. Like in our patients with LUTS weak urinary stream, frequency and urgency were the symptoms with the highest prevalence in the group volunteers with LUTS (fig. 8.1).
The symptoms of the volunteers with LUTS did not differ from those of the patients with LUTS. Nevertheless the volunteers did not seek treatment. We do not know why the prostates of the patients are significantly bigger than those of the volunteers with LUTS. Is this why they became patients?
A shortcoming of our study is still the small number of volunteers. Moreover, we performed a cross-section study and longitudinal relations to (adverse) outcomes are needed to define what is normal and what is abnormal.

Conclusions

Prostate volume, the prevalence of residual volume, URA, symptom scores, AUA symptom index were significantly lower, and maximum free flow rate and effective bladder capacity were significantly higher in elderly symptom-free volunteers compared to the volunteers and patients with LUTS. Except prostate volume, the variables in the volunteers with LUTS approximate those of the patients with LUTS. Prostate volume was significantly lower in the volunteers with LUTS compared to the patients with LUTS, although maximum free flow rate, symptoms, degree of obstruction and prevalence of residual volume did not differ. In all three groups, men with an unstable bladder were present and no difference in prevalence between the groups was found.
Like in patients with LUTS weak urinary stream, frequency and urgency were the symptoms with the highest prevalence in volunteers with LUTS.

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CHAPTER 9

Data from Frequency-Volume Charts Versus Filling Cystometric Estimated Capacities and Prevalence of Instability in Men with Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia

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Abstract

Objective: The aim is to examine associations of filling cystometric estimated compliance, capacities and prevalence of bladder instability with data from frequency-volume charts in a well-defined group of men with lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH).

Methods: Men with LUTS suggestive of BPH, were included if they met the criteria of the International Consensus Committee on BPH, i.e., they voided more than 150 ml during uroflowmetry, their residual volume and prostate size were estimated and they completed frequency-volume charts correctly. From the frequency-volume charts, voiding habits and fluid intake in the daytime and at night were evaluated. Filling cystometric studies were performed in these men as well.

Results: Decreased compliance was an exceptional finding. Cystometric capacity and especially effective capacity (cystometric capacity minus residual volume) corresponded significantly with the maximum voided volume on the frequency-volume charts. Effective capacity was almost twice as high as the average voided volume. Minimum voided volume on frequency-volume charts was not related to filling cystometric data. The presence of instability in supine or sitting positions, or in both positions, was not significantly associated with smaller voided volumes, higher nocturia or diuria.

Conclusions: Filling cystometric capacities were strongly associated with maximal and mean voided volumes derived from frequency-volume charts. The presence of detrusor instability during filling cystometry did not significantly affect voided volumes, diuria or nocturia.

Introduction

The aims of performing filling cystometry in men with lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) are to estimate bladder compliance and bladder capacities and to detect the presence of detrusor instability. Previously[1], we studied the relation between data from frequency-volume charts and symptoms and quality of life in BPH. High diuria, and small voided volumes at night and in daytime appeared to contribute significantly to high symptom scores and low quality of life. Thus, low bladder compliance, small cystometric bladder capacity or small effective bladder capacity (cystometric bladder capacity minus residual volume) and/or the presence of an unstable bladder during filling cystometry are expected to be common in men with severe LUTS.

However, a decrease in bladder compliance does not appear to be a consistent finding in patients with outlet obstruction, although the proportion of men with poor compliance is higher in the group with obstruction and/or detrusor instability than in those with normal urodynamic findings[2]. The probability of having an unstable bladder in men with BPH is about 60%, decreasing to about 25% after surgery[3-5]. However, in a group of 17 healthy older men the prevalence of detrusor instability was 53%[6]. Thus, it seems that the association of detrusor instability with LUTS due to BPH is non-specific. When the subjective evaluation of the patient at 6 months after surgery is taken as criterion for the evaluation of postoperative success or failure, the preoperative predominance of irritative symptoms or the combination of irritative symptoms and detrusor instability did not attain prognostic significance[7]. A preoperative maximum cystometric capacity less than 300 ml only appeared to indicate some post-surgical failure in prostatism[8].

In view of these considerations, the International Consensus Committee on BPH[9] concluded that filling cystometry did not provide useful information in the assessment of patients with LUTS. The Committee decided not to recommend filling cystometry in routine cases. Several explanations are possible for why filling cystometry is not expected to contribute to the diagnostics in men with LUTS suggestive of BPH. One explanation may be the artificial way the bladder is filled. Artificial bladder filling may mask or even provoke detrusor instability. Moreover bladder content sensation may be influenced by the rate of bladder filling and by the temperature of the filling fluid. The presence of a transurethral catheter may influence the outcomes. Results will strongly depend on the measures taken to guarantee the privacy of the patients during the investigations. These considerations suggest that findings during filling cystometry may not be representative for bladder properties during natural bladder filling at home.

If this statement is true, one would expect a lack of association between data obtained during filling cystometry and those obtained from frequency-volume charts. Frequency-volume charts appear to be reliable in the investigation of patients with LUTS suggestive of BPH[10]. The aim of this paper is to examine whether associations exist or whether there is a lack of associations of filling cystometric parameters (compliance, capacities and prevalence of instability) with voided volumes and voiding frequencies derived from frequency-volume charts. We perform the analyses in a group of men who form a reasonable representative sample of the population of men who attend a urology clinic, and for whom there is some suspicion of prostatic obstruction.

Materials and Methods

Methods, definitions and units conform to the standards proposed by the International Continence Society (ICS) except when specifically noted.

In consecutive men presenting to the outpatient department of urology with LUTS, basic standard evaluation (history, quantification of symptoms and quality of life, physical examination and digital rectal examination, urinalysis and renal function assessment) and recommended tests (uroflowmetry and residual urine estimation) conforming to the recommendations of The International Consensus Committee on BPH[11] were performed. Men with LUTS were included if they were older than 50 years without any of the specified exclusion criteria of the International Consensus Committee on BPH[11], they voided a sufficient volume (>150 ml) during one or more free uroflowmetry studies, residual volume was estimated reliably, prostate size was determined by transrectal ultrasound and frequency-volume charts were available showing voiding and also drinking habits during at least one normal 24-hour period. These patients were examined urodynamically as well. Filling cystometric studies were performed with the patient in supine and sitting positions. Bladder pressure was recorded with a 5F catheter and rectal pressure was measured with a 14F catheter, both connected to external pressure transducers. The bladder was filled with saline at 37^{0}C, through a second 5F catheter, at a constant rate of 50 ml/min. In some men an 8F double lumen catheter was used for bladder pressure measurement and bladder filling. Filling was stopped when the patient had a strong desire to void. This filling volume was defined as cystometric capacity (C_{cys}).

In all men, residual volume was estimated by transabdominal ultrasonography or catheterisation during one of the visits at the outpatient department. Conforming to the recommendations of the consensus committee[9], this test was repeated if residual volume was significant. Effective capacity (C_{eff}) was defined as cystometric capacity minus residual volume.

From the frequency-volume charts, the minimum voided volume (V_{min}), the mean voided volume (V_{mean}), the maximum voided volume (V_{max}), mean diuria (N_{diuria}) and mean voided volume in the daytime ($V_{mean,day}$), mean nocturia ($N_{nocturia}$) and mean voided volume at night ($V_{mean,night}$) were estimated. Nighttime was defined as the period between 23:00 and 07:00 h. Voided volumes on the frequency-volume charts at which the patient did not indicate desire to void were excluded from these analyses but were included for estimation of mean total urine production in the daytime ($V_{total,day}$) and of mean total urine production at night ($V_{total,night}$). Mean fluid intake in daytime ($V_{intake,day}$) and mean fluid intake at night ($V_{intake,night}$) were also calculated.

The Kolmogorov-Smirnov goodness of fit test was used to examine whether or not the distribution of a variable was normal. Statistical analyses were done with Kendall and Gibbons distribution-free rank correlation method and Mann-Whitney test. Significance (two-tailed) was set at $p<0.05$.

Results

The included 160 men (age 64.9±8.3 years, range 50 to 89) had an average cystometric capacity of 406±144 ml (range 175 to 850 ml) and an effective cystometric capacity of 355±141 ml (range 100 to 850 ml). The average lowest value (V_{min}) on the frequency-volume chart was 95±58 ml (range 10 to 350 ml), the average highest value (V_{max}) was 351±142 ml (range 100 to 850 ml) and the average mean value (V_{mean}) was 195±74 ml (range 65 to 495 ml). Average diurnal voided volume ($V_{mean,day}$) was 188±77 ml (range 65 to 565 ml) and average nocturnal voided volume ($V_{mean,night}$) 222±101 ml (range 55 to 660 ml). From these parameters only age, mean voided volume (V_{mean}) and average nocturnal voided volume ($V_{mean,night}$) were normally distributed.

Minimum voided volume was on average about 50±20% of mean voided volume. Maximum voided volume was on average 185±55% of mean voided volume.

A significantly low (<40 ml/cm H_2O) bladder compliance was an exceptional finding in our group and therefore was not suited for further analysis.

Table 9.1 shows ratios between voiding data and cystometric capacity (C_{cys}) and between voiding data and effective capacity (C_{eff}).

Of the 160 men, 93 (58%) had a stable bladder and 67 (42%) had an unstable bladder. Table 9.2 shows correlation coefficients between these voiding data and filling cystometric capacities for all men, for men with a stable bladder and for men with an unstable bladder.

Table 9.1 Ratios between data from frequency-volume charts and cystometric capacity (C_{cys}) and between these data and effective capacity (C_{eff}).

Parameter	Value	S.D.	Range
V_{max} / C_{cys}	0.92	0.36	0.3-2.5
V_{min} / C_{cys}	0.26	0.16	0.1-1.0
V_{mean} / C_{cys}	0.51	0.19	0.1-1.3
V_{max} / C_{eff}	1.06	0.45	0.4-3.2
V_{min} / C_{eff}	0.30	0.21	0.1-1.5
V_{mean} / C_{eff}	0.59	0.25	0.2-2.3

Average fluid intakes in daytime or at night of men with a stable bladder did not differ from those of men with an unstable bladder.
Table 9.3 compares voiding data at night and in the daytime in men with a stable bladder to those of men with an unstable bladder.
Voiding parameters in men with a stable bladder (n=93) did not differ significantly from those with an unstable bladder (n=67). Including only men from the unstable group with amplitudes higher than 15 cm H_2O did not affect these findings.
Of the 67 men with an unstable bladder, 11 showed instabilities during filling cystometry in the supine position, 36 in the sitting position and 20 in both the supine and sitting positions. No parameter in these groups appeared to have a significantly different value compared to the value of the corresponding parameter in the group without an unstable bladder.

Table 9.2 Kendall and Gibbons correlation coefficients between parameters obtained from frequency-volume charts and those obtained from filling cystometry in all men, in 93 men with a stable bladder, and in 67 men with an unstable bladder.

	Cystometric capacity			Effective capacity		
Parameter	All men (n=160)	Men with a stable bladder (n=93)	Men with an unstable bladder (n=67)	All men (n=160)	Men with a stable bladder (n=93)	Men with an unstable bladder (n=67)
V_{max}	0.35*	0.39*	0.27*	0.40*	0.45*	0.30*
V_{min}	0.11	0.05	0.14	0.11	0.10	0.09
V_{mean}	0.35*	0.30*	0.37*	0.39*	0.40*	0.33*

* significant at the 0.01 level

Table 9.3 Mean ± SD of voiding data at night and during daytime in men with and without an unstable bladder.

	Men with instabilities (n=67)			Bladder		
	Only in supine position (n=11)	Only in sitting position (n=36)	In supine and in sitting position (n=20)	Unstable (n=67)	Unstable (>15 cm H_2O) (n=46)	Stable (n=93)
$N_{nocturia}$	1.6±1.1	2.4±1.6	2.2±1.1	2.3±1.4	2.2±1.3	2.1±1.2
$V_{mean,night}$ (ml)	243±107	195±75	210±70	207±81	209±76	233±113
N_{diuria}	6.8±1.9	7.3±2.2	6.0±2.5	6.8±2.3	6.7±2.4	6.6±2.9
$V_{mean,day}$ (ml)	200±71	173±57	190±99	182±75	186±78	192±78
V_{min} (ml)	121±45	77±53	110±72	94±62	95±61	96±56
V_{max} (ml)	352±142	331±126	307±100	327±123	327±126	368±152
Age (years)	64.3±7.3	67.1±8.2	67.0±8.6	66.6±8.3	66.4±7.7	63.7±8.2

Discussion

The inclusion criteria we used are recommended by the International Consensus Committee[11]. We consider it not reasonable to change any of these criteria because of the extensive scientific and clinical considerations, which led to the recommendations of the Committee. This means that patients with prior failed invasive treatment of BPH, and patients with suggestion of neurological disease were excluded. In this latter group bladder outlet obstruction may be active. Also, men taking drugs affecting lower urinary tract function were excluded. We also excluded patients who were not able to void more than 150 ml during free flow recording. The number of patients excluded for this reason strongly depends on the efforts made to obtain reliable flow registration. At our outpatient department the incidence of unsuccessful uroflowmetry studies was about 5% in this group. This percentage agrees with the 8% reported by Ezz el Din[12]. Of course men who visited the emergency department because of acute retention with the need for a transurethral catheter were not at all included in our study. Excluding men who not voided a volume of more than 150 ml will lead to an exclusion of those men with (starting) decompensation of the bladder. Thus, it is reasonable to assume that we selected a group of men in whom obstruction is developing or who are in the early phase of obstruction. We judged these men to be a reasonable representative sample of the population of men who attend a urology clinic and for whom there is some suspicion of prostatic obstruction.

