European Association of Urology

GUIDELINES ON BENIGN PROSTATIC HYPERPLASIA

J. de la Rosette, G. Alivizatos, S. Madersbacher,

C. Rioja Sanz, J. Nordling, M. Emberton

UPDATE FEBRUARY 2002

TABLE OF CONTENTS PAGE

1. BACKGROUND

Benign prostatic hyperplasia (BPH) is a condition intimately related to ageing (1). Although it is not life-threatening, its clinical manifestation as lower urinary tract symptoms (LUTS) reduces the patient's quality of life (2). Troublesome LUTS can occur in up to 30% of men older than 65 years (3).

1.1 Prevalence

Although many epidemiological clinical studies have been conducted worldwide over the last 20 years, the prevalence of clinical BPH remains difficult to determine. A standardized clinical definition of BPH is lacking, which makes it intrinsically difficult to perform adequate epidemiological studies. Among the published epidemiological studies, some include probability samples from an entire country, while others represent age-stratified random samples or enrol participants from general practice, hospital populations or responders to selective screening programmes. There is also a lack of homogeneity among these studies in the way in which BPH is assessed, with different questionnaires and methods of administration.

Barry et al. have provided the histological prevalence of BPH, based on a review of five studies relating age to histological findings in human male prostate glands (4). Histological BPH was not found in men under the age of 30 years but its incidence rose with age, reaching a peak in the ninth decade. At that age, BPH was found in 88% of histological samples (4). A palpable enlargement of the prostate has been found in up to 20% of males in their 60s and in 43% in their 80s (5); however, prostate enlargement is not always related to clinical symptoms (2).

Clinical BPH is a highly prevalent disease. By the age of 60 years, nearly 60% of the cohort of the Baltimore Longitudinal Study of Aging had some degree of clinical BPH (6). In the USA, results of the Olmstead County survey, in a sample of unselected Caucasian men aged 40–79 years, showed that moderate-to-severe symptoms can occur among 13% of men aged 40–49 years and among 28% of those older than 70 years (1). In Canada, 23% of the cohort studied presented with moderate-to-severe symptoms (7). The findings for prevalence of LUTS in Europe are similar to those in the USA. In Scotland and in the area of Maastricht, the Netherlands, the prevalence of symptoms increased from 14% of men in their 40s to 43% in their 60s (8,9). Depending on the sample, the prevalence of moderate-to-severe symptoms varies from 14% in France to 30% in the Netherlands (10,11). The proportion of men with moderate-to-severe symptoms doubles with each decade of life (10). Preliminary results of one of the most recent European epidemiological studies on the prevalence of LUTS show that approximately 30% of German males aged 50–80 years present with moderate-to-severe symptoms according to the International Prostate Symptom Score (i.e. I-PSS > 7) (12).

A multicentre study performed in different countries in Asia showed that the age-specific percentages of men with moderate-to-severe symptoms were higher than those in America (13,14). The prevalence increases from 18% for men in their 40s to 56% for those in their 70s (13). Curiously, the average weight of Japanese glands seemed to be smaller than those of their American counterparts (15). Despite methodological differences, some conclusions can be drawn from the studies mentioned above:

- Mild urinary symptoms are very common among men aged 50 years and older.
- Mild symptoms are associated with little bother, while moderate and severe symptoms are associated with increasingly higher levels of inconvenience and interference with living activities (16).
- The same symptoms can cause different troublesome and daily living interference (17).
- The correlation between symptoms, prostate size and urinary flow rate is relatively low (18).

It must be stressed that there is still a need for an epidemiological definition of BPH and its true incidence has yet to be determined (19).

1.2 Is BPH a progressive disorder?

As it is almost impossible to obtain agreement on what it is that defines a man with LUTS/BPH, it seems logical to say that progression cannot be defined in terms of a transition from non-cases to cases. Instead, progression must be measured by documenting deterioration in any number of physiological variables that we associate with the LUTS/BPH syndrome. Traditionally these have included the following:

1. Decrease in maximum flow rate
2. Increase in residual volume
3. Increase in prostate size
4. Deterioration (increase) in symptom score.

In addition, definable events, such as the occurrence of acute urinary retention or prostate surgery, have been used. Less commonly, changes in urodynamic variables and deterioration in disease-specific quality of life have been advocated. Considerable interest currently rests with PSA. It appears to be as good a predictor of progression as any of the variables mentioned above.

1.2.1 Indicators of progression

The strongest evidence to support progression comes from the Olmsted County (20) community-based study and the PLESS placebo group (21).

The strength of evidence for individual parameters as indicators of progression is summarised in Table 1 and is categorised as strong, weak, or none. The actual rates of progression of the individual parameters as determined from the papers reviewed is shown in Table 2. These parameters could potentially be used in decisions about treatment management. Patients who show signs of more pronounced disease progression could be targeted for preventative strategies. The same strategy could be applied to patients who are at increased risk of progression based on recognised risk factors.

Risk factors for progression were found to be age (Olmsted County), PSA (PLESS) and prostate volume (combined 2-year placebo analysis). Other baseline risk factors can be identified, such as symptom severity and decreased urinary flow rate, but current data are not as convincing as those for age, PSA level and prostate volume.

Several other complications, such as renal impairment and bladder dysfunction, have been associated with progression of BPH. Although these are important, they are very rare and therefore could not be evaluated accurately in community-based and clinical studies. The evidence for the progression of BPH has been summarised previously (22).

Table 1. Strength of evidence for specific parameters as indicators of progression of benign prostatic hyperplasia (BPH)

	Parameter	Community- based studies	Clinical trials
LUTS	IPSS	S	N/W*
	BII	S	N/N
	QoL	S	W/S*
BPE	DRE	N	N
	TRUS	S	S
	MRI	N	S/S*
BOO	Qmax	S	W/S*
BPH	Histology	N/A	N/A
Miscellaneous	AUR	S	S/S*
	Surgery	S	W/S*
	Crossover/treatment	S	N

*Conditional risk factors: age and prostate-specific antigen (PSA); S = strong; W = weak; N = no evidence; N/A = not available.
AUR = acute urinary retention; BOO = bladder outlet obstruction; BPE = benign prostatic enlargement; BII = BPH Impact Index; DRE = digital rectal examination; I-PSS = International Prostate Symptom Score; LUTS = lower urinary tract symptoms; MRI = magnetic resonance imaging; Qmax = maximum flow rate; sQoL = quality of life; TRUS = transrectal ultrasonography.

Table 2. Rates of progression of individual parameters in BPH change table

Study	Rate of progression						
	LUTS (points)	Flow rate	Prostate size	Acute urinary retention[a] (Incidence/1000 person years)		Surgery[a] (Incidence/1000 person years)	
				40–49 years	≥ 70 years	40–49 years	≥ 70 years
Olmsted (23–27)	0.18 per year	-2% per year	1.9% per year	3.0	34.7	0.3	10.9
Health Professional (28)	NR	NR	NR	3.3	11.3	NR	NR
PLESS (29)	-1.3 in 4 years[b]	+0.2 mL/s in 4 years[b]	+14% in 4 years	7% over 4 years		10% over 4 years	
2-year studies (30–34)	NR	NR	NR	1.6-4.2%[c] 0.5-3.9%[d]		NR	
North American (35)	NR	NR	NR	NR		10-39%[e]	

[a]Men with moderate to severe symptoms; [b]Flow rate and LUTS responded to placebo treatment by showing an initial improvement, which deteriorated back towards baseline during the course of the placebo-controlled trial; [c]According to baseline prostate volume; [d]According to baseline prostate-specific antigen (PSA) level.

LUTS = lower urinary tract symptoms; NR = not reported.

1.2.2 Conclusions

Based on published data on consequences and complications of the disease, BPH can be considered a progressive disease. There are limited published data on longitudinal studies and the key pieces of evidence that support this notion are the Olmsted County and PLESS studies. A group of patients at increased risk of progression can be identified based on specific risk factors, i.e. age, PSA level and prostate volume. It might be appropriate to identify these patients at risk of progression and initiate early preventative treatment.

1.2.3 REFERENCES

1. **Chute CG, Panser LA, Girman CJ, Oesterling JE, Guess HA, Jacobsen SJ, Lieber MM.**
   The prevalence of prostatism: a population based survey of urinary symptoms. J Urol 1993; 150: 85-89.
2. **Donovan JL, Kay HE, Peters TJ, Abrama P, Coast J, Matos-Ferreira A, Rentzhog L, Bosch JL, Nordling J, Gajewski JB, Barbalias G, Schick E, Silva MM, Nissenkorn I, de la Rosette JJ.**
   Using the ICSQoL to measure the impact of lower urinary tract symptoms on quality of life: evidence from the ICS-'BPH' study. International Continence Society - Benign Prostatic Hyperplasia.
   Br J Urol 1997; 80: 712-721.
3. **Chapple CR.**
   BPH disease management. Eur Urol 1999; 36 (Suppl 3): 1-6.
4. **Barry JJ, Coffey DS, Walsh PC, Ewing LL.**
   The development of human benign prostatic hyperplasia with age. J Urol 1984; 132: 474-479.
5. **Lytton B, Emery JM, Harvard BM.**
   The incidence of benign prostatic hypertrophy. J Urol 1968; 99: 639-645.
6. **Arrighi HM, Metter EJ, Guess HA, Fozzard JL.**
   Natural history of benign prostatic hyperplasia and risk of prostatectomy, the Baltimore Longitudinal Study of Aging. Urology 1991; 35 (Suppl): 4-8.
7. **Norman RW, Nickel JC, Fish D, Pickett SN.**
   Prostate-related symptoms in Canadian men 50 years of age or older: prevalence and relationships among symptoms. Br J Urol 1994; 74: 542-550.
8. **Garraway WM, Collins GN, Lee RJ.**
   High prevalence of benign prostatic hypertrophy in the community. Lancet 1991; 338: 469-471.
9. **Wolfs GGMC, Knottnerus JA, Janknegt RA.**
   Prevalence and detection of micturition problems among 2734 elderly men. J Urol 1994; 152: 1467-1470.
10. **Sagnier PP, McFarlane G, Teillac P, Botto H, Richard F, Boyle P.**
    Impact of symptoms of prostatism on bothersomeness and quality of life of men in the French community. J Urol 1995; 15: 669-673.
11. **Bosch JLHR, Hop WCJ, Kirkels WJ, Schroeder FH.**

The international prostate symptom score in a community-based sample of men between fifty-five and seventy-four years of age. Prevalence and correlation of symptoms with age, prostate volume, flow rate and residual urine volume. Br J Urol 1995; 75: 622–630.

12. **Berges RR, Pientka L.**
Management of the BPH syndrome in Germany: who is treated and how?
Eur Urol 1999; 36 (Suppl 3): 21-27.

13. **Homma Y, Kawabe K, Tsukamoto T, Yamanaka H, Okada K, Okajima E, Yoshida O, Kumazawa J, Gu FL, Lee C, Hsu TC, dela Cruz RC, Tantiwang A, Lim PH, Sheikh MA, Bapat SD, Marshall VR, Tajima K, Aso Y.**
Epidemiologic survey of lower urinary tract symptoms in Asia and Australia using the International Prostate Symptom Score. Int Urol 1997; 4: 40-46.