From 188 men who met all other inclusion criteria, 28 (15%) did not complete the frequency-volume charts correctly during at least 24 h (they reported accumulated volumes, they reported only during parts of days, or they were not willing to complete the charts). The reliability of the frequency-volume charts in the remaining 160 men is demonstrated and discussed extensively elsewhere[10].

Despite the strict selection of our men, minimum voided volume in an individual was about 50% of mean voided volume and maximum voided volume was about twice mean voided volume. This illustrates the well-known large variation of voided volume at an individual level. Variability is not caused by measurement errors but by the nature of the parameter: no person has a unique functional capacity. This also applies to the effective capacity. For these reasons it is not surprising that there is a wide spread in the relations between voiding parameters and filling cystometric parameters. This can be demonstrated by plotting the maximum voided volume against the effective capacity (figure 9.1).

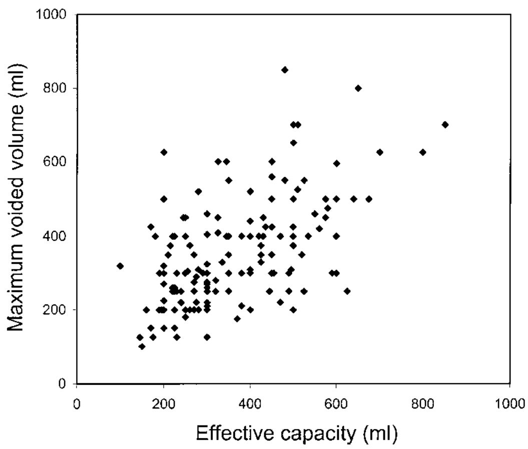

Figure 9.1 Plot of maximum voided volume versus effective capacity.

In figure 9.2 the cumulative percentage of men is plotted for which 100 times the absolute value of (maximum voided volume, V_{max}, minus effective capacity, C_{eff}) divided by maximum voided volume is lower than the upper limit; mathematically formulated: the cumulative percentage of men for which $100 \times |(V_{max} - C_{eff}) / V_{max}| <$ upper limit.

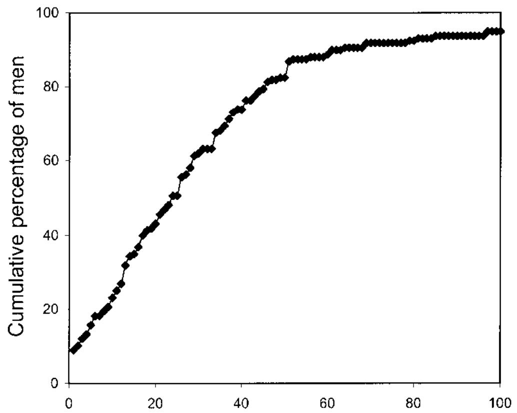

Figure 9.2 Cumulative percentage of men in which $100 \times | (V_{max} - C_{eff}) / V_{max} | <$ upper limit.

For instance: in about 50% of the men the relative difference between maximum voided volume and effective capacity is lower than 25%.

Keeping in mind these large variations, the significant associations found are quite reasonable.

We excluded voided volumes when the patients did not indicate a desire to void. These voidings are likely to have no relation to LUTS.

Most parameters did not show a normal distribution. Therefore, distribution-free statistical tests were used. Since the standard deviation is often reported in the literature, we have listed standard deviations together with the range of the parameter.

We defined the 8-hour period between 23:00 and 07:00 h as nighttime. Shortening this period in our group to 24:00 -06:00 h only resulted in a proportional reduction (about 25%) of mean nocturia and a proportional increase (about 10%) of mean diuria[10]. Mean voided volume at night and in daytime were little affected by this shorter time period[10].

In agreement with the paper of Sullivan and Yalla[2], a decrease in compliance does not appear to be a consistent finding in our patients with LUTS. A compliance of less than 40 ml/cm H_2O was an exceptional finding. Moreover one has to keep in mind that a compliance of 40 ml/cm H_2O may be partially artificial. When the bladder behaves like an ideal sphere and the measurement catheter is positioned at the bottom of the bladder during filling from 0 (diameter 0) until 400 ml (diameter 9 cm), a pressure rise of 9 cm H_2O will be measured due to the increasing water level above the catheter.

In our men, the average cystometric capacity was 406±144 ml, the average effective capacity was 355±141 ml and the average voided volume was 195±74 ml. In a group of 200 incontinent women 55 or more years old, Diokno et al.[13] found an average cystometric capacity of 377 ml and an average voided volume of 196 ml. Average largest voided volume in Diokno's group was 483 ml and in our group 351±142 ml. The similarity of their data and ours is surprising. Moreover, Diokno et al. found a significant positive correlation between the cystometric capacity and maximum voided volume (Pearson's $r=0.493$, $p<0.01$). Calculation of Pearson's r in our group (however, for non-normally distributed samples) revealed a value of 0.497, $p<0.01$.

In 88 consecutive patients (men and females) consulting the out-patient clinic, McCormack et al.[14] found an average cystoscopic capacity of 382±149 ml, an average diurnal voided volume of 176±64 ml and an average nocturnal voided volume of 233±130 ml. Also, the similarity of these findings and our findings (406±144 ml, 188±77 ml and 222±101 ml respectively) is striking.

The strong association between effective capacity (cystometric capacity minus residual volume) and maximum voided volume from the frequency-volume chart (table 9.1 and 9.2) is not surprising. Cystometric capacity is defined as the bladder volume at which the patient has a strong desire to void. In everyday life patients shall void at their "first or normal desire to void" volume. Cystometric determined bladder capacity represents the "strong desire to void" volume, which will not be frequently used by patients in everyday life. As another consequence, functional capacity (average voided volume derived from the frequency-volume charts) is only about half the effective capacity (table 9.1).

Minimum voided volume on frequency-volume charts is not related to cystometric findings (table 9.2) and may be a response to some early urgency to void.

Of the 160 men, 67 (42%) had an unstable bladder as estimated by our filling cystometries. This percentage is lower than the reported preoperative incidence between 49 and 74.3% in 12 clinical studies[9]. However, it is unclear whether these reports are based on patients with BPH who were already selected for operation. In contradiction to the reported preoperative incidence, analysis of data from 185 consecutive unselected men by Rosier et al.[15], revealed concomitant detrusor instability in only 20% of the men.

Correlations between voiding parameters and effective capacity were slightly higher in men with a stable bladder than in men with an unstable bladder (table 9.2). We assume that the voiding habits of men with an unstable bladder may be slightly irregular compared to those of men with a stable bladder. Moreover, cystometric capacity estimated during a period of instability may be lower than this capacity estimated during a stable period.

In men with an unstable bladder, nocturia and diuria were slightly higher and voided volumes slightly lower than in men with a stable bladder, however, the differences were not significant (table 9.3). This finding was not dependent on the amplitude of the instabilities, as including only patients with instabilities higher than 15 cm H_2O did not affect these differences (table 9.3). We could not detect any relation between the position (supine or sitting) in which instabilities occurred and voiding data. That no meaningful differences are found between patients with a stable bladder and patients with an unstable bladder can not be due to the exclusion of men with voided volumes lower than 150 ml during free flowmetry. It is not likely that including the 5% of men who were unsuccessful in voiding a volume of more than 150 ml would change the results significantly. Our results suggest that the detection of detrusor instability in men with LUTS suggestive of BPH is of minor diagnostic importance.

We want to emphasise that conclusions are formulated for our well-defined group of men with LUTS suggestive of BPH.

Conclusions

Decreased compliance was an exceptional finding. Effective capacity (cystometric capacity minus post-void residual volume) was significantly associated with the maximum voided volume on the frequency-volume charts and was almost twice as high as the average voided volume. Minimum voided volume on frequency-volume charts was not related to filling cystometric data. The presence of instability in supine or sitting position or in both positions was not significantly associated with smaller voided volumes, higher diuria or nocturia.

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CHAPTER 10

Data from Frequency-Volume Charts Versus Maximum Free Flow Rate, Residual Volume and Voiding Cystometric Estimated Urethral Obstruction Grade and Detrusor Contractility Grade in Men with Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia

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Abstract

Objective: To examine associations of data from frequency-volume charts with maximum free flow rate, residual volume and voiding cystometric estimated urethral obstruction grade and detrusor contractility in men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia (BPH).

Methods: Included men met the criteria of the International Scientific Committee on BPH. They voided more than 150 ml during uroflowmetry, their residual volume and prostate size were estimated and they completed frequency-volume charts correctly. From the frequency-volume charts voiding habits and fluid intake were evaluated. Pressure-flow studies were performed as well.

Results: Increasing residual volume was coupled with a decrease of maximum voided volume and with a decrease of maximum free flow rate. Cystometric capacity was hardly affected by residual volume. Low contractility did not result in high residual volume. A marked decrease in voided volumes with increasing obstruction grade was observed, due to a decrease of cystometric capacity and an increase of residual volume. Detrusor contractility was hardly associated with voided volumes. A higher voiding frequency was coupled with a higher fluid intake. However, increased standardised frequency (number of voidings per 1000 ml) was associated with a substantial reduction of fluid intake.

Conclusions: Increase of residual volume was coupled with a decrease of maximum voided volume and with a decrease of maximum flow rate. A marked decrease of voided volumes with increasing obstruction grade was observed. Detrusor contractility was hardly associated with residual volume and voided volumes. Increased standardised frequency resulted in a substantial reduction of fluid intake.

Introduction

Frequency-volume charts play an important role in the investigation of people with voiding disorders and give the urologist information about frequency in the daytime and at night together with the voided volumes[1]. They are used for objectively recording patient's symptoms, both as baseline and after therapeutic intervention.

Analyses of frequency-volume charts in elderly focus on relations between increased nocturia, diuresis, and functional bladder capacity[2], on the physiological cause of nocturnal polyuria[3] or on the aetiology of nocturia[4].

From 1991 on, extensive scientific and clinical considerations have led to the international consensus[5] about the diagnostic work-up of elderly men presenting with lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH). In 1997, the International Scientific Committee recommended frequency-volume charts too in the initial diagnostic evaluation of men with LUTS suggestive of BPH when nocturia is the dominant symptom. Reason for this recommendation was that a voiding diary filled out over several 24-hour periods, would help to identify patients with nocturnal polyuria or excessive fluid intake, which were supposed to be common in the ageing man[5].

Recently, it has been shown[6] that frequency-volume charts are completed reliably by men with LUTS suggestive BPH and who met the inclusion criteria of the Scientific Committee. In these men nocturia due to polyuria was an exceptional finding[6]. From further analyses of the frequency-volume charts in the same group, it appeared that not nocturia but high diuria, and small voided volumes at night and in daytime contribute significantly to high symptoms and low quality of life. Quality of life was hardly affected by nocturia[7].

LUTS refer to storage and emptying functions of the bladder. From frequency-volume charts a lot of information is available concerning voiding habits. It seems logical to attach more importance to the frequency-volume charts in the diagnostic work-up of men with LUTS suggestive of BPH, than only to identify patients with nocturnal polyuria or excessive fluid intake. Whereas, for instance, nocturia is strongly associated with BPH[8], hardly any study has been performed with respect to the diagnostic contribution of frequency-volume charts in men with LUTS suggestive of BPH, and concerning the relation of data from these charts with other diagnostic findings.

We wondered whether data from frequency-volume charts in men with LUTS suggestive of BPH, are correlated with filling cystometric and voiding cystometric data. In a previous paper[9] we investigated already the relation between data from frequency-volume charts with filling cystometric estimated capacities and prevalence of instability in

men with LUTS suggestive of BPH. Decreased compliance was an exceptional finding. Effective capacity (cystometric capacity minus residual volume) was strongly associated with maximum voided volume on the frequency-volume charts, which was almost twice as high as the average voided volume. The presence of detrusor instability was not associated with smaller voided volumes or higher diuria or nocturia.
The present paper deals with the associations of data from frequency-volume charts with maximum free flow rate, residual volume and voiding cystometric estimated urethral obstruction grade and detrusor contractility in these men.
Besides we investigated the impact of the amount of fluid intake on nocturia and diuria.

Materials and Methods

Methods, definitions and units conform to the standards proposed by the International Continence Society (ICS) except when specifically noted.
In consecutive men presenting to the outpatient department of urology with LUTS, basic standard evaluation (history, quantification of symptoms and quality of life, physical examination and digital rectal examination, urinalysis and renal function assessment) and recommended tests (uroflowmetry and residual urine estimation) conforming to the recommendations of The International Consensus Committee on BPH from 1991 (republished by The International Scientific Committee in 1998[5]) were performed. Men with LUTS were included if they were older than 50 years without any of the specified exclusion criteria of the International Scientific Committee on BPH[5], they voided a sufficient volume (>150 ml) during one or more free uroflowmetry studies, residual volume was estimated reliably, prostate size was determined by transrectal ultrasound and frequency-volume charts were available showing voiding and also drinking habits during at least one normal 24-hour period. These patients were examined urodynamically as well. Filling cystometric studies were performed with the patient in supine and sitting positions. Pressure-flow studies were done twice with the patient erect. Bladder pressure was recorded with a 5F catheter and rectal pressure was measured with a 14F catheter connected to external pressure transducers. The bladder was filled with saline at 37^0C, through a second 5F catheter, at a constant rate of 50 ml/min. In some men an 8F double lumen catheter was used for bladder pressure measurement and bladder filling. Filling was stopped when the patient had a strong desire to void. This filling volume was defined as cystometric capacity. The first pressure-flow study was done with measuring and filling catheters in the bladder, and the second study was done after removal of the filling catheter. The pressure-flow study with the lowest urethral resistance (usually during voiding with only the measuring catheter in the bladder) was used for further analysis.

In all men residual volume was estimated during one of the visits at the outpatient department by transabdominal ultrasonography or catheterisation. Conforming the recommendations of the Scientific Committee[5] this test was repeated if residual volume was significant. The urodynamic investigation always started with a uroflowmetry and determination of the residual volume by catheterisation. Some patients were not able to arrive with a full bladder and sometimes were not able to produce a flow curve. At the end of the urodynamic investigation the bladder of these patients was refilled via the measurement catheter and after removal of the catheter uroflowmetry was performed. If these patients were known to have significant residual volume, catheterisation was performed once more. The smallest residual volume was used for further analysis.

Effective capacity was defined as cystometric capacity minus residual volume, and relative residual volume as residual volume divided by cystometric capacity.

From pressure-flow studies Schäfer's obstruction grade and contractility grade were estimated[10].

From the frequency-volume charts the minimum voided volume, the mean voided volume, the maximum voided volume, number of voidings in 24 h, mean diuria and mean voided volume in the daytime, mean nocturia and mean voided volume at night were estimated. Nighttime was defined as the period between 23:00 and 07:00 h. Voided volumes on the frequency-volume charts at which patient did not indicate desire to void, were excluded from these analyses, but were included for estimation of mean total urine production in the daytime and of mean total urine production at night. Because we asked the patients also to record their fluid intake, mean fluid intake in daytime and mean fluid intake at night could be calculated too. We defined standardised frequency as number of voidings per 1000 ml.

The Kolmogorov-Smirnov goodness of fit test was used to examine whether or not the distribution of a variable was normal. Statistical analyses were done with the distribution-free Kendall and Gibbons rank correlation method and Mann-Whitney test. Significance (two-tailed) was set at $p<0.05$.

Quadratic curve estimation was performed to quantify the relation between two parameters.

Results

In literature it is usual to calculate mean and standard deviation, despite non-normal distributions. Therefore these values will be listed as well.

Of the 160 included men, 71 (44%) did not have a postvoid residual volume, 57 (36%) did have residual volume but equal or less than 20% of the cystometric capacity, and 32

Table 10.1 Relations between severity of residual volume and age, maximum free flow rate, voided volumes, diuria and nocturia together with filling cystometric capacities.

Relative residual volume	Number of men	Age (years)	Maximum free flow rate (ml/s)	Maximum voided volume (ml)	Mean voided volume (ml) in daytime	Mean voided volume (ml) in nighttime	Minimum voided volume (ml)	Mean diuria	Mean nocturia	Cystometric capacity (ml)	Effective capacity (ml)
0	71	64±9	13.6±5.3	385±160	190±80	220±125	90±65	6.3±2.6	2.0±1.4	395±140	395±140
>0 to 0.2	57	65±8	12.9±5.5	335±105	190±65	220±80	100±50	7.1±2.4	2.1±1.1	400±145	355±140
>0.2	32	68±8	11.1±4.8	305±135	175±90	185±105	95±60	7.0±3.2	2.4±1.4	440±145	265±110

(20%) had residual volume greater than 20% of cystometric capacity. In 52 men (33%) residual urine volume was greater than 50 ml.
Table 10.1 shows the relations between the severity of residual volume and age, maximum free flow rate, voided volumes, diuria, nocturia and capacities.
The increase of cystometric capacity from 395±140 ml (no residual volume) to 440±145 ml (relative residual volume >0.2) was not significant ($p=0.16$), but the decrease of effective capacity from 395±140 ml to 265±110 ml was ($p<0.01$). Also the decrease of maximum voided volume from 385±160 ml to 305±135 ml was significant ($p=0.02$). Mean and minimum voided volume did not depend on residual volume. Also diuria and nocturia were not significantly affected by residual volume.
Maximum urinary flow rate was significantly ($p=0.02$) lower in men with residual volume (relative residual volume >0.2) than in men without residual volume.
The correlation coefficient between maximum free flow rate and obstruction grade was -0.43 ($p<0.01$). Obstruction grade had a substantial impact on voided volumes and on capacities and residual volume (table 10.2).
Especially maximum voided volume and effective capacity were significantly negatively associated with obstruction grade. Despite the variability is high, figure 10.1 shows a significant reduction of maximum voided volume at increasing obstruction grade.
Quadratic curve estimation in the scatter plot of maximum voided volume against obstruction grade (figure 10.1), showed that the average maximum voided volume

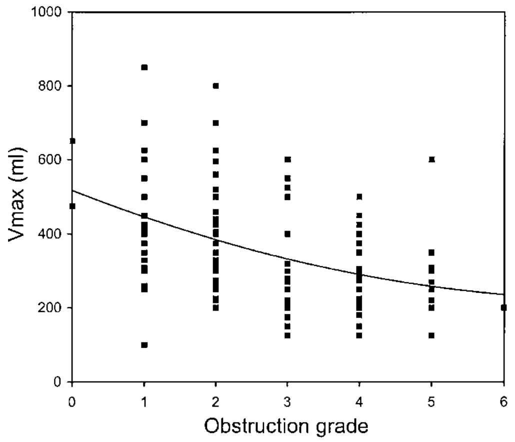

Figure 10.1 Maximum voided volume (Vmax) versus Schäfer's obstruction grade. The curve is obtained by quadratic curve estimation.

Table 10.2 Kendall and Gibbons rank correlation coefficients between bladder outflow parameters and voided volumes, diuria and nocturia together with filling cystometric data and relative residual volume.

Parameter	Maximum voided volume	Mean voided volume in daytime	Mean voided volume in nighttime	Minimum voided volume	Mean diuria	Mean nocturia	Cystometric capacity	Effective capacity	Relative residual volume
Obstruction grade	-0.35**	-0.18**	-0.22**	0.05	0.10	0.10	-0.27**	-0.34**	0.23**
Contractility grade	-0.11	0.06	0.02	0.18**	0.02	0.00	-0.16*	-0.14*	0.11
Maximum free flow rate	0.28**	0.25**	0.26**	0.05	-0.10	-0.13*	0.22**	0.25**	-0.12*

* significant at the 0.05 level

** significant at the 0.01 level

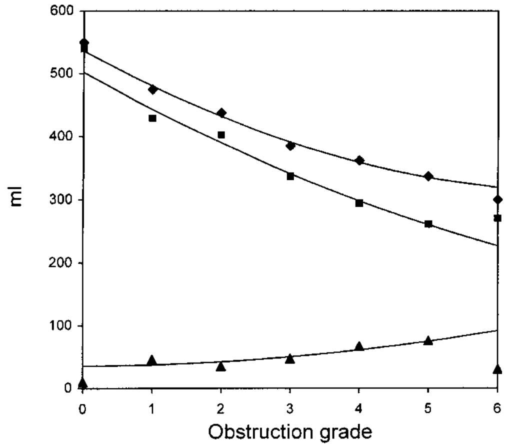

Figure 10.2 Mean values of cystometric capacity (◆), residual volume (▲) and effective capacity (■) as function of Schäfer's obstruction grade. Curves are obtained by quadratic curve fitting using all values (not the mean values).

decreased from 520 ml at obstruction grade 0, to 235 ml at obstruction grade 6. Cystometric capacity is negatively and relative residual volume is positively associated with obstruction grade, resulting in a substantial reduction of effective capacity from 500 ml (grade 0), to 230 ml (grade 6) (figure 10.2).

Mean voided volumes in daytime and at night are significantly negatively related with obstruction. The positive correlations between obstruction grade and diuria and nocturia were not significant. Table 10.3 shows relations between obstruction grade and mean voided volume in 24 h, number of voidings in 24 h, total urine production in 24 h and total fluid intake in 24 h. We introduced a standardised frequency of voiding by the number of voidings per 1000 ml.

Contractility grade had hardly impact on voiding parameters (tables 10.2 and 10.3). Maximum free flow rate was significantly positively correlated with all voided volumes (except minimum voided volume), with cystometric and effective capacities, and with urine production and fluid intake. Increase in voiding frequency and in residual volume resulted in a decrease of maximum free flow rate (tables 10.2 and 10.3)

We found a positive correlation ($p=0.03$) between number of voidings in 24 h and total fluid intake in 24 h (figure 10.3) but a negative correlation ($p<0.01$) between fluid intake in 24 h and standardised frequency (figure 10.4).

Table 10.3 Kendall and Gibbons rank correlation coefficients between bladder outflow parameters and mean voided volume, 24 h frequency, standardised frequency, total 24 h urine production and total 24 h fluid intake.

Parameter	Mean voided volume in 24h	Number of voidings in 24h	Number of voidings per 1000 ml	Total urine production in 24h	Total fluid intake in 24h
Obstruction grade	-0.23**	0.11	0.23**	-0.11	-0.16**
Contractility grade	0.05	0.01	-0.05	0.09	0.07
Max. free flow rate	0.27**	-0.13*	-0.27**	0.17**	0.18**

* significant at the 0.05 level

** significant at the 0.01 level

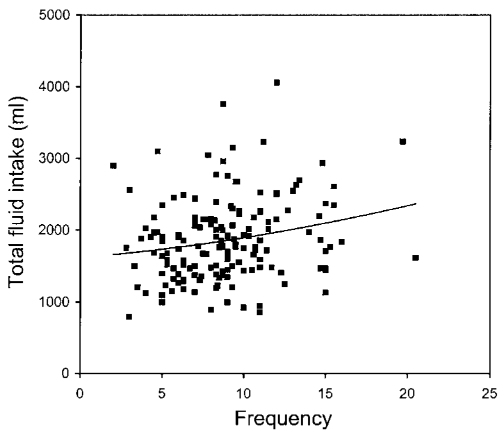

Figure 10.3 Scatter plot of total fluid intake in 24 h versus number of voidings in 24 h. The curve is obtained by quadratic curve fitting.

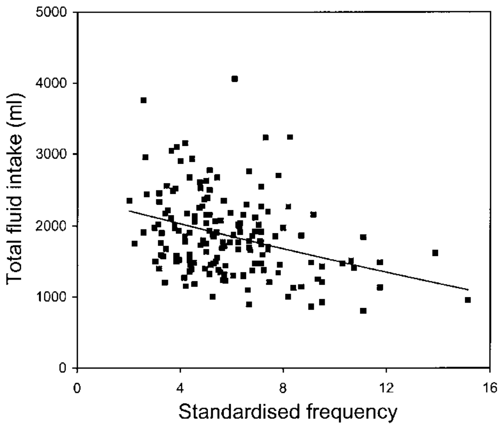

Figure 10.4 Scatter plot of total fluid intake in 24 h versus number of voidings per 1000 ml (standardised frequency). The curve is obtained by quadratic curve estimation.