14. **Tsukamoto T, Kumamoto Y, Masumori N, Miyakr H, Rhodes T, Girman GJ, Guess HA, Jacobsen HJ, Lieber MM.**
Prevalence of prostatism in Japanese men in a population based study with comparison to a similar American study. J Urol 1995; 154: 391-395.

15. **Masumori N, Tsukamoto T, Kumamoto Y, Miyake H, Rhodes T, Girman CJ, Guess HA, Jacobsen SJ, Lieber MM.**
Japanese men have smaller prostate volumes but comparable urinary flow rates relative to American men: results of community based studies in 2 countries. J Urol. 1996 Apr;155(4):1324-7.

16. **Guess HA.**
Population-based studies of benign prostatic hyperplasia. In: Kirby R et al. (eds). Textbook of Benign Prostatic Hyperplasia. Isis Medical Media: Oxford, 1996; 117-124.

17. **Guess HA, Chute CG, Garraway WM, Girman CJ, Panser LA, Lee RJ, Jacobsen SJ, McKelvie GB, Oesterling JE, Lieber MM.**
Similar levels of urological symptoms have similar impact on Scottish and American men although Scots report less symptoms. J Urol 1993; 150: 1701-1705.

18. **Girman CJ, Jacobsen SJ, Guess HA, Oesterling JE, Chute CG, Panser LA, Lieber MM.**
Natural history of prostatism: relationship among symptoms, prostate volume and peak urinary flow. J Urol 1995; 153: 1510-1515.

19. **Oishi K, Boyle P, Barry JM et al.**
Epidemiology and natural history of benign prostatic hyperplasia. In: Denis L, Griffiths K, Khoury S et al. (eds). Fourth International Consultation on BPH, Paris, July 1997. Health Publications: Plymouth, 1998, pp. 25-59.

20. **Jacobsen SJ, Girman CJ, Guess HA, Rhodes T, Oesterling JE, and Lieber MM.**
Natural history of prostatism: longitudinal changes in voiding symptoms in community dwelling men. J Urol 1996; 155: 595-600.

21. **McConnell JD, Bruskewitz R, Walsh P, Andriole G, Lieber M, Holtgrewe HL, Albertsen P, Roehrborn CG, Nickel JC, Wang DZ, Taylor AM, Waldstreicher J.**
The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostatic hyperplasia. New Engl J Med 1998; 338: 557-563.

22. **Anderson JB, Roehrborn CG, Schalken JA, Emberton M.**
The progression of benign prostatic hyperplasia: examining the evidence and determining the risk. Eur Urol 2001; 39: 390-399.

23. **Jacobsen SJ, Jacobson DJ, Girman CJ, Roberts RO, Rhodes T, Guess HA, Lieber MM.**
Natural history of prostatism: risk factors for acute urinary retention. J Urol 1997; 158: 481-487.

24. **Jacobsen SJ, Jacobson DJ, Girman CJ, Roberts RO, Rhodes T, Guess HA, Lieber MM.**
Treatment for benign prostatic hyperplasia among community dwelling men: the Olmsted County Study of urinary symptoms and health status. J Urol 1999; 162: 1301-1306.

25. **Jacobsen SJ, Girman CJ, Guess HA, Rhodes T, Oesterling JE, Lieber MM.**
Natural history of prostatism: longitudinal changes in voiding symptoms in community dwelling men. J Urol 1996; 155: 595–600.

26. **Rhodes T, Girman CJ, Jacobsen DJ, Roberts RO, Lieber MM, Jacobsen SJ.**
Longitudinal prostate volume in a community-based sample: 7 year followup in the Olmsted County Study of urinary symptoms and health status among men.
J Urol 2000; 163 (suppl 4): 249. [abstract 1105]

27. **Roberts RO, Jacobsen SJ, Jacobson DJ, Rhodes T, Girman CJ, Lieber MM.**
Longitudinal changes in peak urinary flow rates in a community-based cohort. J Urol 2000; 163: 107-113.

28. **Meigs JB, Barry MJ, Giovannucci E, Rimm EB, Stampfer MJ, Kawachi I.**
Incidence rates and risk factors for acute urinary retention: the Health Professional Followup Study. J Urol 1999; 162: 376-382.

29. **McConnell JD, Bruskewitz R, Walsh P, Andriole G, Lieber M, Holtgrewe HL, Albertsen P, Roehrborn CG, Nickel JC, Wang DZ, Taylor AM, Waldstreicher J.**
The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostatic hyperplasia. New Engl J Med 1998; 338: 557-563.
30. **Arrighi HM, Guess HA, Metter EJ, Fozard JL.**
Symptoms and signs of prostatism as risk factors for prostatectomy. Prostate 1990; 16: 253-261.
31. **Anderson JB, Roehrborn CG, Schalken JA, Emberton M.**
The progression of benign prostatic hyperplasia: examining the evidence and determining the risk. Eur Urol 2001; 39: 390-399.
32. **Roehrborn CG, Boyle P, Bergner D, Gray T, Gittelman M, Shown T, Melman A, Bracken RB, deVere White R, Taylor A, Wang D, Waldstreicher J.**
Serum prostate-specific antigen and prostate volume predict long-term changes in symptoms and flow rate: results of a four-year, randomized trial comparing finasteride versus placebo. PLESS Study Group. Urology 1999; 54: 662-669.
33. **Roehrborn CG, McConnell JD, Lieber M, Kaplan S, Geller J, Malek GH, Castellanos R, Coffield S, Saltzman B, Resnick M, Cook TJ, Waldstreicher J.**
Serum prostate-specific antigen is a powerful predictor of acute urinary retention and the need for surgery in men with clinical benign prostatic hyperplasia. PLESS Study Group. Urology 1999; 53: 473-480.
34. **Roehrborn CG, McConnell JD, Bonilla J Rosenblatt S, Hudson PB, Malek GH, Schellhammer PF, Bruskewitz R, Matsumoto AM, Harrison LH, Fuselier HA, Walsh P, Roy J, Andriole G, Resnick M, Waldstreicher J.**
Serum prostate-specific antigen is a strong predictor of future prostate growth in men with benign prostatic hyperplasia. PROSCAR long-term efficacy and safety study. J Urol 2000; 163: 13-20.
35. **Gormley GJ, Stoner E, Bruskowitz RC, Imperato-McKinley J, Walsh PC, McConnell JD, Adriole GL, Geller J, BrackenBR, Tenover JS et al.**
The effect of finasteride in men with benign prostatic hyperplasia. The Finasteride Study Group. New Engl J. Med. 1992 Oct 22;327(17):1185-91.

2. RISK FACTORS

2.1 For developing the disease

The aetiology of BPH is multifactorial. Currently, there is no strong evidence that smoking, vasectomy, obesity or high alcohol intake are risk factors in the development of clinical BPH. Results of the different epidemiological studies are controversial, probably because of differences in sampling and methods of analysis. In most cases only insufficient marginal differences can be established (1).

Chronic conditions, such as hypertension or diabetes, have been related to clinical BPH, but given the frequent occurrence of these conditions in ageing men a large proportion of patients can be expected to suffer from such an association (2,3).

Recently, it has been stated that diabetes and clinical BPH are associated more frequently than would be expected based on chance alone. Although more severe BPH symptoms (increased I-PSS and post-void residual) seem to be found in diabetic males even after age adjustment, the fact that both conditions increase with age and can cause partially similar voiding symptoms, produces a considerable bias (3).

The only true factors related to the development of the disease are age and hormonal status (4). The crucial role of the testis has been recognized for more than a century and current research has extended into the field of molecular biology (5). Both of these risk factors are currently beyond prevention.

2.2 For surgical treatment

Although the number of surgical procedures for BPH has declined in the USA and Europe over the last decade (6), they still represent the second most common major operation in aged men (7). Ultimately, three in 10 men may undergo surgery for this condition (2).

Surgical risk depends on age and the presence of clinical symptoms. In the absence of clinical symptoms, the likelihood of being treated surgically is about 3% (8,9). The need for surgery increases with symptoms and is twice as high in men with a high baseline-symptom score than for those with a low score (10). For men presenting with urinary retention, the cumulative incidence for prostatectomy is 60% at 1 year and 80% at 7 years (11). Multivariate analysis carried out on a sample of 16,219 men, aged at least 40 years, with a mean follow-up of 12 years, showed a positive association with surgery for age, low body mass index, non-smokers, urine pH greater than 5, and a history of kidney X-ray and/or tuberculosis, for each of the five clinical

urinary symptoms studied (12).

In the Veterans Normative Aging Study, in a cohort of 2,280 men, the main predictor for surgery was the presence of urinary symptoms. The risk of requiring subsequent surgery also varied with age, the odds ratio being 1.8 for nocturia and 4.3 for hesitancy in young men (aged < 65 years). Among older men, only nocturia (odds ratio 2.4) was predictive of surgery (13). In the Baltimore study, the three predictive symptoms for surgery were change in size and force of the urinary stream, sensation of incomplete voiding and digital rectal enlargement of the prostate. Men with one factor had a cumulative incidence of surgery of 9%, those with two factors of 16%, and those with three factors of 37%. Nevertheless, the same study showed that increasing age was the predominant risk factor for surgery (8).

From the above, it can be concluded that the risk of needing surgery for BPH increases with age and with the degree of clinical symptoms at baseline. Nocturia and changes in urinary stream seem to be the most important predictive symptoms.

2.3 REFERENCES

1. **Oishi K, Boyle P, Barry JM et al.**
   Epidemiology and natural history of benign prostatic hyperplasia. In: Denis L, Griffiths K, Khoury S et al. (eds). Fourth International Consultation on BPH, Paris, July 1997.
   Health Publications: Plymouth, 1998, pp. 25-59.
2. **Boyle P.**
   Epidemiology of benign prostatic hyperplasia: risk factors and concomitance with hypertension.
   Br J Clin Pract 1994; 74(suppl): 18-22.
3. **Michel MC, Mehlburger L, Schumacher H, Bressel HU, Goepel M.**
   Effect of diabetes on lower urinary tract symptoms in patients with benign prostatic hyperplasia.
   J Urol 2000; 163: 1725-1729.
4. **Isaacs JT, Coffey DS.**
   Etiology and disease process of benign prostatic hyperplasia. Prostate 1989; (Suppl 2): 33-50.
5. **Voller MCW, Schalken JA.**
   Molecular genetics of benign prostatic hyperplasia. In: Kirby R et al. (eds). Textbook of Benign Prostatic Hyperplasia. Isis Medical Media: Oxford, 1996, pp. 109-113.
6. **Holtgrewe HL, Ackermann R, Bay-Nielsen H et al.**
   Report from the Committee on the Economics of BPH. In: Cockett ATK et al. (eds). Third International Consultation on Benign Prostatic Hyperplasia (BPH).
   Scientific Communication International: Jersey, 1996, pp. 51-70.
7. **Meigs JB, Barry MJ.**
   Natural history of benign prostatic hyperplasia. In: Kirby R et al. (eds). Textbook of Benign Prostatic Hyperplasia. Isis Medical Media: Oxford, 1996, pp. 125-135.
8. **Arrighi HM, Metter EJ, Guess HA, Fozzard JL.**
   Natural history of benign prostatic hyperplasia and risk of prostatectomy, the Baltimore Longitudinal Study of Aging. Urology 1991; 35 (Suppl): 4-8.
9. **Diokno A, Brown M, Goldstein N, Herzog A.**
   Epidemiology of bladder emptying symptoms in elderly men. J Urol 1992; 148: 1817-1821.
10. **Wasson J, Reda D, Bruskewitz RC, Elinson J, Keller AM, Henderson WG.**
    A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. The Veterans Affairs Cooperative Study Group on Transurethral Resection of the Prostate.
    N Engl J Med 1994; 334: 75-79.
11. **Craigen A, Hickling J, Saunders C, Carpenter R.**
    The natural history of prostatic obstruction: a prospective survey. J R Coll Gen Pract 1969; 18: 226-232.
12. **Sidney S, Quesenberry C Jr, Sadler MC, Lydick EG, Guess HA, Cattolica EV.**
    Risk factors for surgically treated benign prostatic hyperplasia in a prepaid health care plan.
    Urology 1991; 38 (Suppl 1): 13-19.
13. **Epstein RS, Lydick E, de Labry L, Vokonas PS.**
    Age-related differences in risk factors for prostatectomy for benign prostatic hyperplasia: the VA Normative Aging Study. Urology 1991; 38 (Suppl 1): 9-12.