In table 10.4 correlations are listed between total fluid intake in 24 h and nocturia, standardised nocturia, diuria and standardised diuria.

Table 10.4 Kendall and Gibbons rank correlations of total fluid intake in 24 h with nocturia, nocturia per 1000 ml, diuria and diuria per 1000 ml.

Parameter	Correlation coefficient with fluid intake
Nocturia	0.14*
Nocturia per 1000 ml	-0.26**
Diuria	0.12*
Diuria per 1000 ml	-0.19**

* significant at the 0.05 level
** significant at the 0.01 level

Discussion

The reliability of the frequency-volume charts in our population was discussed in a previous paper[6].
Of the men, 52 (33%) had residual urine greater than 50 ml. This percentage is lower than the reported incidence of 52% in unobstructed and 69% in obstructed men over the age of 55[11]. Our condition that men were included only if they could void a volume of at least 150 ml during free flowmetry may have excluded men with severe and prolonged obstruction or with impaired detrusor contractility. In a reasonable number of these excluded men, however, bladder properties may have been changed resulting in (partly) decompensated bladders. We assume that our group included men who were able to compensate more or less for the impaired outflow conditions and thus the incidence of severe residual volume will be low. Our inclusion criteria are recommended by the International Scientific Committee on BPH[5]. We consider it not reasonable to change any of these criteria because of the extensive scientific and clinical considerations, which led to the recommendations of the Committee.
As residual volume increased, cystometric capacity increased (table 10.1). However, this increase was only 10% and not significant. Effective bladder capacity decreased with about 30% ($p<0.01$) (table 10.1). This significant decrease is reflected by a significant decrease (20%) in maximum voided volumes on frequency-volume charts ($p=0.02$) (table 10.1). The not significant increase of cystometric capacity with 10% together with the significant decrease of effective capacity with 30% suggest that in BPH the development of residual volume in the initial phase of BPH, is not compensated by a higher capacity. It also argues for expressing the severity of residual volume as percentage of cystometric capacity, i.e. relative residual volume.
In functional capacity (mean voided volume), only a not significant ($p=0.15$) decrease of 10% is observed. Also diuria and nocturia are slightly but not significantly higher in the presence of postvoid residual volume (table 10.1). In contrast with effective capacity and maximum voided volume, the remaining voiding data on frequency-volume charts are hardly associated with the prevalence of residual volume.
The small decreases of mean voided volumes in daytime and at night (table 10.1) are coupled with a similar proportional increase in diuria and nocturia, resulting in an unchanged 24 h urine production.
Increasing residual volume is coupled to decreasing flow rate (table 10.1). This agrees with findings reported by Drach and Steinbronn[12] and by those reported by Neal et al.[13] and may be explained by the concomitant reduction of maximum voided volume. Maximum free flow rate decreases when voided volume decreases[14]. Low contractility

degree did not result in high residual volume (table 10.2). This is in agreement with the findings of Neal et al.[13] that low voiding pressures did not correlate with increased residual volumes.

Obstruction grade was significantly related with all voided volumes, except minimum voided volume (tables 10.2 and 10.3). Effective capacity was significantly reduced by an increasing obstruction grade. This reduction is partly due to an increase in residual volume when obstruction grade increases (table 10.2). From the other hand cystometric capacity decreases with increasing obstruction grade (table 10.2). Increase in residual volume and concomitant decrease in cystometric capacity with increasing obstruction grade result in an even higher decrease of effective capacity (figure 10.2). The relation between effective capacity and obstruction grade is similar to that between maximum voided volume and obstruction grade (figure 10.1). This agrees with the earlier reported strong association between effective capacity and maximum voided volume[9]. The decrease in cystometric capacity with increasing obstruction grade in our population is in accordance with the marked decrease in capacity of rabbit bladders after creation of a mild outlet obstruction[15].

We used quadratic curve estimation to quantify the relation between two variables. Higher order curve estimation is meaningless because of the wide variability of the parameters. The curves, especially those in figures 10.3 and 10.4, approximate linear curves.

Despite the negative correlation between obstruction grade and mean voided volume, only a not significant positive correlation was found between obstruction grade and number of voidings in 24 h (table 10.3). This implies that patients with a high obstruction grade produce less urine in 24 h then those with a low obstruction grade. Indeed a negative, but not significant correlation is found between total urine production in 24 h and obstruction grade. Anyhow men with a high obstruction grade have a significant lower fluid intake than those with a low obstruction grade (table 10.3).

It seems logical to assume that a higher frequency is coupled with a higher fluid intake and actually this coupling exists (figure 10.3). However if we investigate the relation between standardised frequency and fluid intake, a substantial reduction in fluid intake is observed at increasing standardised frequency (figure 10.4). Obviously, men in whom voided volumes are becoming smaller due to increasing outlet obstruction try to compensate the raised frequency by reducing their fluid intake. This implies that adaptation of patient's behaviour to his personal situation should be involved in the interpretation of symptoms. This applies to diuria and nocturia as well (table 10.4).

In contrast to obstruction grade, detrusor contractility degree is much less associated with voided volumes and capacities in our population.

Like expected a high negative correlation existed between obstruction degree and

maximum free flow rate. However, it is not only the increased outlet obstruction that contributes to the decrease of maximum free flow rate. Maximum flow rate increases when voided volume increases (in the range of 50 to 500 ml[14]). This range roughly corresponds with the range of the maximum voided volumes in our population (table 10.1). We found a sharp decrease of maximum voided volume as obstruction grade increases. This decrease in turn will contribute to lower maximum flow rates as well.
In our group maximum flow rate is negatively correlated to relative residual volume (table 10.2), which in turn is positively related to obstruction grade and negatively to maximum voided volumes (table 10.2).
These examples illustrate the complex mutual interactions between changes in parameters during the development of obstructive BPH.
We want to emphasise that conclusions are formulated for our group of strictly selected men with LUTS suggestive of BPH.

Conclusions

Increasing residual volume was coupled to a decrease of maximum voided volume and to a decrease of maximum free flow rate. Cystometric capacity was hardly affected by residual volume. Low contractility did not result in high residual volume. A marked decrease in voided volumes with increasing obstruction grade was observed, due to a decrease of cystometric capacity and an increase of residual volume. Men with a high obstruction grade have a lower fluid intake than those with low obstruction grade. In contrast to obstruction grade, detrusor contractility is much less associated with voided volumes. A higher voiding frequency is coupled with a higher fluid intake. However, increased standardised frequency (number of voidings per 1000 ml) resulted in a substantial reduction of fluid intake.
The mutual interactions between parameters during the development of benign prostatic hyperplasia are complex.

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CHAPTER 11

The Non-Invasive Assessment of Benign Prostatic Obstruction in Elderly Men with Lower Urinary Tract Symptoms

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In preparation

Abstract

Objective: Urodynamically, men with lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) are classified as unobstructed, equivocal or obstructed. Aim was to investigate what combination of easily available non-invasive parameters allows such classification in optimal agreement with urodynamic classification.

Methods: Mandatory and recommended tests were performed in 369 men with LUTS suggestive of BPH. The provisional classification of the International Continence Society (ICS), the group specific resistance factor URA, and Schäfer's obstruction grade, were estimated from urodynamic studies. Effective capacity was defined as voided volume at strong desire. In a subgroup of 160 men frequency-volume charts were analysed. A further group of 95 men were used for validation.

Results: The combination: prostate size (ml) minus 3 times maximum urinary free flow rate (ml/s) minus 0.1 times effective capacity (ml), was optimal in the classification compared to urodynamic classification. Extension of this formula to more than 3 parameters did not result in a better selection. The method of quantifying urethral resistance did not affect the selecting power of the combination. Replacement of effective capacity by two times mean voided volume estimated from the frequency-volume chart did not affect the results.

Conclusion: Bladder outlet obstruction number (BOON) for optimal non-invasive classification of men with LUTS suggestive of BPH, can be calculated with a formula composed of 3 readily available parameters: prostate size (ml) minus 3 times maximum urinary free flow rate (ml/s) minus 0.2 times mean voided volume (ml).

Introduction

In the past, methods were developed to non-invasively diagnose bladder outlet obstruction in men with lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH). The clinical prostate score (CLIPS), introduced by Rosier et al.[1], was composed of scores for prostate volume, maximum urinary flow rate, post-void residual volume and voided volume. The score had a superior correlation with urodynamically objectivated bladder outlet obstruction than isolated parameters. The bladder outlet obstruction number (BOON), introduced by van Venrooij and Boon[2], was calculated from prostate size, maximum urinary free flow rate and relative residual volume. Relative residual volume was defined as residual volume divided by bladder volume at strong desire to void (times 100%). Schacterle et al.[3] combined maximum urinary flow rate and American Urological Association symptom index[4] for identifying obstruction and non-obstruction. The proportion of patients that was correctly diagnosed appeared to be small. Steele et al.[5] combined symptom score, maximum free flow rate and prostate volume for predicting bladder outflow obstruction.
Disagreement exists about which parameters to use, and about the number of parameters needed for optimal classification of men according to obstruction grade. Anyhow, parameters should be easily to estimate and should be accepted as useful in daily urological practice.
The American Urological Association symptom index and quality of life question[4] are accepted as mandatory tools in the clinical evaluation of benign prostatic hyperplasia[6]. Transrectal ultrasonography is accepted as a reliable method to estimate prostate size[6]. Uroflowmetry, with measurement of the maximum flow rate, has become the most frequently used urodynamic examination. However, maximal flow rate depends on voided volume[7]. Therefore, flow rate recordings with a voided volume of at least 150 ml are recommended[8]. Some patients may not void an adequate volume (>150 ml). The number depends on the efforts made on the outpatient clinic and could be decreased to about 5% in our department[2].
In a significant number of patients, reliable estimation of residual urine is difficult[9]. Drainage of the bladder by catheter gives a quantitative value, but is invasive and the bladder may be incompletely drained in about 25% of patients[10]. Therefore, determination of residual urine by ultrasonography is recommended, but in the outpatient department estimation of residual urine immediately after voiding is sometimes difficult to realise.
A number of methods are developed to quantify degree of obstruction from pressure-flow relations[11]. Because these methods are based on the passive urethral resistance

relation[12], all methods give the same results in classifying clearly obstructed and clearly non-obstructed pressure-flow relations. In classifying intermediate urethral resistance a lack of agreement exists[13].

The International Continence Society (ICS) Subcommittee on Standardisation of Terminology of Pressure-Flow Studies recommends the provisional ICS method for definition of obstruction[11] in benign prostatic hyperplasia: patients are obstructed when the AG-number, defined as detrusor pressure (cm H_2O) at maximum flow minus 2 times maximal flow (ml/s), is higher than 40. If the AG-number is lower than 20, patients are considered to be non-obstructed. All other cases are considered to be equivocal. The group-specific resistance factor (URA)[14] can be used to classify the pressure-flow relation as well. The boundary value URA=29 cm H_2O separates obstructed and equivocal bladder outlet, and URA=21 cm H_2O[13] between equivocal and unobstructed. Finally, obstruction grade (range 0- no obstruction to 6- severe obstruction) as proposed by Schäfer[15], can be used to classify patients: men with an obstruction grade of 0 or 1 do not have bladder outlet obstruction, those with an obstruction grade of 3 or more have obstruction, and those with obstruction grade 2 are equivocal[13].

We ranked different parameters according to their correlation with obstruction grade. Parameters with the highest correlation were used to create linear combinations with still higher correlation with obstruction grade. We studied the optimal number of parameters to be used in these combinations. We compared the reliability of the combination with the reliability of the other classification methods. The impact of using the different definitions of obstruction on our findings was evaluated as well.

Materials and Methods

Methods, definitions and units conform to the standards proposed by the International Continence Society except when specifically noted.