3. DIAGNOSIS

Diagnostic investigations have been classified as:

- Mandatory: this test should be performed in every patient
- Recommended: there is evidence to support the use of this test
- Optional: this test is done at the discretion of the clinician
- Not recommended: there is no evidence to support the use of this test.

3.1 Symptom scores

Assessment of a man should include a detailed history and examination. The examination should include a digital rectal examination (DRE) of the prostate. An attempt should be made to estimate the size of the prostate in order to determine whether it is enlarged. It is acknowledged that DRE is inaccurate when compared to transrectal ultrasound assessment of prostate size. The shape and consistency of the gland should be noted and the size and position of any palpable nodules documented.

Probably the best way to assess symptom severity is with a validated symptom score. A number of instruments exist that can measure symptom severity, bother and quality of life (Table 3) (1). Most instruments in current use conform to acceptable standards of validity, reliability and responsiveness; in other words they measure what they purport to measure, are stable over time and are able to reflect clinically important changes (2).

Table 3 BPH symptom scores. Adapted from McConnell et al. (1).

Aspect	Occurrence or frequency	Disease-specific health-related quality of life (QoL)	
		Impact of individual symptoms	Impact (global)
Lower urinary tract symptoms (excluding continence)	I-PSS (7 questions) DAN-PSS-1 ICS male Clinical Prostate Score Bladder Outlet Obstruction Number	DAN-PSS-1 ICS male Symptom Problem Index	I-PSS (1 QoL question) ICS QoL BPH QoL 9 BPH Impact Index
Continence	DAN-PSS-1 ICS male BSFI ICS sex BPH QoL 9 RSSF	DAN-PSS-1 ICS male BSFI ICS sex RSSF	ICS QoL BSFI BPH QoL 9 RSSF
Activities of daily living			BPH QoL 9 ICS QoL SF36

BPH = benign prostatic hyperplasia; BSFI = Brief Sexual Function Inventory; DAN-PSS-1 = Danish Prostate Symptom Score-1; ICS = International Continence Score; I-PSS = International Prostate Symptom Score; RSSF = Radiumhemmets Scale of Sexual Functioning.

3.1.1 I-PSS

The I-PSS has become the international standard. It is derived from the American Urological Association (AUA) 7 score described by Barry and his colleagues in the early 1990s (3). By adding the scores (with equal weighting) to its constituent questions, a summary or index score is generated which has been shown to be an accurate reflection of a man's overall symptoms over the preceding month (4). The extent to which the self-reported scores reflect actual events has been questioned. Men report nocturia with accuracy but tend to overstate daytime frequency. Correlation of the self-reported score to intermittency or to the strength of stream was poor (5).

Age and cultural factors may be important. The I-PSS appears less reliable in men over 65 years old (6) and careful linguistic validation needs to be undertaken prior to its use in non-North American cultures (7).

Numerous authors have reported and commented upon the poor correlations between I-PSS and other physiological variables. For example, there are numerous reports of symptom severity (as expressed by I-PSS) correlating poorly with peak urinary flow rate, average flow rate, post-void residual volume, prostate size or pressure-flow relationships (1, 8–10). This lack of correlation has troubled many investigators and has led some

to raise questions about the validity of the I-PSS. Correlations of similar magntude have been seen in many other disease areas, e.g. peak respiratory flow correlates poorly with patient's own reports of the severity of their asthma. The lack of correlation can be explained in two ways. Firstly, IPSS and physiological measures measure different things. Secondly, there are statistical issues related to the clustering of values or data points, which will also result in poor correlation.

A validated symptom score assesses symptom severity. It can be used to monitor change in symptoms over time or following an intervention.

3.1.2 Danish Prostate Symptom Score (DAN-PSS)

The DAN-PSS system is a self-administrated quality-of-life questionnaire comprising 12 questions related to voiding problems and the perceived bother related to each individual symptom (Table 4) (10). The difference between the DAN-PSS and the AUA/I-PSS system is that each symptom in the DAN-PSS system is both quantified and qualified by determining a symptom score and a 'bother' score. The DAN-PSS questionnaire has demonstrated a high degree of construct validity, correlating with the Madsen–Iversen score system and with the patient's answers to questions about how bothersome their symptoms have been. The DAN-PSS system has discriminated clearly between patients with BPH and control subjects, and has been sensitive to changes following BPH treatment. However, it has not been able to predict bladder outlet obstruction (11). The DAN-PSS and I-PSS indexes are correlated, and the DAN-PSS seems to be more sensitive to changes after pharmacological treatment than the I-PSS, Madsen-Iversen and Boyarsky symptom indexes (12).

3.1.3 Quality-of-life assessment

The impact of urinary symptoms on the quality of life is generally evaluated by means of question 8 of the I-PSS. However, this question measures the extent to which patients tolerate their symptoms rather than evaluating their quality of life. A number of health-related, quality-of-life instruments have been used for clinical research. One of the best known is the generic measure, the Medical Outcomes Study 36-item short-form health survey (SF36) (14). It is a self-completed questionnaire used to measure general health status and quality of life. It has been used in a number of studies addressing men with lower urinary tract symptoms. Using this score, a postal population survey among 217 men aged 55 years and over with LUTS showed that, depending on the respondent's activity, 9–49% of those with moderate or severe urinary symptoms reported interference with some of their daily activities. Increasing symptom severity was associated with worsening physical condition, social functioning, vitality, mental health and perception of general health. Increasing 'bothersomeness' was associated with a worsening of all dimensions of general health status and quality of life. The association between the outcome of this population survey and the degree of 'bothersomeness' was stronger than that with the I-PSS symptom score.

3.1.4 Symptom score as decision tool for treatment

Can symptom severity alone be used to allocate treatment? The US Agency for Health Care Policy and Research Guidelines (1) tried to do this. Three categories of symptom severity were described: mild (0–7), moderate (8–19) and severe (20–35). The authors suggested that patients with mild symptoms were most appropriately managed by a watchful waiting approach. Patient with moderate symptoms might benefit from pharmacotherapy, while patients with severe symptoms may derive most benefit from prostatectomy. Although notions of appropriateness have not been well-studied, the proposed policy appears to hold true for patients with mild symptoms but is less reliable for men with moderate or severe symptoms (15).

3.1.5 Symptom score as outcome predictor

Symptom score may be one of the more powerful predictors of symptomatic outcome (16). As men with mild symptoms have little room for improvement it is of little surprise that they do not experience high levels of symptom reduction following surgery. A man with a pre-operative I-PSS of 17, or more, has an 87% chance of experiencing a substantial symptom reduction (17). There is little evidence that physiological measures improve the chances of predicting a favourable symptomatic outcome.

3.1.6 Conclusions

Evaluating symptom severity with a symptom score is an important part of the initial assessment of a man. It is helpful in allocating treatment, and in both predicting and monitoring the response to therapy.

3.1.7 Recommendations

Standard	Clinical history, symptom assessment, physical examination.
Recommended	Validated symptom score, e.g. I-PSS.

Table 4 The Danish Prostate Symptom Score. Adapted from Hansen et al. (10).

Each question allows the patient to choose one of four answers.
For each question the patient scores 0–3 for severity of symptoms (A) and 0–3 for the degree of bother (B).

1A Hesitancy: Do you have to wait for urination to start?
Answers: 0 No; 1 Rarely; 2 Daily; 3 Every time

1B If you have to wait to start urination, is this a problem for you?
Answers: 0 No problem; 1 Small problem; 2 Moderate problem; 3 Major problem

2A Weak stream: Do you consider your urinary stream as:
Answers: 0 Normal; 1 Weak; 2 Very weak; 3 Dribbling

2B If your stream is weak or dribbling, is this a problem for you?
Answers: 0 No problem; 1 Small problem; 2 Moderate problem; 3 Major problem

3A Incomplete emptying: Do you feel you empty your bladder completely?
Answers: 0 Always; 1 Occasionally; 2 Rarely; 3 Never

3B If you feel that you do not empty your bladder completely, is this a problem for you?
Answers: 0 No problem; 1 Small problem; 2 Moderate problem; 3 Major problem

4A Straining: Do you have to strain to start and/or maintain urination?
Answers: 0 No; 1 Rarely; 2 Daily; 3 Always

4B If you have to strain, is this a problem for you?
Answers: 0 No problem; 1 Small problem; 2 Moderate problem; 3 Major problem

5A Daytime frequency: What is the longest interval between each urination, from when you wake up until you go to bed?
Answers: 0 More than 3 h; 1 2–3 h; 2 1–2 h: 3 Less than 1 h

5B Do you consider your frequency of urination a problem?
Answers: 0 No problem; 1 Small problem; 2 Moderate problem; 3 Major problem

6A Nocturia: How many times do you have to urinate during the night?
Answers: 0 None; 1 One to two times; 2 Three to four times; 3 Five times or more

6B If you have to urinate during the night, is this a problem for you?
Answers: 0 No problem; 1 Small problem; 2 Moderate problem; 3 Major problem

7A Urge: Do you experience an imperative (strong) urge to urinate?
Answers: 0 Never; 1 Rarely; 2 Daily; 3 Always

7B If you have an imperative (strong) urge to urinate, is this a problem for you?
Answers: 0 No problem; 1 Small problem; 2 Moderate problem; 3 Major problem

8A Urge incontinence: Is the urge to urinate so strong that urine starts to flow before you reach the toilet?
Answers: 0 Never; 1 Rarely; 2 Daily; 3 Every time

8B If the urge to urinate is so strong that urine starts to flow before you reach the toilet, is this a problem for you?
Answers: 0 No problem; 1 Small problem; 2 Moderate problem; 3 Major problem

9A Dysuria: Do you feel pain or have a burning feeling when you urinate?
Answers: 0 Never; 1 Rarely; 2 Daily; 3 Always

9B If it hurts or burns when you urinate, is this a problem for you?
Answers: 0 No problem; 1 Small problem; 2 Moderate problem; 3 Major problem

10A Post-micturition dribbling: Do you experience dribbling after voiding, when you feel you have finished urination?
Answers: 0 Never; 1 In the toilet; 2 Small amounts in the trousers; 3 Large amounts in the trousers

10B If you experience dribbling after voiding, is this a problem for you?
Answers: 0 No problem; 1 Small problem; 2 Moderate problem; 3 Major problem

11A Stress incontinence: Do you experience leakage of urine when physically active (e.g. lifting, sneezing, coughing)?
Answers: 0 Never; 1 Rarely; 2 Often; 3 Always

11B If you experience urinary leakage when physically active, is this a problem for you?
Answers: 0 No problem; 1 Small problem; 2 Moderate problem; 3 Major problem

12A Overflow/seeping incontinence: Do you experience leakage of urine without urge or physical activity?
Answers: 0 Never; 1 Rarely; 2 Often; 3 Always

12B If you experience urinary leakage without urge or physical activity, do you consider this a problem?
Answers: 0 No problem; 1 Small problem; 2 Moderate problem; 3 Major problem

3.2 Prostate-specific antigen (PSA) measurement

Before selecting the proper treatment for men with LUTS, every urologist will perform a DRE and most will measure the serum value of PSA

3.2.1 Factors influencing the serum levels of PSA

In cases where the architecture of the prostatic gland is disrupted, PSA will 'leak' into the circulation. This occurs when prostatic carcinoma is present but also in BPH, prostatitis and after urinary retention. This is why PSA is not considered as being cancer-specific, but organ-specific. Other known causes of PSA serum elevations are biopsy of the prostate gland and ejaculation (18). In addition, small and clinically insignificant changes occur after DRE.

Two other important factors, age and race, must also be considered when evaluating PSA values in men with LUTS (19,20). African–Americans with no evidence of prostate carcinoma have higher PSA values after their fourth decade of life, and therefore age-specific reference ranges must be adapted and interpreted according to race and ethnicity (21). A recent community-based study of African-American men contradicts the beliefs of racial PSA differences, since only minor variations in PSA reference ranges were found (22).

3.2.2 PSA and prediction of prostatic volume

Stamey et al. were the first to correlate PSA serum values and volume of prostatic tissue (23). In their studies in the late 1980s, they found that the serum PSA contribution from BPH was 0.30 ng/mL per gram of tissue and 3.5 ng/ml per cm^3 of cancer tissue. Roehrborn et al. have shown that PSA and prostate volume have an age-dependent, log-linear relationship and that PSA has a good predictive value for assessing prostatic volume (24). Prediction of prostate volume can also be based on total and free PSA. Both PSA forms were found to be able to predict the TRUS prostate volume (± 20%) in more than 90% of the cases (25).

3.2.3 PSA and probability of having prostate cancer

The chance of having prostate cancer is strongly related with the serum value of PSA. Table 5 shows the probability of prostate cancer among men with normal digital rectal examination (Adapted from Barry [26]). The sensitivity of PSA to diagnose prostate cancer is better than that of DRE, but both methods have poor specificity.

In order to avoid unnecessary biopsies, Potter et al. (10) have used three clinical parameters – age, PSA and DRE – and have calculated the likelihood of detecting prostate cancer on sextant TRUS-guided biopsies among 2054 men (Table 6).

Table 5 Probability of prostate cancer among men with normal DRE. Adapted from Barry (26).

PSA (ng/mL)	Probability of prostate cancer (%)
0–2.4	Not known
2.5–4	12–23
4.1–10	25
> 10.0	> 50

*PSA = prostate-specific antigen.

Table 6 Probability of prostate cancer as a function of age, PSA and DRE. Adapted from Potter et al. (27).

PSA (ng/mL)	DRE –	DRE +	DRE –	DRE +	DRE –	DRE +	DRE –	DRE +
< 2.5	9	37	12	39	15	42	20	44
2.6–4.0	9	41	12	42	16	44	20	47
4.1–6.0	10	41	14	44	17	47	22	48
6.1–10.0	11	-	15	48	19	50	25	42
10.1–20.0	13	55	19	54	25	58	31	60
> 20.0	22	82	45	74	43	81	59	84

*DRE = digital rectal examination; PSA = prostate-specific antigen.

3.2.4 PSA and prediction of BPH-related outcomes

In a series of studies, Roehrborn et al. (28,29) have shown that PSA and prostatic volume can be used to evaluate the risks of either needing surgery or developing acute urinary retention. These parameters were also

related with long-term changes in symptom scores and flow rates. In a recent epidemiological study, elevated free PSA levels could predict clinical BPH, independent of total PSA levels (30). Djavan et al. have also shown that patients with higher PSA values had a better chance of a favorable outcome after treatment with microware thermotherapy (31).

3.2.5 Conclusions

1. Various factors (cancer, BPH, infection, trauma, age, race) may influence serum PSA levels.
2. The level of PSA correlates with the volume of the prostate gland
3. The higher the PSA level, the greater is the probability of having prostate cancer
4. The PSA level can predict the natural history of BPH.

3.2.6 Recommendations

The measurement of PSA is recommended when a diagnosis of prostatic carcinoma will change the decision made about which therapeutic option to use.

3.2.7 REFERENCES

1. **McConnell JD, Barry MJ, Bruskewitz RC et al.**
   Benign Prostatic Hyperplasia: Diagnosis and Treatment. Quick Reference Guide for Clinicians. AHCPR publication no. 94-0583. Agency for Health Care Policy and Research, Public Health Service, US Department of Health and Human Services: Rockville, MD, February 1994.
2. **Kirshner B, Guyatt G.**
   A methodological framework for assessing health indices. J Chronic Dis 1985; 38: 27-36.
3. **Barry MJ, Fowler FJ Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, Cockett AT.**
   The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the Americal Urological Association. J. Urol. 1992 Nov;148(5):1549-57; discussion 1564.
4. **Barry MJ, Fowler FJ Jr, Mulley AG Jr, Jenderson JV Jr, Wennberg JE.**
   Patient reactions to a programe designed to facilitate patient participation in treatment decisions for benign prostatic hyperplasia. Med. Care. 1005;33(8):771-82.
5. **Matzkin H, Greenstein A, Prager-Geller T, Sofer M, Braf Z.**
   Do reported micturition symptoms on the American Urological Association Questionnaire correlate with 24-hour home uroflowmetry recordings? J Urol. 1996;155(1):197-9.
6. **Barry MJ, Cockett AT, Holtgrewe HL, McConnell JD, Sihelnik SA, Winfield HN.**
   Relationship of symptoms of prostatism to commonly used physiological and anatomical measures of the severity of benign prostatic hyperplasia. J Urol. 1993;150(2 Pt 1):351-8.
7. **Sagnier PP, McFarlane G, Teillac P, Botto H, Richard F, Boyle P.**
   Impact of symptoms of prostatism on bothersomeness and quality of life of men in the French community. J Urol 1995; 15: 669-673.
8. **Barry M.J., Cockett AT, Holtgrewe HL, McConnell JD, Sihelnik SA, Winfield HN.**
   Relationship of symptoms of prostatism to commonly used physiological and anatomical measures of the severity of benign prostatic hyperplasia. J Urol. 1993;150(2 Pt 1):351-8.
9. **Chute CG, Panser LA, Girman CJ, Oesterling JE, Guess HA, Jacobsen SJ, Lieber MM.**
   The prevalence of prostatism: a population based survey of urinary symptoms. J Urol 1993; 150: 85-89.
10. **Sirls LT, Kirkemo AK, Jay J.**
    Lack of correlation of the American Urological Association Symptom 7 Index with urodynamic gladder outlet obstruction. Neurourol Urodyn. 1996;15(5):447-56.
11. **Hansen BJ, Flyger H, Brasso K, Schou J, Nordling J, Thorup Andersen J, Mortensen S, Meyhoff HH, Walter S, Hald T.**
    Validation of the self-administratered Danish Prostatic Symptom Score (DAN-PSS-1) system for use in benign prostatic hyperplasia. Br J Urol 1995, 76: 451–458.
12. **Pannek J, Berges RR, Haupt G and Senge T.**
    Value of the Danish Prostate Symptom score compared to the AUA symptom score and pressure/flow studies in the preoperative evaluation of men with symptomatic benign prostatic hyperplasia. Neurourol. Urodyn 1998; 16: 9–18.
13. **Hansen BJ, Mortensen S, Mensink HJA, Flyger H, Riehmann M, Hendolin N, Nordling J, Hald T.**
    Comparison of the Danish prostatic symptom score with the International Prostatic Symptom Score, the Madsen-Iversen and Boyarsky symptom indexes. Br J Urol 1998; 81: 36-41.

14. **Hunter DJW, McKee M, Black NA, Sanderson CFB.**
Health status and quality of life of British men with lower urinary tract symptoms: results from the SF 36. Urology 1995; 45: 962–971.
15. **Kaplan SA, Olsson CA, Te AE.**
The American Urological Association symptom score in the evaluation of men with lower urinary tract symptoms: at 2 years of follow-up, does it work? J. Urol. 1996 Jun;155(6):1971-4.
16. **Emberton M, Black N.**
Impact of non-response and of late-response by patients in a multi-centre surgical outcome audit. Int J Qual Health Care. 1995 Mar;7(1):47-55.
17. **Hakenberg OW, Pinnock CB, Marshall VR.**
Does evaluation with the International Prostate Symptom Score predict the outcome of transurethral resection of the prostate? J Urol. 1997 Jul;158(1):94-9.
18. **Herschman JD, Smith DS, Catalona WJ.**
Effect of ejaculation on serum total and free prostate specific antigen concentrations. Urology 1997; 50: 239-243.
19. **Oesterling JE, Jacobsen SJ, Chute CG, Guess HA, Girman CJ, Panser LA, Lieber MM.**
Serum prostate specific antigen in a community-based population of healthy men: establishment of age-specific reference ranges. JAMA 1993; 270: 860–866.
20. **Laguna P and Alivizatos G.**
Prostate specific antigen and benign prostatic hyperplasia. Curr Opin Urol 2000; 10: 3-8.
21. **Eastham JA, Sartor O, Richey W, Moparty B, Sullivan J.**
Racial variation in prostate specific antigen in a large cohort of men without prostate cancer. J La State Med Soc 2001; 153: 184–189.
22. **Cooney KA, Strawderman MS, Wojno KJ, Doerr KM, Taylor A, Alcser KH, Heeringa SG, Taylor JM, Wei JT, Montie JE, Schottenfeld D.**
Age-specific distribution of serum prostate-specific antigen in a community-based study of African-American men. Urology 2001; 57: 91–96.
23. **Stamey TA, Yang N, Hay AR, McNeal JE, Freiha FS, Redwine E.**
Prostate specific antigen as a serum marker for adenocarcinoma of the prostate. N Engl J Med 1987; 317: 909-914.
24. **Roehrborn CG, Boyle P, Gould AL, Waldstreicher J.**
Serum prostate specific antigen as a predictor of prostate volume in men with benign prostatic hyperplasia. Urology 1999; 53: 581-589.
25. **Morote J, Encabo G, Lopez M, de Torres IM.**
Prediction of prostate volume based on total and free serum prostate specific antigen: is it reliable? Eur Urol 2000; 38: 91-95.
26. **Barry MJ.**
Prostate specific antigen. Testing for early diagnosis of prostate cancer. N Engl J Med 2001; 344: 1373-1377
27. **Potter SR, Horniger W, Tinzl M, Bartsch G, Partin A.**
Age, prostate specific antigen and digital rectal examination as determinants of the probability of having prostate cancer. Urology 2001; 57: 1100-1103.
28. **Roehrborn CG, McConnell JD, Lieber M, Kaplan S, Geller J, Malek GH, Castellanos R, Coffield S, Saltzman B, Resnick M, Cook TJ, Waldstreicher J.**
Serum prostate specific antigen concentration is a powerful prediction of acute urinary retention and need for surgery in men with clinical benign prostatic hyperplasia. PLESS Study Group. Urology 1999; 53: 473-480.
29. **Roehrborn CG, Malice MP, Cook TJ, Girman CJ.**
Clinical predictors of spontaneous acute urinary retention in men with LUTS and clinical BPH: A comprehensive analysis of the pooled placebo groops of several large clinical trials. Urology 2001; 58: 210-216.
30. **Meigs JB, Mohr B, Barry MJ, Collins MM, McKinlay JB.**
Risk factors for clinical benign prostatic hyperplasia in a community-based population of healthy aging men. J Clin Epidemiol 2001; 54: 935-944.
31. **Djavan B, Bursa B, Basharkhah A, Seitz C, Remzi M, Ghawidel K, Hruby S, Marberger M.**
Pretreatment prostate-specific antigen as an outcome predictor of targeted transurethral microwave thermotherapy. Urology 2000; 55: 51-57.