In men with LUTS suggestive of BPH, basic standard evaluation and recommended tests, conforming to the recommendations of The International Consensus Committee on benign prostatic hyperplasia (BPH) from 1993 (updated[8] in 1997) were performed. According to the clinical judgement of the urologists, when the results of the evaluation were suggestive of bladder outflow obstruction due to BPH, the patients were evaluated urodynamically as well. Filling cystometric studies were performed with the patient in the supine and erect positions. Pressure-flow studies were done twice with the patient erect. Bladder pressure was recorded with a 5F catheter and rectal pressure was measured with a 14F catheter connected to exter-

nal pressure transducers. The bladder was filled with saline at 37^0C, through a second 5F catheter, at a constant rate of 50 ml/min. Filling was stopped when the patient had a strong desire to void. The first pressure-flow study was done with the measuring and filling catheters in the bladder, and the second study was done after removal of the filling catheter. Schäfer's obstruction grade[15] and the group-specific resistance factor (URA)[14] were estimated and pressure-flow studies were classified as well according to the provisional ICS definition[11]. Patients were included in the study if they were 50 years of age or older, without any of the other specified exclusion criteria (International Consensus Committee on BPH[8]), they voided a sufficient volume (>150 ml) during 1 or more free uroflowmetry studies, reliable pressure-flow relationships were obtained, bladder volume at strong desire was estimated, residual urine was estimated reliably at repeated tests by transabdominal ultrasonography and/or catheterisation and prostate size was determined by transrectal ultrasound. Effective capacity was defined as the bladder volume at strong desire to void minus residual volume. Thus effective capacity represents the voided volume at strong desire. Functional capacity represents the mean voided volume calculated from frequency-volume charts.
Consecutively, 369 men (65.6±8.0 years of age, range 50 to 90) were included for the analyses of the different classification methods. From the last 160 consecutive men (65.1±8.3 years of age, range 50 to 85), frequency-volume charts were analysed. Finally, a group of 95 men (65.5±7.3 years of age, range 50 to 84) was used for validation. Correlations among parameters were calculated with the distribution-free rank correlation test of Kendall and Gibbons. The level of significance (two-tailed probability) was $p=0.05$.

Results

In the appendix it is mathematically proven that a linear combination of two parameters may correlate better with another parameter than each parameter alone. If one of the parameters does not correlate at all, such combination will not result in a higher correlation coefficient.
Table 11.1 shows Kendall and Gibbons' correlations of variables and combination of variables with AG-number, URA and Schäfer's obstruction grade.
Hardly any correlation was found between symptom score or quality of life score and urethral resistance parameters. Thus including symptom score or quality life score in a linear combination with the aim to increase correlation with obstruction grade has no sense (see appendix).

Table 11.1 Kendall and Gibbons correlations of variables and combination of variables with AG-number, URA and Schäfer's obstruction grade.

Variable	AG-number	URA	Schäfer's obstruction grade
Effective capacity (C_{eff})	-0.28**	-0.26**	-0.29**
Maximal free flow rate (Qmax)	-0.36**	-0.42**	-0.37**
Prostate volume (V)	+0.25**	+0.23**	+0.28**
Relative residual volume (Rrel)	+0.21**	+0.24**	+0.22**
Residual volume (R)	+0.18**	+0.21**	+0.19**
Symptom index	+0.02	+0.08*	+0.07
Quality of life score	+0.01	-0.01	+0.01
V-3xQmax	0.41**	0.43**	0.43**
V-3xQmax-0.1xC_{eff}	0.45**	0.45**	0.46**
V-3xQmax-0.1xC_{eff}+0.25xRrel	0.45**	0.46**	0.46**
Clinical prostate score[1]	0.40**	0.45**	0.42**

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

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

By numerical analysis[2], almost maximal correlation with urethral resistance was found for the combination: prostate volume (V) - 3 times maximal urinary flow rate (Q) minus 0.1 times effective capacity (C_{eff}). We defined the expression V-3Q-0.1C_{eff} as bladder outlet obstruction number (BOON). Extension of the bladder outlet obstruction number with relative residual volume makes no sense (see table 11.1). The optimal number of parameters in a linear combination in order to improve correlation with urethral grade appears to be 3.

The discriminating power of the BOON in the classification of men in unobstructed, equivocal and obstructed men in relation to the urodynamic classifications by ICS, URA and Schäfer, is illustrated in table 11.2.

Table 11.2 Unobstructed, equivocal and obstructed men according to the provisional definition of the ICS, according to URA and according to Schäfer's grade in relation to BOON.

		Provisional definition of the ICS			URA			Schäfer's grade		
	Number of men	Number of unobstructed men	Number of equivocal men	Number of obstructed men	Number of unobstructed men	Number of equivocal men	Number of obstructed men	Number of unobstructed men	Number of equivocal men	Number of obstructed men
All men	369 (100%)	66 (18%)	111 (30%)	192 (52%)	72 (19%)	84 (23%)	213 (58%)	68 (18%)	97 (27%)	204 (55%)
Men with BOON>-40	231 (63%)	14	55	162	14	42	175	18	45	168
	(100%)	(6%)	(24%)	(70%)	(6%)	(18%)	(76%)	(8%)	(19%)	(73%)
Men with BOON>-20	116 (31%)	1	16	99	1	13	102	3	12	101
	(100%)	(1%)	(14%)	(85%)	(1%)	(11%)	(88%)	(3%)	(10%)	(87%)
Men with BOON>-10	84 (23%)	0	8	76	0	8	76	0	7	77
	(100%)	(0%)	(10%)	(90%)	(0%)	(10%)	(90%)	(0%)	(8%)	(92%)
Men with BOON≤ -40	138 (37%)	52	56	30	58	42	38	50	52	36
	(100%)	(38%)	(40%)	(22%)	(42%)	(30%)	(28%)	(36%)	(38%)	(26%)
Men with BOON≤ -60	75 (20%)	34	30	11	38	23	14	34	27	14
	(100%)	(45%)	(40%)	(15%)	(51%)	(31%)	(18%)	(45%)	(36%)	(19%)
Men with BOON≤ -80	31 (8%)	19	10	2	20	5	6	17	11	3
	(100%)	(61%)	(32%)	(7%)	(65%)	(16%)	(19%)	(55%)	(35%)	(10%)

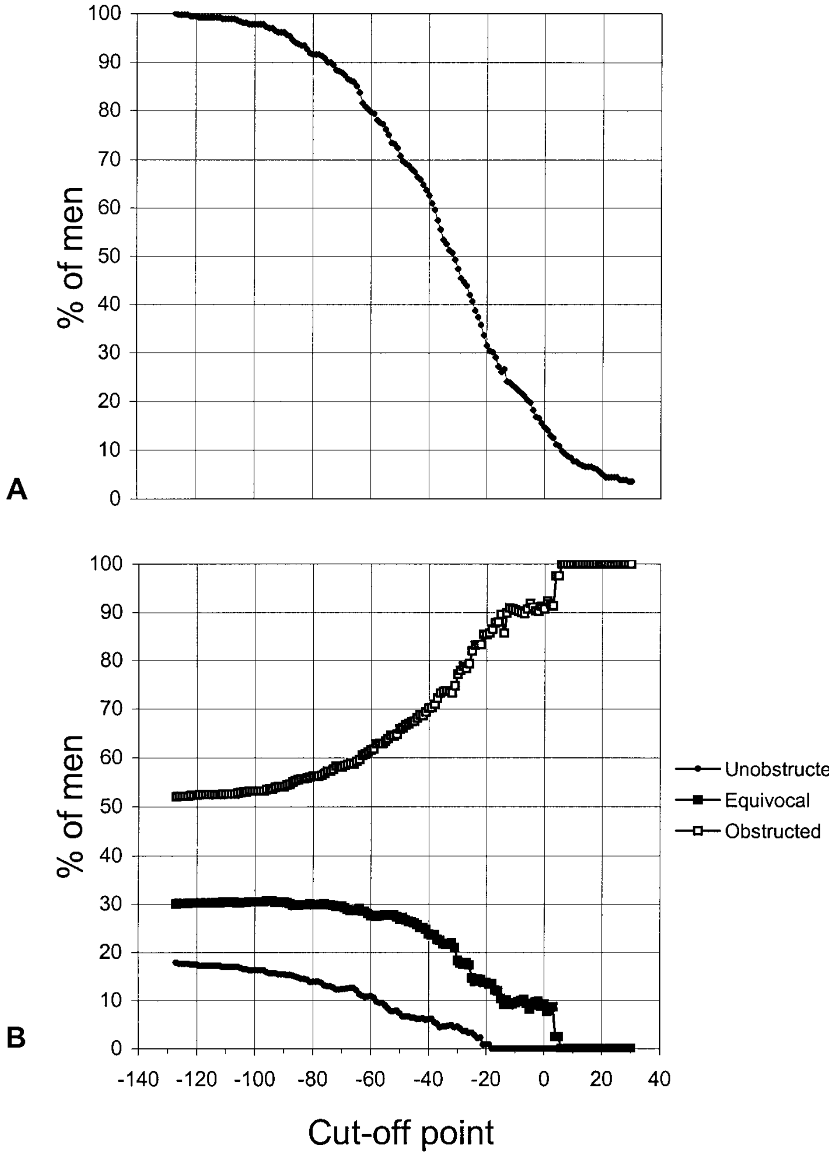

Figure 11.1 A. Proportional number (%) of men with BOON>cut-off point. B. Proportional number (%) of men with BOON>cut-off point who are obstructed, equivocal or unobstructed according to the ICS definition.

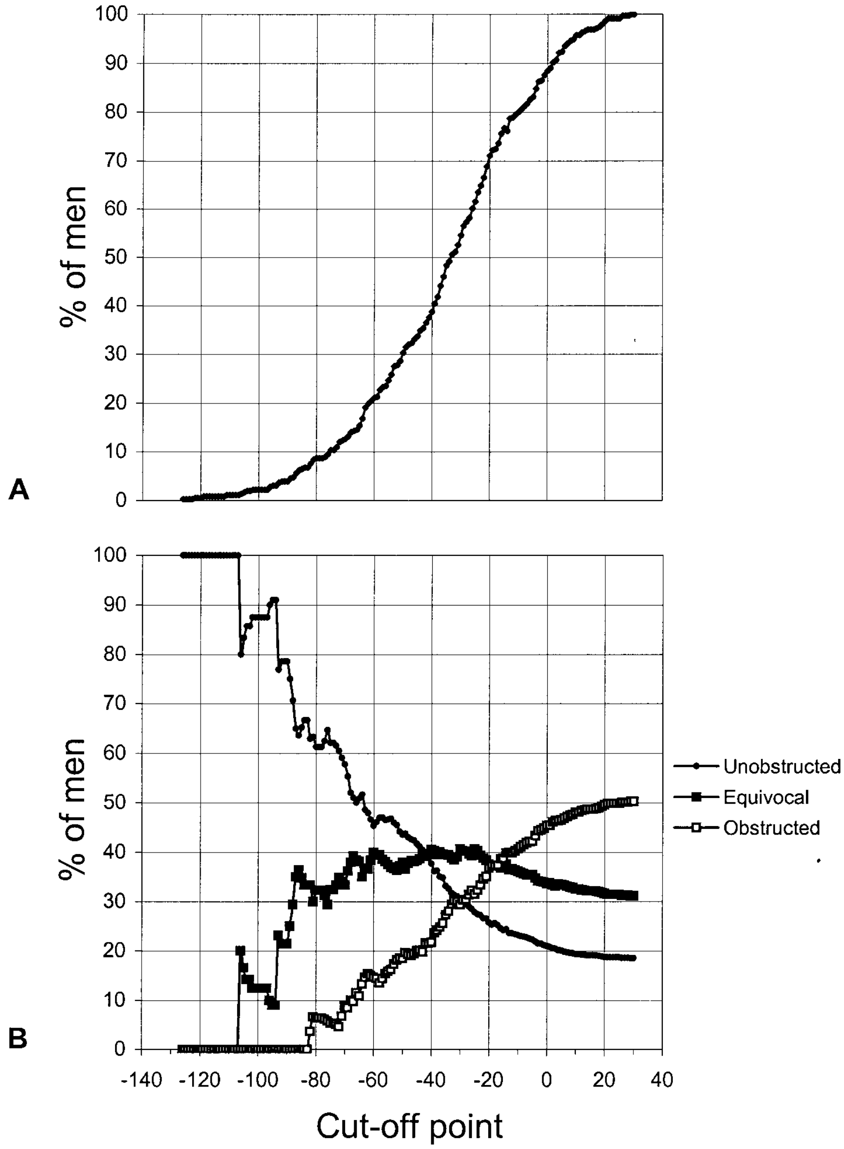

Figure 11.2 A. Proportional number (%) of men with BOON≤ cut-off point. **B.** Proportional number (%) of men with BOON≤ cut-off point who are obstructed, equivocal or unobstructed according to the ICS definition.

Figure 11.1A shows the proportional number of patients with BOON>cut-off point, and figure 11.1B the percentages of men who are obstructed, equivocal or unobstructed according to the provisional definition of the ICS[11].