3.3 Creatinine measurement

It is well-accepted today that bladder outlet obstruction due to BPH might cause hydronephrosis and renal failure (1). Ten years ago, it was shown that patients with BPH and renal insufficiency had a 25% risk of

developing post-operative complications compared with the 17% risk in patients with normal renal function (2). Earlier studies also showed a much higher mortality among BPH patients who underwent surgical treatment when renal insufficiency was present at the same time (3,4).

Most studies have found that the incidence of azotaemia in men with BPH varies from 15-30% (5,6). However, these figures might be overestimates as these studies involved patients undergoing surgical treatment (i.e. those with severe symptoms and with urinary retention). A recent study evaluated 246 men presenting with BPH symptoms and found that approximately one in 10 (11%) had renal insufficiency (7). It was also shown that neither the symptom score nor the quality-of-life assessment was associated with serum creatinine levels in patients with BPH. When renal dysfunction was present, diabetes and hypertension were the most probable causes of the elevated creatinine level among this group of patients. This study also noted that it was rather rare to find patients with high creatinine levels due to bladder outlet obstruction only.

Comiter et al. (8) reported a study in which voiding dysfunction of a non-neurogenic aetiology did not appear to be a risk factor for elevated BUN (blood urea/nitrogen) and creatinine levels. Bruskewitz et al. (9) also found that an isolated serum creatinine level could not predict the outcome after TURP, as measured by an improvement in quality of life. Despite all of the above, it is probably unwise to avoid measuring serum creatinine levels in patients undergoing BPH evaluation in an effort to minimize costs. Koch et al. (10) studied the additional value of renal ultrasonography in the assessment of patients with BPH and concluded that only those with an elevated creatinine level needed such an investigation.

3.3.1 Conclusions

As it is difficult to select those with renal insufficiency from among evaluable BPH patients, it is probably cost effective to measure serum creatinine levels in all patients. In this way, proper therapy can be offered to the right men and the costs of long-term renal damage and post-surgical complications can be avoided. This point is increasingly emphasized, as the use of certain α-blockers might cause additional problems in men with renal insufficiency. In the report from the AHCPR (11) and in the recommendations of the Fourth International Consultation on BPH (12), the measurement of creatinine is highly recommended.

3.3.2 REFERENCES

1. **Sacks SH, Aparicio SAJR, Bevan A, Oliver DO, Will EJ, Davison AM.**
   Late renal failure due to prostatic outflow obstruction: a preventable disease. Br Med J 1989; 298: 156-159.
2. **Mebust WK, Holtgrewe HL, Cockett AT, Peters PC.**
   Transurethral prostatectomy: immediate and post-operative complications. A comparative study of 13 participating institutions evaluating 3,885 patients. J Urol 1989; 141: 243-247.
3. **Holtgrewe HL, Valk WL.**
   Factors influencing the mortality and morbidity of transurethral prostatectomy: a study of 2015 cases. J Urol 1962; 87: 450-459.
4. **Melchior J, Valk WL, Foret JD, Mebust WK.**
   Transurethral prostatectomy in the azotemic patient. J Urol 1974; 112: 643-646.
5. **Roehrborn CG.**
   Initial diagnostic evaluation of men with lower urinary tract symptoms. In: Cockett ATK et al. (eds). Proceedings of the Third International Consultation on Benign Prostatic Hyperplasia (BPH). Scientific Communication International: Geneva, 1996, pp. 167-254.
6. **Mukamel E, Nissenkorn I, Boner G, Servadio C.**
   Occult progressive renal damage in the elderly male due to benign prostatic hypertrophy. J Am Geriatr Soc 1979; 27: 403-406.
7. **Gerber GS, Goldfisher ER, Karrison TG, Bales GT.**
   Serum creatinine measurement in men with lower urinary tract symptoms secondary to benign prostatic hyperplasia. Urology 1997; 49: 697-702.
8. **Comiter GV, Sullivan MP, Schacterle RS, Cohen LH, Valla SV.**
   Urodynamic risk factors for renal dysfunction in men with obstructive and non-obstructive voiding dysfunction. J Urol 1997; 158: 181-185.
9. **Bruskewitz RC, Reda DJ, Wasson JH, Barrett L, Phelan M.**
   Testing to predict outcome after transurethral resection of the prostate. J Urol 1997; 157: 1304-1308.
10. **Koch WF, Ezz El Din K, de Wildt MJAM, Debruyne FM, de la Rosette JJ.**
    The outcome of renal ultrasound in the assessment of 556 consecutive patients with benign prostatic hyperplasia. J Urol 1995; 155: 186-189.
11. **McConnell JD, Barry MJ, Bruskewitz RC.**
    Benign Prostatic Hyperplasia: Diagnosis and Treatment. Quick Reference Guide for Clinicians. AHCPR

publication 94-0583. Agency for Health Care Policy and Research, Public Health Service, US Department of Health and Human Services: Rockville, MD, February 1994.

12. **Koyanagi T, Artibani W, Correa R et al.**
In: Denis L, Griffiths K, Khoury S et al. (eds). Proceedings of the Fourth International Consultation on BPH, Paris, July 1997. Health Publications: Plymouth, 1998, pp. 179-265.

3.4 Urinalysis

Since LUTS is not only observed in patients with BPH, but also frequently in men with urinary tract infections, whether related or not to benign enlargement of the gland, and in at least 25% of patients with carcinoma of the bladder, analytical and microscopic urine analysis was considered to be mandatory.

However, microscopic urine analysis has not been accepted as a screening test for the early detection of severe urological diseases, such as malignancies. This is mainly due to the low specificity of this highly sensitive test, causing unnecessary further diagnostic measures in a large number of patients.

Overall, we concluded that this inexpensive test which does not require sophisticated technical equipment should be incorporated in the primary evaluation of any patient presenting with LUTS

3.4.1 Conclusions

Urinalysis may be included in the primary evalution. However, it should be noted that there is little evidence in the literature to support this conclusion.

3.5 Digital rectal examination (DRE)

Digital rectal examination (DRE) is an important examination in men with LUTS for two reasons. Firstly, it can help to determine the co-existence of prostatic carcinoma. Secondly, it enhances the capacity to estimate prostate volume, and in this way may assist in choosing the right treatment, as prostate size has been shown to be a determining factor for certain treatment options.

3.5.1 DRE and cancer detection

The positive predictive value (PPV) of a suspicious DRE to actually diagnose prostate cancer is 26-34% (1). These figures are based on screening studies and it is believed that DRE will have a higher PPV for cancer among men with LUTS as these patients are usually older.

Fowler et al. (2000) found that when DRE is the only indication of malignancy, prostate cancer detection is equivalent in black and white men (2).

Potter et al. (2001) used three clinical parameters, age, PSA and DRE, to determine the probability of having prostate cancer and constructed a nomogram to help in the decision whether or not to perform a prostate biopsy. In this study, DRE had a significant influence on the likelihood of a positive biopsy in all PSA and age ranges (3).

In the 'Early Detection Project Group' of the German Urological Association, the PPV was 16% for DRE, 17% for PSA and 51% for the combination of both. This study recommends the combination of PSA (cut-off value 4.0 ng/ml) and DRE in the early detection of prostate cancer (4).

An important new issue is the value of DRE in detecting cancer in patients with PSA levels less than 4.0 ng/ml. Preliminary results from the European Randomized Study of Screening for Prostate Cancer (ERSPC) in Europe have questioned the value of DRE for screening at low PSA levels (5,6).

3.5.2 DRE and prostate size evaluation

A number of options are currently available for the treatment of patients with BPH. Response to certain types of therapy, e.g. finasteride, depends on the actual prostate volume. In patients for whom invasive therapy, such as surgery, is recommended, an estimation of the prostate gland volume will help the urologist to select the most suitable form of treatment with the lowest cost and best outcome.

Correct estimation of the prostatic volume by DRE is not an easy task and therefore investigators for the PLCO (Prostate, Lung, Colorectal and Ovarian Cancer) trial have described quality-control procedures for DRE examination (7).

It is well-accepted that TRUS is more accurate in determining prostate volume than DRE. Roehrborn, has analyzed the data from four studies in which estimations of prostate volume by DRE were compared with those performed by TRUS (8). Although different methods and criteria were used in the four studies, it was concluded that underestimation of DRE increased with increasing TRUS volume, particularly if the volume was greater than 30 ml. For this reason, Roehrborn developed a model of visual aids to help urologists predict prostate volume more accurately (9). Similar models to assist training for DRE examination have been proposed by other groups as well (10).

Finally, Frank et al. (2001) have compared the knee-elbow to the left-lateral position of the patient in

examining and evaluating the prostate. They concluded that both methods were equal in completeness of examination, pain, and embarrassment (11).

3.5.3 Conclusions

1. DRE is an important examination in excluding prostatic carcinoma and other pelvic pathologies.
2. DRE is useful in evaluating the size of the prostate gland but proper training is needed.

3.5.4. Recommendations

DRE is considered as a standard procedure in the evaluation of men with LUTS.