Figures 11.2A and 11.2B show these numbers for BOON≤ cut-off point.
Kendall and Gibbons' correlation coefficient between the clinical prostate score (CLIPS) of Rosier et al.[1] and URA in our 369 men was 0.45. Rosier reports a Pearson's correlation coefficient of 0.53 in his group (in our group, Pearson's correlation coefficient was 0.54 between URA and CLIPS). Modifying CLIPS by omission of post-void residual volume and by doubling the weight of voided volume did not change correlation with URA in our group. Table 11.3 shows the discriminating power of the CLIPS and of the modified CLIPS when URA is used for defining obstruction.
We applied the threshold values proposed by Schacterle et al.[3] on our group. Of 38 men (out of 369) with both maximal urinary flow lower than 10 ml/s and symptom score higher than 20, 26 men (68%) were obstructed. In our group we could only select 24 men (6.5%) according to the cut-off values proposed by Steele[5]: maximum urine flow of 10 or less ml/s and prostate volume of 40 ml or greater and symptom index of greater than 20. But even in these 24 men, only 18 (75%) were obstructed.

Table 11.3 Total number of men and number of obstructed men according to URA>29 cm H_2O in relation to clinical prostate score (CLIPS) and modified CLIPS.

	Number of men	Number of obstructed men
All men	369 (100%)	213 (58%)
Men with CLIPS>4	242 (66%)	182
	(100%)	(75%)
Men with CLIPS>9	139 (36%)	118
	(100%)	(85%)
Men with CLIPS>12	93 (23%)	86
	(100%)	(92%)
Men with modified CLIPS>4	231 (63%)	179
	(100%)	(77%)
Men with modified CLIPS>9	138 (37%)	116
	(100%)	(84%)
Men with modified CLIPS>11	88 (24%)	83
	(100%)	(94%)

Table 11.4 Unobstructed, equivocal and obstructed men according to the provisional definition of the ICS in relation to BOON with mean voided volume incorporated in stead of effective capacity.

	Number of men	Number of unobstructed men	Number of equivocal men	Number of obstructed men
All men	95 (100%)	17 (18%)	23 (24%)	55 (58%)
Men with BOON>-40	50 (53%)	1	11	38
	(100%)	(2%)	(22%)	(76%)
Men with BOON>-20	28 (29%)	0	4	24
	(100%)	(0%)	(14%)	(86%)
Men with BOON>-10	17 (18%)	0	3	14
	(100%)	(0%)	(18%)	(82%)

From the study of the 160 men who reported reliably[16] their voidings on frequency-volume charts, it appeared that a strong individual association existed between calculated mean voided volume and voided volume at strong desire[17]. Mean voided volume was half the voided volume at strong desire[17]. We replaced voided volume at strong desire in our formula for BOON by 2 times mean voided volume estimated from the frequency-volume chart. We validated the use of the formula BOON=prostate volume minus 3 times maximum free flow rate minus 0.2 times mean voided volume in a further group of 95 consecutive men. In table 11.4 the results of this validation are listed.

Discussion

The combination: prostate size (ml) minus 3 times maximum urinary free flow rate (ml/s) minus 0.1 times effective capacity (ml) was optimal in the classification of unobstructed, equivocal and obstructed men compared to urodynamic classification. Extension of this combination with more parameters did not increase the selection power.

As no correlation exists between symptom score and obstruction grade, including symptom score does not make sense (appendix). Consequently, in our group the combi-

nation of maximal urinary flow rate with symptom score to discriminate obstructed and unobstructed men, as proposed by Schacterle et al.[3], did not work.
The selecting power of our bladder outlet obstruction number (BOON) is similar to the power of the clinical prostate score (CLIPS)[1]. The CLIPS contains comparable parameters as our BOON plus post-void residual volume. Application of the clinical prostate score thus has the disadvantage that it requires reliable estimation of residual volume. However, in our group, omission of post-void residual volume score in the CLIPS, did not decrease its correlation with obstruction grade. In the same way, extension of our BOON with post-void residual volume did not increase its correlation with obstruction grade (see table 11.1). The clinical prostate score thus can be simplified and its applicability increased by omission of post-void residual volume. We prefer the application of BOON above the modified CLIPS because of its simplicity.
In contrast to the claim of Steele et al.[5], we could only select 6.5% of our men who had values above their cut-off points. But even after this selection, still 25% (and not 0%) of the men were equivocal or unobstructed. Possibly the selection criteria of Steele et al. differ largely from those of Rosier et al. and of us.
Regardless which method is used and thus which definition is applied for obstruction, equivocal and nonobstruction, the selecting power of bladder outlet obstruction number BOON is relatively similar (table 11.2).
Effective capacity was defined as the voided volume at strong desire to void. At home a lower bladder content may trigger the patient to empty his bladder and only a few times he will wait until strong desire. This explains why voided volume at strong desire is twice the mean voided volume calculated from the frequency-volume chart.
Estimation of mean voided volume from frequency-volume charts is easy. Ultrasonography is accepted as a useful investigation of the prostate and is a reliable method to estimate prostate size[6]. Uroflowmetry with measurement of maximum urinary flow rate has become the most frequently used urodynamic examination. This means that in most urological practises the parameters mean voided volume, prostate volume and maximum urinary flow rate are easy to access. Using the easily applicable formula: prostate volume minus 3 times maximum urinary flow rate minus 0.1 times voided volume at strong desire (or 0.2 times mean voided volume at home), it is possible to predict the chance to have or not to have bladder outlet obstruction. This chance can easily be estimated by applying the figures 11.1 and 11.2. BOON may contribute to the non-invasive selection of men in whom it is unlikely that their LUTS are due to bladder outlet obstruction and in whom further investigation is indicated.

Conclusions

Bladder outlet obstruction number (BOON) may be calculated with an easily applicable formula composed of readily available parameters: prostate size, maximum urinary flow and voided volume at strong desire. The easy to use formula is BOON=prostate size (ml) - 3 x maximum urinary flow rate (ml/s) - 0.1 x voided volume (ml) at strong desire. The voided volume at strong desire is twice the mean voided volume calculated from frequency-volume charts. Replacement of voided volume at strong desire by twice the mean voided volume, did not affect the selection power of the formula. Extension of the formula to more than 3 parameters did not result in a better correlation of the formula with obstruction grade and thus in a better classification of men. The results are hardly dependent on the method used to quantify the urethral resistance and thus to classify obstructed, equivocal and non-obstructed men.

Appendix

Pearson's correlation coefficient (r) between 2 variables X and Y is defined:

$$r(X,Y) = Cov(X,Y)/[Var(X)*Var(Y)]^{1/2}$$

in which Cov(X,Y) is the covariance of X and Y, and Var(X) and Var(Y) are the variances of X and Y respectively. For variance and covariance additional laws apply:

$$Var(X+W) = Var(X) + Var(W) + 2Cov(X,W)$$

$$Cov(X+W,Y) = Cov(X,Y) + Cov(W,Y)$$

Suppose that there is a significant positive correlation with correlation coefficient c_1 between OG (obstruction grade) and a parameter A and also between OG and a parameter B (correlation coefficient c_2). Suppose $c_1 \geq c_2$, thus $c_2=\gamma c_1$ with $0<\gamma\leq 1$.

We shall prove that under certain conditions a linear combination of A and B, $A+\alpha B$ with $\alpha>0$, results in a correlation with OG with a correlation coefficient higher than c_1.

We introduce a new variable β, defined by:

$$\beta^2 = Var(B)/Var(A)$$

If $B' = B/\beta$ then:

$$Var(B') = Var(A)$$

If:

$$\alpha' = \alpha\beta$$

then:

$$r(OG,A+\alpha B) = r(OG,A+\alpha' B')$$

According to the definition:

$$r(OG,A+\alpha'B') = [Cov(OG,A+\alpha'B')]/[Var(OG)*Var(A+\alpha'B')]^{1/2}$$

By applying the additional laws and using var(A)=Var(B'), the right-hand expression in this equation can be changed into:

$$[r(OG,A)+\alpha' r(OG,\alpha' B')] / [1+\alpha'^2+2\alpha' r(A,B')]^{1/2}$$

Substitution of r(OG,A) = c_1, r(OG,α'B') = r(OG,B) = γc_1 and r(A,B') = r(A,B) results in:

$$r(OG,A+\alpha'B') = [c_1 + \gamma\alpha' c_1]/[1+\alpha'^2+2\alpha' r(A,B)]^{1/2}$$

Thus the combination A+α'B' will result in an improvement of the correlation with OG with a factor:

$$[1 + \gamma\alpha'] / [1 + 2\alpha' r(A,B) + \alpha'^2]^{1/2}$$

Minimum and maximum values for r(OG,A+α'B') are found for:

$$\delta/\delta\alpha' \, [r(OG,A+\alpha'B')] = 0$$

or:

$$\alpha' = [\gamma - r(A,B)] / [1-\gamma r(A,B)]$$

Because A and B are positively correlated with OG, it is reasonable to assume that the correlation between A and B is positive too, thus r(A,B)≥ 0. The improvement of the correlation is maximal if r(A,B)=0 and equals:

$$[\gamma^2 + 1]^{1/2}$$

If $\gamma = 0$ no improvement can be obtained. The maximum improvement is about 40% ($\gamma=1$). We may combine a third parameter c_3 that correlates with OG (correlation coefficient $c_3 \leq c_2 \leq c_1$) with A+α'B' and so on. However, the improvement will be limited to only a few parameters due to a decreasing γ and an expected increase of the correlation coefficient between the combination and the next parameter. This is clearly illustrated in table 11.1 of the Chapter.

We assume that our calculations also apply to Kendall and Gibbons correlation coefficient.

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CHAPTER 12

General Discussion and Conclusions

(Superscript numbers refer to the chapters in this thesis)

Benign prostatic hyperplasia (BPH) affects a considerable number of elderly men. In a lot of these men, BPH is associated with lower urinary tract symptoms (LUTS). Depending on the degree of bothersomeness of these LUTS, the patient will seek medical treatment. Due to the ageing population, BPH creates not only a substantial, but also an increasing demand on the health care system. Investigation of the contribution of the results of different examination methods to the final diagnosis of men with LUTS suggestive of BPH is necessary. Patronised by the World Health Organisation (WHO), the International Scientific Committee of the International Consultation on BPH, from 1991 onwards, formulated recommendations concerning the evaluation of LUTS suggestive of BPH based upon such research. Every two years the recommendations are adapted to new scientific developments and views.
The investigations, reported in this thesis, focussed on symptoms and diagnostics in clinical BPH in well-defined groups of men with LUTS suggestive of BPH. We included only men who fulfilled the criteria of the International Scientific Committee[1]. We were somewhat astonished about the number of men who had to be excluded[5] because they were already taking medication active on the lower urinary tract before diagnosis has been completed. We do not know whether this was due to an increasing preference for medication over surgery or that it was just to tide over waiting times for health care. We only included men who were able to produce at least one voiding with a volume of more than 150 ml. The latter criteria led to an exclusion of about 5%. Except for one man who had a bladder capacity of 1100 ml, the maximum capacity in the other men was 900 ml[6]. Most men (81%) had no residual volume, or had a residual volume lower than 100 ml[6]. These data give support to our assumption that our groups included men who were able to compensate more or less for the impaired outflow conditions due to BPH and that we excluded men with severe and prolonged obstruction. In a reasonable number of these excluded men, bladder properties might have been changed resulting in (partly) decompensated bladders. **With our selection procedure aetiology to patients' complaints was reduced to a minimum of variables in contrast to other studies, and thus our groups were well suited for studying symptoms, bothersomeness and diagnostics and their mutual interactions in BPH.** Only 5% of our men were excluded because they did not void more than 150 ml. Thus **the men included in our study form a reasonably representative sample of the population of men who attend a urologic clinic, and for whom there is some suspicion of prostatic obstruction.**

Knowledge about the presence or absence of bladder outlet obstruction is still considered as decisive in the choice of treatment. The only reliable method (until now) for directly diagnosing bladder outlet obstruction in BPH is simultaneous measurement of the driving pressure and the resulting urinary flow rate. However, pressure-flow studies are considered too invasive and to cause discomfort to the patient. **However, our experience was that urodynamics was associated with low objective and subjective morbidity, provided that specific precautions were fulfilled[1]**. Taking into account these precautions, patients who were not able to produce a reliable pressure-flow registration were exceptional. We found 53% of our patients to be obstructed, 27% to be equivocal and 20% to be unobstructed[6]. This distribution emphasises the need for pressure-flow studies.