3.5.5 REFERENCES

1. **M. Resnick, R. Ackerman, J Bosch, J Cidre, K. Foo, I. Frand.**
   Fifth International Consultation on BPH. In: Chatelain C, Denis L, Foo S, Khoury S, McConnell J (eds). Benign Prostatic Hyperplasia. Plymbride Distributions, 2000, pp. 169-188.
2. **Fowler JE JR, Bigler SA, Farabaugh PB, Wilson SS.**
   Prostate cancer detection in Black and White men with abnormal digital rectal examination and prostate specific antigen less then 4 ng/ml. J Urol 2000; 164: 1961-1963.
3. **Potter SR, Horniger W, Tinzl M, Bartsch G, Partin AW.**
   Age, prostate-specific antigen, and digital rectal examination as determinants of the probability of having prostate cancer. Urology 2001; 57: 1100-1104.
4. **Luboldt HJ, Bex A, Swoboda A, Husing J, Rubben H.**
   Early detection of prostate cancer in Germany. A study using digital rectal examination and 4.0 ng/ml prostate-specific antigen as cutoff. Eur Urol 2001; 39: 131-137.
5. **Vis AN, Hoedemaeker RF, van der Kwast TH, Schröder FH.**
   Defining the window of opportunity in screening for prostate cancer validation of a predictive tumor classification model. Prostate 2001; 46: 154-162.
6. **Shröder FH, Roobol-Bouts M, Vis AN, van der Kwast T, Kranse R.**
   Prostate-specific antigen-based early detection of prostate cancer validation of screening without rectal examination. Urology 2001; 57: 83-90.
7. **Weissfeld JL, Fagerstrom RM, O'Brien B.**
   Quality control of cancer screening examination procedures in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial. Control Clin Trials 2000; 21(Suppl 6): S390-399.
8. **Roehrborn CG.**
   Accurate determination of prostate size via digital rectal examination and transpectal ultrasound. Urology 1998; 51(Suppl 4A): 19-20.
9. **Roehrborn CG, Sech S, Montoya J, Rhodes T, Girman CJ.**
   Interexaminer reliability and validity of a three-dimensional model to assess prostate volume by digital rectal examination. Urology 2001; 57: 1087-1092.
10. **Burdea G, Patounakis G, Popescu V, Wiss RE.**
    Virtual reality-based training for the diagnosis of prostate cancer.
    IEEE Trans Biomed Eng 1999; 46: 1253-1260.
11. **Frank J, Thomas K, Oliver S, Andrews S, Choong S, Taylor R, Emberton M.**
    Couch or crouch? Examining the prostate, a randomized study comparing the knee-elbow and the left-lateral position. BJU Int 2001; 87: 331-333.

3.6 Imaging of the urinary tract

Imaging of the entire (including the upper) urinary tract, particularly prior to prostate surgery, has been an integral part of the diagnostic assessment of elderly men with LUTS due to BPH during past decades (1–12). In parallel with endoscopy, the role of routine imaging of the upper and lower urinary tract in all patients with LUTS has been increasingly questioned in recent years (5,6,9,13). Ideally, an imaging modality for patients with LUTS should provide both imaging of the urinary tract and demonstrate the morphological effects of prostate pathology upon the rest of the lower and/or upper urinary tract.

3.6.1 Upper urinary tract

A recent survey of 24 urological centres in the UK found that 21 of 24 centres (79%) used either intravenous urography (IVU) or sonography, and that 16 of 24 centres (67%) used plain films as routine procedures prior to

prostatectomy (14). Similar findings, particularly a high rate of IVU, have been reported in the USA (15). The most common argument in favour of routine imaging of the upper urinary tract was 'not to miss anything'.

Data from several large-scale studies have led to doubts concerning the role of routine upper urinary tract imaging in patients with LUTS. Wilkinson and Wild (12) reported on 175 patients with LUTS with no urinary retention and identified no abnormalities on renal ultrasound and IVU that would have altered the therapeutic approach. Similar data have been published by Koch et al., who performed renal ultrasound scans in a consecutive series of 556 elderly men with LUTS; 14 (2.5%) had hydronephrosis (13). Serum creatinine levels appeared to be correlated with dilatation of the renal pelvis. The authors concluded that renal ultrasound is only indicated in patients with an elevated serum creatinine level and/or post-void residual urine volume (13).

A recent review was carried out on data from 25 published reports on the findings of IVU. A total of 6,131 men from nine ultrasound series were involved, including 778 patients with LUTS due to BPH. The mean patient age in these series was 68.4 years (16). Overall, 74.3% of all IVUs and 70% of all the ultrasound studies performed were normal. Hydronephrosis was found in 7.6% of IVU and 6.8% of ultrasonography patients; 30% had measurable degrees of renal insufficiency. Poor or no renal function was found in 12.3% and 0.8%. Renal cysts were seen in 4.5% and 15.3%, and solid renal masses were identified in 0.81% and 0.51% of IVU and of ultrasonography patients, respectively.

These data need to be correlated with the incidence of renal cell cancer in the general population. Based on several autopsy and epidemiological studies, it has been estimated that the risk of elderly men developing renal cell cancer ranges from 0.18% to 0.56%. These figures are comparable with the results of large-scale studies in elderly men with LUTS and indicate that the incidence of renal carcinoma is not increased in these patients.

Other malignancies found during routine examination of the urinary tract are bladder and ureteral cancer, usually seen in about 1% of cases. However, most of the cancers suspected during imaging were not identified during endoscopy. A number of tumours were identified during endoscopy that had been overlooked during imaging.

IVU adverse events

A review of 10 reported studies involving over 2.1 million patients revealed an incidence of adverse effects due to contrast medium in approximately 6% of patients, an incidence of serious adverse effects in 1 in 1,000-2,000, and a risk of dying from an allergic reaction of 1 in 100,000-200,000 (17,18). The average radiation dose is 1.58 rem. Low-osmolar contrast material (LOCM) resulted in a six-fold improvement in safety compared with high-osmolar contrast material (18). Furthermore, in patients with pre-existing renal failure, the use of LOCM reduces the risk of nephrotoxicity (18).

IVU or renal ultrasound

Several arguments support the use of renal ultrasound. Among the most important are:

- Better characterization of renal masses
- Possibility of investigating the liver and retroperitoneum
- Simultaneous evaluation of the bladder, post-void residual urine volume and prostate
- Costs
- Avoidance of irradiation
- No side-effects.

3.6.2 Lower urinary tract

Urinary bladder voiding cysto-urethrogram

This investigation suffers from the fact that the information on the lower urinary tract is only indirect and gives, at best, only limited urodynamic information. It is therefore not recommended in the routine diagnostic work-up of elderly men with LUTS. More recently, the measurement of bladder wall thickness by transabdominal ultrasound has gained considerable interest as a non-invasive tool to assess bladder outflow obstruction (19). Manieri et al. (20) concluded that bladder wall thickness appeared to be a useful predictor of bladder outlet obstruction, with a value exceeding that of uroflowmetry. Reliable data on inter- and intra-observer variability, as well as reproducibility, are still lacking and, therefore, measurement of bladder wall thickness is currently not part of the recommended diagnostic work-up of patients with LUTS.

3.6.3 Urethra

Retrograde urethrography gives only indirect information on the effect of benign prostatic enlargement (BPE) on adjacent structures.

3.6.4 Prostate

Imaging of the prostate is performed to assess:

- Prostate size
- Prostate shape
- Occult carcinoma
- Tissue characterization.

Choice of imaging modalities
The prostate can be imaged using:
- Transabdominal ultrasound
- TRUS
- Computed tomography (CT) and magnetic resonance imaging (MRI) (including transrectal MRI).

In daily routine practice, however, only imaging of the prostate by TRUS, or, if this is not available, by transabdominal ultrasound, is currently used (21).

Prostate size
A large body of evidence documents the accuracy of TRUS in calculating the volume of the prostate (22,23). TRUS has significantly higher accuracy than that of cystoscopy, IVU, rectal examination and or urethral pressure profile (24). The prostate volume estimated by DRE and endoscopy is known to underestimate prostates over 40 mL in size (24). Prostate volume can be estimated by serial planimetry, orthogonal plane, rotational body (single plane, ellipsoid) and three-dimensional methods (23).

Clinical relevance of prostate size
A number of studies indicate that prostate size is a (weak) outcome predictor in the emerging field of less invasive procedures. Outcome is usually more favourable in patients with smaller prostates, particularly for visual laser ablation (VLAP), interstitial laser coagulation (ILC), transurethral electrovaporization (TUVP) and (TUNA®). However, there is no generally accepted volume for which these less invasive procedures are contraindicated. In contrast, it has been demonstrated that high-energy (TUMT) is more suitable for patients with larger prostates. With transurethral/open prostatectomy, the critical volume is approximately 80 mL, while for transurethral incision of the prostate (TUIP) or TURP the critical volume is 25-30 mL. For finasteride therapy, the critical volume is 40 mL.

Prostate shape
Watanabe (25) introduced the concept of the presumed circle area ratio (PCAR). This is based on the usual normal triangular-shaped appearance of the prostate in the absence of BPE. In BPE, the shape of the prostate is changed by the continuous growth of the transition zone. Watanabe reported that pathological residual urine is seen if the PCAR is greater than 0.75 or less than 75, and that BPE is very unlikely to be the cause of the post-void residual urine volume. More likely causes include bladder cancer or prostate cancer. However, validation of these data by others is still lacking.

3.6.5 REFERENCES

1. **Andersen JT, Jacobsen O, Standgaard L.**
   The diagnostic value of intravenous pyelography in infravesical obstruction in males.
   Scand J Urol Nephrol 1977; 11: 225-230.
2. **Bohne AW, Urwiller RD, Pantos TG.**
   Routine intravenous urograms prior to prostatectomy. J Urol 1961; 86: 171-172.
3. **Bundrick TJ, Katz PG.**
   Excretory urography in patients with prostatism. Am J Radiol 1986; 147: 957-959.
4. **Butler MR, Donnelly B, Domaranchat A.**
   Intravenous urography in evaluation of acute retention. Urology 1978; 12: 464-466.
5. **Christofferson I, Moller I.**
   Excretory urography: a superfluous routine examination in patients with prostatic hypertrophy.
   Eur Urol 1981; 7: 65-67.
6. **DeLacey G, Johnson S.**
   Prostatism: how useful is routine imaging of the urinary tract? Br Med J 1988; 296: 965-967.
7. **Donker PJ, Kakiailatu F.**
   Preoperative evaluation of patients with bladder outlet obstruction with particular regard to excretory urography. J Urol 1978; 120: 685–686.
8. **Marshall V, Singh M, Blandy JP.**
   Is urography necessary for patients with acute retention of urine before prostatectomy?
   Br J Urol 1974; 46: 73-76.
9. **Morrison JD.**

Help or habit? Excretion urography before prostatectomy. Br J Clin Pract 1980; 34: 239-241.
10. **Pinck BD, Corrigan MJ, Jasper P.**
Pre-prostatectomy excretory urography: does it merit the expense? J Urol 1980; 123: 390-391.
11. **Wasserman NF, Lapointe S, Eckmann DR, Rosel PR.**
Assessment of prostatism: role of intravenous urography. Radiology 1987; 165: 831-835.
12. **Wilkinson AG, Wild SR.**
Is pre-operative imaging of the urinary tract worthwhile in the assessment of prostatism?
Br J Urol 1992; 70: 53-57.
13. **Koch WF, Ezz el Din K, de Wildt MJ, Debruyne FM, de la Rosette JJ.**
The outcome of renal ultrasound in the assessment of 556 consecutive patients with benign prostatic hyperplasia. J Urol 1996; 155: 186-189.
14. **Wilkinson AG, Wild SR.**
Survey of urological centres and review of current practice in the pre-operative assessment of prostatism. Br J Urol 1992; 70: 43-45.
15. **Holtgrewe HL, Mebust WK, Dowd JB, Cockett AT, Peters PC, Proctor C.**
Transurethral prostatectomy: practice aspects of the dominant operation in American urology.
J Urol 1989; 141: 248-253.
16. **Koyanagi T, Artibani W, Correa R et al.**
In: Denis L, Griffiths K, Khoury S et al. (eds). Proceedings of the Fourth International Consultation on BPH, Paris, July 1997. Health Publications: Plymouth, pp. 179-265.
17. **Barrett BJ, Carlisle EJ.**
Meta-analysis of the relative nephrotoxicity of high- and low-osmolarity iodinated contrast media.
Radiology 1993; 188: 171-178.
18. **Thomson HS, Dorph S.**
High-osmolar and low-osmolar contrast media. Acta Radiol 1993; 34: 205-209.
19. **Kojima M, Inui E, Ochiai A, Naya Y, Ukimura O, Watanabe H.**
Noninvasive quantitative estimation of infravesical obstruction using ultrasonic measurement of bladder weight. J Urol 1997; 157: 476-479.
20. **Manieri C, Carter SS, Romano G, Trucchi A, Valenti M, Tubaro A.**
The diagnosis of bladder outlet obstruction in men by ultrasound measurement of bladder wall thickness. J Urol 1998; 159: 761-765.
21. **Scheckowitz EM, Resnick MI.**
Imaging of the prostate. Benign prostatic hyperplasia. Urol Clin North Am 1995; 22: 321-332.
22. **Aarnink RG, de la Rosette JJ, Debruyne FM, Wijkstra H.**
Reproducibility of prostate volume measurements from transrectal ultrasonography by an automated and a manual technique. Br J Urol 1996; 78: 219-223.
23. **Aarnink RG, Beerlage HP, de la Rosette JJ, Debruyne FM, Wijkstra H.**
Transrectal ultrasound of the prostate: innovations and future applications. J Urol 1998; 159: 1568-1579.
24. **Roehrborn CG.**
Accurate determination of prostate size via digital rectal examination and transrectal ultrasound.
Urology 1998; 51: 19-22.
25. **Watanabe H.**
New concept of BPH: PCAR theory. Prostate 1998; 37: 116-125.

3.7 Voiding charts (diaries)

Voiding charts (diaries) are simple to complete and can provide useful objective clinical information (1,2). There is no standard frequency volume chart available. However, recent data indicate that a 24-hour voiding chart is sufficient and that longer time periods provide only little additional information (3). There is a close correlation between LUTS, as assessed by symptom scores, and data generated by voiding charts, such as frequency and nocturia. The ICS BPH study reported an exact correlation in 41% of the number of voids, 61% for the time of voids and 68% for episodes of nocturia (2). Voiding charts allow, for example, the identification of patients with nocturnal polyuria, one of the causes of nocturia in elderly men (4–6).

3.7.1 Conclusions

Recording of a 24-hour frequency volume chart in the course of an initial consultation is considered to be a standard investigation. A frequency volume chart is non-invasive, inexpensive, and provides important insight into LUTS.

3.7.2 REFERENCES

1. **Abrams P, Klevmark B.**
   Frequency volume charts: an indispensable part of lower urinary tract assessment.
   Scand J Urol Nephrol 1996; 179: 47-53.
2. **Reynard JM, Yang Q, Donavan JL, Peters TL, Schäfer W, de la Rosette JJ, Dabhoiewala NF, Osawa D, Lim AT, Abrams P.**
   The ICS-BPH study: uroflowmetry, lower urinary tract symptoms and bladder outlet obstruction.
   Br J Urol 1998; 82: 619-623.
3. **Gisholf KWH, van Venrooij GEPM, Eckhardt MD, Boon TA.**
   Analysis and reliability of data from 24-hour frequency-volume charts in men with lower urinary tract symptoms due to benign prostatic hyperplasia. Eur Urol 2000; 38: 45-52.
4. **Van Venrooij GEPM, Eckhardt MD, Gisholf KWH, Boon TA.**
   Data from frequency-volume charts versus symptom scores and quality of life score in men with lower urinary tract symptoms due to benign prostatic hyperplasia. Eur Urol 2001; 39: 42-47.
5. **Blanker MH, Bohnen AM, Groeneveld FPMJ, Bernsen RMD, Prins A, Bosch JLHR.**
   Normal voiding patterns and determinants of increased diurnal and nocturnal voiding frequency in elderly men. J Urol 2000; 164: 1201-1205.
6. **Matthiesen TB, Rittig S, Mortensen JT, Djurhuus JC.**
   Nocturia and polyuria in men referred with lower urinary tract symptoms, assessed using a 7-day frequency-volume chart. Br J Urol Int 1999; 83: 1017-1022.

3.8 Urodynamic studies

Pressure-flow studies are regarded as an additional diagnostic test and are considered optional by both the AHCPR (1) and the Fifth International Consultation on BPH (2). Flow rates only determine the probability of obstruction, whereas pressure-flow studies can categorize the degree of obstruction and identify patients in whom a low flow rate may be due to a low-pressure detrusor contraction. Flow rates may be particularly limited in predicting obstruction in specific situations, such as in elderly patients, individuals with low voided volumes, or men with a Qmax of more than 10 mL/s, as well as in the presence of neurological disease. Although pressure-flow studies are the only means of diagnosing obstruction accurately, debate continues as to their role in predicting treatment outcomes. Recent methodological studies looking on intraindividual variation in pressure-flow results (3,4,5) as well as intra- and interindividual observer accuracy in interpretation of pressure-flow curves (6) have demonstrated a considerable methodological variation. This makes it more difficult to judge the influence of infravesical obstruction on lower urinary tract symptoms in patients with BPH. For this reason, and because pressure-flow studies are regarded as invasive, they remain optional. In specific patient subgroups, the case for pressure-flow studies is stronger.

The methodology for performing pressure-flow studies is now standardized (7) and requires the simultaneous recording of both intravesical and intra-abdominal pressure. Detrusor pressure at the point of maximum flow must be recorded in order to diagnose obstruction. Different nomograms exist with which to classify patients into categories of obstruction. Those developed by Schafer (8), Abrams and Griffiths (9) and Rollema and van Mastrigt (URA - Urethral Resistance Index) (10) are most commonly used, and they all correlate closely. The ICS (International Continence Society) nomogram (11) has now been adopted as the standard nomogram to aid comparison of different data sets, and should be used in clinical practice.

3.8.1 Outcome

Pressure-flow studies do not predict the response to medical therapy and have no role in this setting. However, it is known that patients with high-pressure and low-flow urodynamics have the best outcome from prostatectomy. Patients with low-pressure and low-flow urodynamics may also have a successful outcome following prostatectomy, but the probability is lower.

Most work in relation to pressure-flow studies and treatment of BPH relates to TURP. Studies from Neal et al. (12,13), Abrams et al. (14), Jensen (15), Robertson et al. (16) and Langen et al. (17) all report improved outcomes in patients who are obstructed prior to surgery, based on pressure-flow studies

3.8.2 Conclusions

Pressure-flow studies remain optional tests in straightforward cases presenting for the first time with LUTS. These studies are the most useful investigations available for the purpose of counselling patients regarding the outcome of surgical therapies for BPH. The ICS nomogram should be used for the diagnosis of obstruction in order to standardize data for comparative purposes.

3.8.3 REFERENCES

1. **McConnell JD, Barry MJ, Bruskewitz RC.**
   Benign Prostatic Hyperplasia: Diagnosis and Treatment. Quick Reference Guide for Clinicians. AHCPR publication no. 94-0583. Agency for Health Care Policy and Research, Public Health Service, US Department of Health and Human Services: Rockville, MD, February 1994.
2. **Chatelain C, Denis L, Foo KT, Khoury S, McConnell J (eds.).**
   Proceedings of the Fifth International Consultation on BPH, Paris, July 2000. Health Publications, Plymouth 2001: 524.
3. **Hansen F, Olsen L, Atan A, Nordling J.**
   Pressure-flow studies: Short term repeatability. Neurourol Urodyn 1999;18:205-14.
4. **Sonke GS, Kortmann BB, Verbeek AL, Kiemeney LA, Debruyne F, de La Rossette JJ.**
   Variability of pressure-flow studies in men with lower urinary tract symptoms.
   Neurourol Urodyn 2000;19:637-51.
5. **Eri LM, Wessel N, Berge V.**
   Test-retest variation of pressure flow parameters in men with bladder outlet obstruction.
   J Urol 2001;165:1188-92.
6. **Kortmann BB, Sonke GS, Wijkstra H, Nordling J, Kallestrup E, Holm NR, de La Rosette JJ.**
   Intra- and Inter-investigator variation in the analysis of pressure-flow studies in men with lower urinary tract symptoms. Neurourol Urodyn 2000;19:221-32.
7. **Rowan D, James ED, Kramer AE, Sterling AM, Suhel PF.**
   Urodynamic equipment: technical aspects. Produced by the International Continence Society Working Party on Urodynamic Equipment. J Med Eng Technol 1987; 11: 57-64.
8. **Schafer W.**
   A new concept for simple but specific grading of bladder outflow condition independent from detrusor function. J Urol 1993; 149: 574-577.
9. **Abrams P, Griffiths DJ.**
   The assessment of prostatic obstruction from urodynamic measurements and from residual urine.
   Br J Urol 1979; 51: 129-134.
10. **Rollema HJ, van Mastrigt R.**
    Improved indication and follow-up in transurethral resection of the prostate using the computer program CLIM: a prospective study. J Urol 1992; 148: 111-116.
11. **Griffiths D, Hofner K, van Mastrigt R, Rollema HJ, Spangberg A, Gleason D.**
    Standardization of terminology of lower urinary tract function: pressure-flow studies of voiding, urethral resistance and urethral obstruction. International Continence Society Subcommittee on Standardization of Terminology of Pressure-Flow Studies. Neurourol Urodyn 1997; 16: 1-18.
12. **Neal DE, Styles RA, Powell PH, Thong J, Ramsden PD.**
    Relationship between voiding pressure, symptoms and urodynamic findings in 253 men undergoing prostatectomy. Br J Urol 1987; 60: 554-559.
13. **Neal DE, Ramsden PD, Sharples L, Smith A, Powell PH, Styles RA, Webb RJ.**
    Outcome of elective prostatectomy. BMJ 1989; 299: 762-767.
14. **Abrams PH, Farrar DJ, Turner-Warwick RT, Whiteside CG, Feneley RC.**
    The results of prostatectomy: a symptomatic and urodynamic analysis of 152 patients.
    J Urol 1979; 121: 640-642.
15. **Jensen KM-E.**
    Clinical evaluation of routine urodynamic investigations in prostatism.
    Neurourol Urodynam 1989; 8: 545-578.
16. **Robertson AS, Griffiths C, Neal DE.**
    Conventional urodynamics and ambulatory monitoring in the definition and management of bladder outflow obstruction. J Urol 1996; 155: 506-511.
17. **Langen PH, Schafer W, Jakse G.**
    Urodynamic assessment in patients undergoing transurethral resection of the prostate: a prospective study. In: Benign Prostatic Hyperplasia: Conservative and Operative Management. Jakse G, et al. (eds). Springer-Verlag:New York, 1992, 75-84.