There are different methods of analysing pressure-flow studies to define bladder outlet obstruction. In our group of men, high agreement existed between the different methods of classification[6]. Differences between the methods were marginal and are not likely to influence a decision whether or not to perform surgery[6]. **In normal clinical practice, the high agreement between the methods leaves the urologist free to choose between the group specific urethral resistance factor URA, the Schäfer nomogram or the (simple applicable) AG-number in order to evaluate urethral resistance and thus to classify men as obstructed, equivocal or unobstructed[6]**.

Despite the strict selection procedures, we reconfirmed the reported absence of a correlation between prostate volume and symptoms or quality of life, and between degree of bladder outlet obstruction and symptoms or quality of life[4]. Additionally, the presence of residual volume and/or an unstable bladder was not reflected in significantly more symptoms or a lower quality of life[4]. The subjective interpretation of symptoms by the patient will surely contribute to the lack of such associations: there was no association between score on incomplete emptying and the actual presence or absence of residual volume. If there were significant correlations between symptoms and urodynamic parameters, on average the correlation with the cumulative symptom index and quality of life remained poor. This can be attributed to the opposite implications of urodynamics on symptoms: a high bladder contractility results in a high score on urgency but in a low score on weak urinary stream and intermittency. **The lack of associations does not mean that the value of urodynamics is questionable, it just demonstrates that urodynamics and symptoms and quality of life reflect different aspects of BPH.**

Correlations between objective parameters, obtained by urodynamics, are more pronounced[7]. In contrast to the still generally accepted assumptions (based on digital rectal examinations), **obstruction grade increased significantly with increasing prostate volume,** which agrees with recent published findings based on studies performed with rectal ultrasound. Maximum urinary free flow rate was strongly negatively correlated with obstruction grade. **Patients with significant residual volume have larger prostates and higher outlet obstruction grades. Surprisingly, no correlation between the severity of residual volume and contractility grade was found. We found a remarkable reduction of effective bladder capacity (voided volume at strong desire to void) at increasing degrees of bladder outlet obstruction[7].**

To decide what is pathological in elderly men requires a knowledge of what can be considered as normal. Therefore, we studied 14 elderly, symptom-free population-based men[8] and found 5 of them to be obstructed. Additionally, 6 of them exhibited an unstable bladder and 6 had significant residual volume. Nevertheless, mean prostate volume in these men was found to be 21 ml (in our patients 38 ml) and a mean cumulative symptom score of 3 was found (in our patients 17). **Typical urodynamic findings in men with LUTS suggestive for BPH are thus also common in healthy elderly men without LUTS. Effective capacity in the symptom-free group was significantly higher than in the men with LUTS. Since normality in urodynamics may include so many different features, the interpretation of urodynamic evaluations should be made with caution.**

Up to now, decision making for treatment has been mainly based on symptoms and the degree of bladder outlet obstruction. However, what characterises men who seek treatment for BPH is not their obstruction degree or possible risk for upper urinary tract damage, but rather worry and embarrassment about urinary symptoms. We used validated methods to quantify these effects of disease[5]. **The symptoms with the highest prevalence were weak urinary stream, frequency and urgency. Hesitancy had the lowest prevalence. The symptoms urgency, nocturia and hesitancy were the most bothersome.** The majority of men experienced only a little physical discomfort due to their urination problems. Patients were only discouraged from doing things they would usually do when the symptom index (range 0 to 35) exceeded 20 (which was the case in 30% of the men). **Bother about incomplete emptying and bother about frequency have a high impact on well-being, in contrast to weak urinary stream and, surprisingly, hesitancy.** Confirming the earlier reported lack of association between score on incomplete emptying and the actual presence or absence of residual volume, bothering about incomplete emptying was also not associated with the actual residual volume. Obviously, an increase in frequency is interpreted by the patient as caused by incomplete emptying.

Since bothersomeness and well-being should be regarded as the outstanding parameters to measure outcome after treatment, **we strongly recommend the addition of**

questions directed at bothersomeness and health-related quality of life, to the symptom questions.
For this purpose validated questionnaires are available[5]. Bother due to LUTS and impact on a patient's quality of life should contribute to treatment decisions.

In a subgroup of the men, it has been demonstrated that **reporting on frequency-volume charts during just 24 hours is reliable and sufficient to gain insight into the voiding habits during normal daily life of a man with LUTS suggestive of BPH**[2]. In our group nocturia due to polyuria was an exceptional finding. When data from frequency-volume charts were associated with symptoms and quality of life, then **high diuria and small voided volumes at night and in daytime contributed to high symptoms and a low quality of life**[3]. We suppose that frequent voiding of small volumes interferes with daily social life and therefore with quality of life. Again, a high negative correlation was found between mean voided volume at night and in daytime and score on incomplete emptying. Also in this subgroup the latter score was hardly dependent on the presence or absence of residual volume. This suggests once more that frequent voiding of small volumes may be (wrongly) interpreted as caused by inability to empty the bladder completely.
Comparing data from frequency-volume charts with filling cystometric estimated parameters revealed that cystometric capacity (bladder volume at strong desire to void) and especially **effective capacity (cystometric capacity minus residual volume=voided volume at strong desire) corresponded significantly to the maximum voided volume reported on the frequency-volume chart. Effective capacity was twice as high as the mean voided volume calculated from the charts**[9]. Effective capacity represents the "strong desire to void" volume, which will not be frequently used by patients in everyday life. Patients shall void at their "first or normal desire to void" volume, resulting in a voided volume that is half of that voided at strong desire. This means that bladder capacities can easily be calculated from data from frequency-volume charts and residual volume. Interestingly, **the presence of instability was not associated with smaller voided volumes or higher nocturia or diuria derived from frequency-volume charts**[9]. As has been mentioned earlier, symptom-free elderly male volunteers also showed detrusor instability[8]. **It seems that the association of detrusor instability with BPH is non-specific. In contrast to some results published by others, decreased bladder compliance was an exceptional finding in our group**[9]. These findings support the opinion that filling cystometry is of minor diagnostic importance in BPH, when reliable frequency-volume charts are available.
Association of data from frequency-volume charts with data obtained by pressure-flow

studies[10] showed **a substantial reduction of the reported maximum voided volume at increasing obstruction grade, due to an increase in residual volume and a simultaneous decrease in bladder capacity.** These effects can lead in themselves to complaints of frequency, nocturia and small voided volumes and the (wrong) feeling of an inability to empty the bladder completely. **We suppose that the declining volume of the bladder at the onset and early phase of BPH is the major cause of bothersomeness and a loss of general well-being.** Evidently, the shrinking bladder leads men to a substantial reduction in fluid intake[10]. This illustrates that **interpretation of the symptoms should be done carefully taking into account possible adaptations of the patient's behaviour with regard to troublesome symptoms** (such as less urgency, frequency and nocturia due to reduction of fluid intake).
Frequency-volume charts with reporting on fluid intake, deserve more attention than only to identify patients with nocturnal polyuria or excessive fluid intake. In our group, patients with nocturnal polyuria and excessive fluid intake were exceptional. The maximum voided volume in voiding diaries is a reliable reflection of the effective capacity. Functional bladder capacity (average voided volume derived from the voiding diary) is only 50% of the effective capacity. Frequency-volume charts allow for quantification of frequency and nocturia. **We strongly recommend the use of frequency-volume charts during one representative 24 h period in the initial evaluation of men with LUTS suggestive of BPH.**

A shortcoming of our study is that our observations apply to the total group of studied patients. It is difficult to interpret the results for an individual patient, because the variability is high. Besides, we performed a cross-section study. As a consequence, it is difficult to find out the cause and effect relations between the parameters.

Urodynamic evaluations may improve diagnosis of patients with LUTS, and may guide selection of patients for specific treatment modalities. Whereas filling cystometry is of minor diagnostic importance, pressure-flow studies should be done before invasive treatments are considered. As has been mentioned above, these investigations can be done with low subjective and objective morbidity and with reliable results. Nevertheless we realise that, due to a number of factors, the barrier to perform a pressure-flow study in our clinic may be lower than in other clinics. Therefore, we investigated the possibility of non-invasive assessment of benign prostatic obstruction in elderly men with LUTS[11]. Based upon the associations of parameters with obstruction grade[4,7,9,10], we investigated which linear combination of easily available non-invasive parameters allowed the classification of men as obstructed, equivocal or unobstructed in optimal agreement with urodynamic classification. This has led to the development of **the bladder outlet obstruction number BOON, defined as BOON=prostate volume (Vprostate, in ml) minus 3 times maximum urinary free flow rate (Qmax, in ml/s) minus 0.1 times voided volume at strong desire (Vstrong, ml), or BOON=Vprost - 3xQmax - 0.1xVstrong. Extension of this formula to more than 3 parameters did not result in a better classificiation. Replacement of voided volume at strong desire by 2 times mean voided volume (Vmean) calculated from frequency volume charts, thus:**

BOON = Vprost - 3xQmax - 0.2xVmean,

did not affect the results. In chapter 11 nomograms are given with which an urologist can predict what chance a man has with a known BOON to be obstructed, equivocal or unobstructed.
When the BOON is not conclusive enough, we strongly advise the performing of pressure-flow studies to be aware of low bladder contractility without obstruction or other causes for LUTS. It is generally accepted that men with low flow/ low pressure BPH might not realise the same benefit from surgical treatment as do obstructed patients. **By performing urodynamics, patients can be informed before treatment in an optimal manner.**

Samenvatting voor niet-ingewijden

De prostaat is een klier ter grootte van een walnoot die zich vlak onder de blaas rond de plasbuis bevindt. Normaal weegt de prostaat ongeveer 15 gram. Na het dertigste levensjaar kan de prostaat gaan groeien tot zelfs meer dan 100 gram. Deze meestal goedaardige vergroting van de prostaat wordt benigne prostaathyperplasie (BPH) genoemd. BPH kan aanleiding geven tot meerdere klachten, zoals een zwakke urinestraal, vaak moeten plassen, 's nachts vaak het bed uit moeten om te plassen, de urine moeilijk op kunnen houden en nadruppelen. Ook kan BPH andere aandoeningen veroorzaken, zoals blaasontsteking of het ontstaan van blaasstenen. Deze verschijnselen kunnen als zeer hinderlijk ervaren worden en een grote invloed hebben op het dagelijks leven van de patiënt en diens kwaliteit van leven.

Om de diagnose BPH te kunnen stellen, maakt de uroloog gebruik van verschillende onderzoeken. Door middel van geluidsgolven (echografisch) onderzoek wordt de grootte van de prostaat bepaald. De ernst van verschillende klachten, en de hinder die een patiënt daarvan ondervindt, worden in kaart gebracht met behulp van vragenlijsten. Door de patiënt in een aangepast toilet te laten plassen, kunnen de sterkte van de urinestraal en de uitgeplaste hoeveelheid worden gemeten. Daarna kan de in de blaas achtergebleven hoeveelheid urine worden bepaald. Patiënten vullen bovendien gedurende een aantal dagen een plasdagboek in. Dit dagboek geeft informatie over tijdstippen en de dan geplaste hoeveelheden overdag en 's nachts en over de hoeveelheden vocht die de patiënt drinkt.

Belangrijk bij BPH is het onderzoek naar het gedrag van de blaas als deze gevuld wordt en wanneer deze zich ledigt (urodynamisch onderzoek: UDO). Dit onderzoek kan de oorzaak van de klachten achterhalen. Hiertoe wordt een dun slangetje (een catheter) door de plasbuis tot in de blaas geschoven. Met deze catheter kan de blaasdruk worden gemeten en de blaas worden gevuld tot de patiënt goede aandrang heeft. De patiënt wordt dan gevraagd te plassen. Het slangetje is zo dun dat de patiënt er gemakkelijk langs kan plassen. De blaasdruk wordt tijdens het plassen gemeten. Omdat de patiënt in het aangepaste toilet plast, wordt ook de sterkte van de uitgeplaste straal gemeten. Het UDO geeft onder andere informatie over de blaasinhoud bij aandrang (de blaascapaciteit), eventuele ongewenste samentrekkingen van de blaasspier (blaaskrampen), de knijpkracht van de blaasspier, de hinder die de blaasspier ondervindt bij het plassen door de vergrote prostaat (de obstructie) en de achtergebleven hoeveelheid urine in de blaas (het residu). Een zwakke straal bij het plassen kan veroorzaakt worden door een vergrote prostaat die in de weg zit (obstructie). Het kan echter ook gebeuren dat de prostaat niet in de weg zit, maar de blaasspier verzwakt is. Urodynamisch onderzoek is (tot nu toe) de enige methode om een zwakke blaasspier te onderscheiden van obstructie, als oorzaak van de klachten.

Internationaal staan onderzoek en behandeling van de aandoening BPH volop in de

belangstelling. Een internationale commissie van de Wereld Gezondheidsorganisatie spreekt zich iedere twee jaar onder andere uit over welke van de diagnostische onderzoeken belangrijk of minder belangrijk zijn, afhankelijk van de dan geldende wetenschappelijke inzichten.
BPH kan behandeld worden met medicijnen of met een operatie die vaak via de plasbuis uitgevoerd kan worden. De kans dat een man in zijn leven voor BPH behandeld moet worden, wordt geschat op 30%. In Nederland vonden in 1999 ongeveer 10.000 prostaatoperaties plaats. De kosten hiervan waren ruim 32 miljoen Euro. Aangezien de kans op BPH toeneemt als men ouder wordt, zal het aantal patiënten wereldwijd toenemen door de vergrijzing. Onderzoek en behandeling van patiënten met BPH zullen daardoor een toenemende vraag naar de gezondheidszorg veroorzaken. Het goed in kaart brengen van de klachten en de hinder ervan voor de patiënt en een goede diagnose van BPH zijn vereist voor verbeteringen in behandeling van deze veel voorkomende aandoening.

De doelstellingen van dit proefschrift waren:
1. het bestuderen van verschillende diagnostische onderzoeksmethoden en hun onderlinge overeenkomsten en verschillen bij mannen met klachten veroorzaakt door BPH;
2. het onderzoeken van de ernst van de klachten, de hinder die patiënten ervan hebben en de invloed hiervan op hun welzijn;
3. het in maat en getal uitdrukken van de diagnostische bijdrage van de verschillende (combinaties van) onderzoeksmethoden.

We hebben onderzoek gedaan bij 565 mannen boven de 50 jaar die van 1993 tot 2000 de polikliniek urologie in het Universitair Medisch Centrum in Utrecht bezochten met klachten veroorzaakt door BPH.
De onderzochte patiënten voldeden aan strenge eisen: ze moesten meer dan 150 ml kunnen plassen bij de meting van de stevigheid van de urinestraal, ze mochten geen prostaatkanker of neurologische ziektes hebben en ze mochten niet aan hun prostaat geopereerd zijn. Ook patiënten die medicatie innamen die de urinewegen beïnvloeden, werden uitgesloten. Met onze strenge eisen hoopten we mannen met ernstige en lang bestaande obstructie uit te sluiten. Bij een deel van deze mannen zal de blaas immers niet goed meer werken en zijn er al veranderingen opgetreden in de blaasspier. Onze onderzochte patiëntengroep zal daardoor een juiste afspiegeling zijn van mannen die zich bij een urologische kliniek melden met klachten mogelijk veroorzaakt door BPH.
Uitgebreide diagnostiek werd uitgevoerd, waaronder echografie van de prostaat, klachtenvragenlijsten, meting van de sterkte van de urinestraal, residu-bepaling en urodyna-

misch onderzoek. We hebben geprobeerd de onderzoeken zo betrouwbaar mogelijk uit te voeren. Veel aandacht werd besteed aan de privacy en het comfort van de patiënt tijdens de onderzoeken. Daarnaast werd er altijd gecontroleerd of de onderzoeksresultaten wel betrouwbaar waren, bijvoorbeeld door de patiënt te vragen of hij geplast had zoals thuis. Als dat niet het geval was, werd het onderzoek herhaald. Indien er bijvoorbeeld na het plassen urine achterbleef in de blaas werd altijd onderzocht of dat elke keer zo was.

De bestudeerde patiëntengroep bleek gemiddeld 66 jaar oud te zijn. De hoogste leeftijd was 90 jaar. Het gemiddelde prostaatgewicht was 38 gram (variërend van 10 tot 155 gram). De urinestraalsterkte bedroeg gemiddeld 12 ml per seconde, terwijl een man zonder BPH gemakkelijk 30 ml per seconde haalt. De gemiddelde blaascapaciteit was 415 ml, terwijl deze normaal ruim 500 ml is.

Urodynamisch onderzoek wordt door veel urologen gezien als tijdrovend, duur en belastend voor de patiënt. Onze ervaring is echter dat urodynamisch onderzoek niet belastend hoeft te zijn, mits er voorzorgsmaatregelen getroffen worden die de privacy en het comfort van de patiënt bevorderen.

De aan- of afwezigheid van obstructie in de plasbuis door de vergrote prostaat is belangrijk bij de keuze van de behandeling. In onze patiëntengroep bleek 53% van de patiënten een obstructie te hebben, 20% had geen obstructie en bij 27% was dit twijfelachtig.

Er zijn verschillende rekenmethoden bedacht door natuurkundigen en urologen om de gegevens over blaasdruk en de sterkte van de urinestraal (waarmee de mate van obstructie bepaald wordt) te bekijken. Wij vonden een grote mate van overeenstemming tussen deze methoden. De gevonden kleine verschillen zullen naar verwachting de beslissing over wel of niet opereren niet beïnvloeden.

Ondanks onze strenge eisen bij de samenstelling van de patiëntengroep vonden wij, net als in de literatuur, geen verband tussen de grootte van de prostaat en de ernst van de klachten en de kwaliteit van leven van de patiënt. Ook vonden wij geen verband tussen de mate van obstructie en de ernst van de klachten. Daarnaast bleek ook het achterblijven van urine in de blaas na het plassen (het residu) of blaaskrampen niet tot meer klachten of een slechtere kwaliteit van leven te leiden.

De zwakke verbanden tussen urodynamische bevindingen en de ernst van de klachten, kan verklaard worden door tegengestelde uitwerkingen die een urodynamische bevinding te weeg kan brengen. Een grote knijpkracht van de blaas kan tot een ernstige klacht over vaak moeten plassen leiden terwijl er dan geen klacht is over een zwakke urinestraal. Daarnaast kan de patiënt een verkeerde voorstelling van de werkelijkheid hebben. Zo bleken patiënten die goed leeg plassen toch net zo vaak het gevoel te heb-

ben niet goed te kunnen leegplassen als die patiënten die daadwerkelijk niet goed leegplasten. Het ontbreken van verbanden wil niet zeggen dat de waarde van urodynamisch onderzoek twijfelachtig is. Het toont alleen aan dat urodynamica en het in kaart brengen van klachten elkaar aanvullen in de diagnostiek.
Er zijn wel verbanden gevonden tussen andere gemeten grootheden. Bij een toenemend prostaatgewicht neemt ook de mate van obstructie toe. De sterkte van de urinestraal in de groep patiënten nam af bij een toenemende obstructie. Patiënten met een aanzienlijk residu bleken grotere prostaten en een grotere obstructie te hebben dan patiënten die hun blaas helemaal leeg plasten. Daarnaast was het opmerkelijk dat de blaascapaciteit (sterk) afnam bij toenemende obstructie.

Om te achterhalen of uitkomsten van onderzoeken afwijkend zijn, is het belangrijk te weten wat de blaasfunctie is van oudere mannen zonder klachten. Veertien gezonde vrijwilligers hebben we urologisch onderzocht. Het gemiddelde prostaatgewicht was 21 gram. Vijf vrijwilligers bleken een obstructie te hebben. Tevens bleken zes vrijwilligers blaaskrampen te vertonen en hadden zes een aanzienlijk urineresidu. Typische urodynamische bevindingen bij patiënten met klachten veroorzaakt door BPH blijken dus ook voor te komen bij gezonde oudere mannen. Urodynamische bevindingen moeten dus behoedzaam worden geïnterpreteerd en altijd worden gecombineerd met de bevindingen van andere onderzoeken.

Tot nu toe werd de beslissing om een patiënt met BPH te behandelen voornamelijk gebaseerd op de ernst van de klachten en de mate van obstructie door de prostaat. Echter, de mannen met BPH komen niet naar de uroloog omdat ze een obstructie vermoeden of bang zijn voor risico op schade aan hun urinewegen. Ze komen omdat ze zich zorgen maken en omdat ze hinder van hun klachten ondervinden. We hebben deze zorgen en hinder in onze groep onderzocht. De klachten die het meest voorkwamen, waren een zwakke urinestraal, vaak moeten plassen en loze aandrang. De klachten die de patiënten het hinderlijkst vonden, waren vaak moeten plassen, waaronder 's nachts en het moeten persen om de urinestraal op gang te brengen.
Ongeveer 30% van de patiënten liet zich door de klachten ervan weerhouden de dingen te doen die ze gewend waren te doen. De zorgen die patiënten zich maken over het niet goed leeg kunnen plassen en het vaak moeten plassen hadden een grote invloed op het welzijn van de patiënten, in tegenstelling tot bijvoorbeeld de zorgen die patiënten zich maken over een zwakke urinestraal. Wij pleiten voor de toevoeging aan de diagnostiek van vragen over de hinder van en de zorgen over de klachten en de gevolgen hiervan voor de kwaliteit van leven.

In een subgroep van 160 patiënten toonden we aan dat het invullen van een plasdagboek gedurende 24 uur betrouwbaar en toereikend is om inzicht te krijgen in het plasgedrag tijdens het dagelijks leven van een man met klachten veroorzaakt door BPH. Toen de gegevens verkregen van plasdagboeken vergeleken werden met de antwoorden op vragen over klachten, bleek dat vooral het overdag vaak moeten plassen en kleine plasjes overdag en 's nachts aanleiding waren tot ernstige klachten.
Het uitgeplaste volume bij sterke aandrang tijdens het UDO bleek overeen te komen met de grootste geplaste hoeveelheid ingevuld in het plasdagboek. Mensen zullen in hun dagelijks leven meestal gaan plassen bij eerste of normale aandrang en niet wachten tot ze sterke aandrang hebben. De grootste geplaste hoeveelheid bleek ongeveer twee keer zo groot te zijn als de gemiddelde geplaste hoeveelheid van het plasdagboek. Het vaststellen van blaaskrampen tijdens het UDO hield geen verband met kleinere plashoeveelheden of een groter aantal keren plassen in het plasdagboek. Aangezien gezonde mannelijke vrijwilligers ook blaaskrampen lieten zien, lijkt het erop dat blaaskrampen niet kenmerkend zijn voor BPH. Bovenstaande resultaten tonen aan dat urodynamische metingen tijdens het vullen van de blaas bij BPH niet belangrijk zijn voor de diagnostiek, mits er betrouwbaar ingevulde plasdagboeken beschikbaar zijn.
We veronderstellen dat de afnemende blaasinhoud bij het voortschrijden van de aandoening de belangrijkste oorzaak is van de hinder die patiënten gaan ondervinden van BPH. De krimpende blaas leidt ertoe dat veel patiënten hun vochtinname verminderen. Bij de beoordeling van de klachten dient rekening gehouden te worden met het feit dat patiënten hun gedrag aangepast kunnen hebben aan hinderlijke klachten. Wij pleiten voor het gebruik van plasdagboeken gedurende een normale periode van 24 uur bij onderzoek van patiënten met klachten veroorzaakt door BPH. Dit is immers de enige manier om een inzicht te krijgen in het aantal keren dat een patiënt overdag en 's nachts plast en hoeveel de patiënt drinkt.

Een tekortkoming van ons onderzoek is het feit dat bovenstaande resultaten voor de totale groep patiënten gelden. Het is moeilijk onze resultaten voor een enkele patiënt weer te geven aangezien er een enorme spreiding is van de onderzochte grootheden tussen mensen.

Urodynamisch onderzoek kan de diagnose bij patiënten met urologische klachten verbeteren. Urodynamisch onderzoek zal gedaan moeten worden indien een operatie wordt overwogen. We realiseren ons echter wel dat, om verschillende redenen, urodynamisch onderzoek in andere klinieken niet zo vanzelfsprekend is als in onze kliniek. Daarom hebben we onderzocht of het mogelijk was de mate van obstructie in de plasbuis te voorspellen op basis van gegevens verkregen uit een aantal onderzoeken die toch al worden uitgevoerd. Dit heeft geleid tot een eenvoudige formule waarin het volume van de prostaat, de sterkte van de urinestraal en de grootste uitgeplaste hoeveelheid (of twee maal de gemiddeld geplaste hoeveelheid) op het plasdagboek kunnen worden ingevuld. Met het getal dat daar uitkomt (de BOON) kan de uroloog aan de hand van twee grafieken (uit hoofdstuk 11) voorspellen of een patiënt wel of niet een obstructie heeft. Als de BOON niet voldoende uitsluitsel geeft, raden wij met klem aan wèl urodynamisch onderzoek uit te voeren om op de hoogte te zijn van mogelijke andere oorzaken van de klachten. Door urodynamisch onderzoek uit te voeren, kunnen patiënten goed worden geïnformeerd over hun aandoening en over de verwachtingen na behandeling van de aandoening.

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Curriculum Vitae

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