3.9 Endoscopy

The standard endoscopic procedure for diagnostic evaluation of the lower urinary tract (urethra, prostate, bladder neck and bladder) is a urethrocystoscopy. This investigation can confirm causes of outflow obstruction while eliminating intravesical abnormalities.

3.9.1 LUTS caused by bladder outlet obstruction

Voiding complaints in elderly men are most frequently caused by BPH resulting in benign prostatic obstruction. This obstruction has a critical role in altering voiding, resulting in significant (pathological) changes in the urinary tract of some patients and symptoms alone in others. However, the role of BPH in the voiding dysfunction experienced by elderly men is often unclear (1). Hyperplasia may be associated with striking lateral lobe enlargement, but symptoms may be negligible if the degree of obstruction is not severe. Conversely, BPH may be associated with a relatively small prostate and marked obstructive symptoms if the obstructing tissue originates exclusively within the central zone of the peri-urethral gland area (2).

It is generally accepted that therapies aimed at removing obstruction will relieve LUTS in most men. Patients with BPH or other forms of bladder outlet obstruction may develop certain signs seen by urethrocystoscopy, indicating the presence of such obstruction. These signs may include:

- Enlargement of the prostate gland with visual obstruction of the urethra and the bladder neck
- Obstruction of the bladder neck by a high posterior lip of the bladder neck
- Muscular hypertrophy of the detrusor muscle, indicated by the presence of muscular trabeculation and the formation of cellules as well as diverticula
- Formation of bladder stones
- Retention of (post-void residual) urine.

Thus, urethrocystoscopy may provide information about the cause, size and severity of obstruction, patency of the bladder neck, prostatic occlusion of the urethra and estimated prostate size (3). Several studies have addressed these issues.

3.9.2 Morbidity of urethrocystoscopy

Berge et al. (4) studied 85 patients and found that the risk of acquiring clinically significant urinary tract infection was 2.4% after urethral instrumentation alone.

3.9.3 Relationship between trabeculation and peak flow rate

Shoukry et al. (5) evaluated 122 patients of mean age 64 years with LUTS using three post-operative uroflowmetry tests and symptom evaluation. Urethrocystoscopy was also performed in these patients. The pre-operative peak flow rate was normal in 25% of 60 patients who had no bladder trabeculation, 21% of 73 patients with mild trabeculation and 12% of 40 patients with marked trabeculation on cystoscopy. All 21 patients who presented with diverticula had an ‘obstructive’ peak flow rate prior to surgery.

Anikwe (6) showed that there was no significant correlation ($p > 0.5$) between the degree of trabeculation, as graded from I to IV, and the peak pre-operative flow rate in 39 men aged 53–83 years with LUTS. There appeared to be a trend towards lower peak flow rates in men with higher degrees of trabeculation.

3.9.4 Relationship between trabeculation and symptoms

Simonsen et al. (7) found a correlation between the presence of trabeculation and the number of obstructive symptoms. When patients were grouped by age, it was noted that trabeculation significantly increased with increasing age ($p < 0.5$). In another study, none of the trabeculation ratings were predictive of symptom severity, while moderate-to-severe trabeculation was predictive of larger prostate size and reduced flow rate (8).

3.9.5 Relationship between trabeculation and prostate size

Anderson and Nordling (9) examined the correlation between cystoscopic findings and the presence of trabeculation. While the cystoscopically estimated weight correlated with the presence of trabeculation ($p = 0.003$), the bladder neck to verumontanum distance and the cystoscopic appearance of occlusion did not correlate significantly ($p > 0.5$). Homma et al. (10) showed that patients had a high likelihood of outlet obstruction when their prostate size was greater than 30 mL or if their posterior urethra was severely obstructed on endoscopy.

3.9.6 Relationship between trabeculation and obstruction

El Din et al. (11) evaluated urethroscopic findings and the results of urodynamic studies in 492 elderly men with LUTS. They noted a clear correlation between cystoscopic appearance (grade of trabeculation and grade of urethral obstruction) and urodynamic indices, detrusor instability and low compliance. It should be noted, however, that bladder outlet obstruction is present in approximately 15% of patients with normal cystoscopic findings, while approximately 8% of patients have no obstruction at all even if severe trabeculation is present, suggesting the inadvisability of drawing the same conclusion in all patients. They believe that the value of urethrocystoscopy is limited and advise against its use in the diagnosis of bladder outlet obstruction. Instead, it should be used primarily to exclude bladder pathology and to decide between interventional approaches.

3.9.7 Bladder diverticula and obstruction

The detection of large bladder diverticula might be of therapeutic importance. For example, the presence of a large bladder diverticulum might dictate the type of intervention. It is, however, evident that other diagnostic modalities, such as cystography, intravenous pyelography (IVP) or transabdominal sonography, are equally sensitive, or more sensitive, at detecting large bladder diverticula, without carrying the risks of invasive urethrocystoscopy. No data are available to document the sensitivity or specificity of cystography, IVP, cystoscopy or transabdominal sonography for evaluating large bladder diverticula.

Quirinia and Hoffmann (12) reported on 104 patients with BPH of whom 51% had diverticula by cystography. Although the presence of diverticula was related to age, upper tract dilation, increasing amounts of residual urine and bladder instability, there was no relationship with bladder capacity, peak flow rate or prostate size. At present, no final decision about the value of cystoscopy in the assessment of bladder diverticula can be made. Equally poorly documented is the impact that the presence or absence of bladder diverticula might have on outcome after prostate surgery.

3.9.8 Bladder stones and obstruction

There is no doubt that the presence of bladder stones can be assessed accurately by urethrocystoscopy. Bladder stones are a clear indicator of bladder outlet obstruction. While it is not always clear whether the obstruction is of an organic, anatomical or neurogenic nature, the presence of stones in the bladder indicates an abnormality in the bladder-emptying mechanism and is usually preceded by the presence of residual urine or recurrent urinary tract infections. However, there is also no doubt that bladder stones are detected equally well by IVP or by the non-invasive method of transabdominal sonography. In fact, stones composed of poorly radio-opaque or radiolucent material are seen very well by transabdominal sonography, while being missed on a renal ultrasound.

The crux of the matter has to be whether or not the detection of bladder stones dictates the surgical procedure of choice. It is obvious that the presence of a large bladder stone should guide the surgeon towards an open procedure rather than a lengthy electrohydraulic lithotripsy. However, the majority of all bladder stones are rather small, and can be removed during TURP through the sheath of the resectoscope, or by destroying them with endoscopic instruments prior to washing them out. It is therefore questionable whether or not urethrocystoscopy should be performed to assess the presence or absence of bladder stones prior to surgery for BPH, particularly as most patients with bladder stones will have microscopic haematuria that will have been detected during the standard basic evaluation.

3.9.9 Intravesical pathology

The detection of other pathology (urethral or intravesical) is advantageous and can be accomplished by endoscopy better than with most other modalities. In a study by Ezz El Din et al. (13), urinalysis and a cystoscopy were performed in 750 consecutive patients with BPH. Only three patients had a bladder tumour while 49 had urinary calculi. There was no correlation between any clinical parameter and the finding of microscopic haematuria. It was concluded that haematuria is a frequent finding in the assessment of BPH patients and that additional tests should only be performed if indicated (e.g. in the case of abnormal urine cytology).

3.9.10 Conclusions

Diagnostic endoscopy of the lower urinary tract should be considered an optional test for the following reasons:

- The outcomes of the intervention are unknown
- The benefits do not outweigh the harm of the invasive study
- Patients' preferences are expected to be divided.

3.9.11 REFERENCES

1. **Grayhack JT.**
   Benign prostatic hyperplasia. The scope of the problem. Cancer 1992; 70(Suppl 1): 275-279.
2. **Bostwick DG.**
   Pathology of benign prostatic hyperplasia. In Textbook of Benign Prostatic Hyperplasia. Kirby R et al. (eds). Oxford: Isis Medical Media, 1996, pp. 91-104.
3. **Larsen EH, Bruskewitz RC.**
   Urodynamic evaluation of male outflow obstruction. Krane RJ, Siroky B (ed.).
   Clinical Neurourol 1991;427-443.
4. **Berge V, Eri LM, Tveter KJ.**

Complications of invasive, urodynamic examinations and prostate biopsies in patients with benign prostatic hyperplasia. Scand J Urol Nephrol Suppl 1995; 172: 95-98.

5. **Shoukry I, Susset JG, Elhilali MM, Dutartre D.**
Role of uroflowmetry in the assessment of lower urinary tract obstruction in adult males.
Br J Urol 1975; 47: 559-566.

6. **Anikwe RM.**
Correlations between clinical findings and urinary flow rate in benign prostatic hypertrophy.
Int Surg 1976; 61: 392-394.

7. **Simonsen O, Moller-Madsen B, Dorflinger T, Norgaard JP, Jorgensen HS, Lundhus E.**
The significance of age on symptoms and urodynamic and cystoscopic findings in benign prostatic hypertrophy. Urol Res 1987; 15: 355-358.

8. **Barry MJ, Cockett AT, Holtgrewe HL, McConnell JD, Sihelnik SA, Winfield HN.**
Relationship of symptoms of prostatism to commonly used physiological and anatomical measures of the severity of benign prostatic hyperplasia. J Urol 1993; 150: 351-358.

9. **Andersen JT, Nordling J.**
Prostatism. II. The correlation between cysto-urethroscopic, cystometric and urodynamic findings.
Scand J Urol Nephrol 1980; 14: 23-27.

10. **Homma Y, Gotoh M, Takei M, Kawabe K, Yamaguchi T.**
Predictability of conventional tests for the assessment of bladder outlet obstruction in benign prostatic hyperplasia. Int J Urol 1998; 5: 61-66.

11. **el Din KE, de Wildt MJ, Rosier PF, Wijkstra H, Debruyne FM, de la Rosette JJ.**
The correlation between urodynamic and cystoscopic findings in elderly men with voiding complaints.
J Urol 1996; 155: 1018-1022.

12. **Quirinia A, Hoffmann AL.**
Bladder diverticula in patients with prostatism. Int Urol Nephrol 1993; 25: 243-247.

13. **Ezz el Din K, Koch WF, de Wildt MJ, Debruyne FM, de la Rosette JJ.**
The predictive value of microscopic haematuria in patients with lower urinary tract symptoms and benign prostatic hyperplasia. Eur Urol 1996; 30: 409-413.

3.10 RECOMMENDATIONS FOR DIAGNOSIS

1. Among all the different urinary symptom score systems currently available, the use of I-PSS is recommended because of its worldwide distribution and use.

2. In patients undergoing investigation for LUTS, the minimal requirement is to assess the upper urinary tract function with a creatinine measurement and/or an ultrasonographic examination. Urinalysis may be included in the primary evaluation. However, it should be noted that there is little evidence in the literature to support this conclusion.

3. DRE is a minimal requirement in patients undergoing investigation for LUTS.

4. There is a consensus that if imaging of the upper urinary tract is performed, ultrasonography is the method of choice.

5. Imaging of the upper urinary tract is recommended in patients with LUTS and one of the following:
   * History of, or a current, urinary tract infection
   * History of urolithiasis
   * History of urinary tract surgery
   * History of urothelial tumour (including IVU)
   * Haematuria (including IVU)
   * Urinary retention.

6. CT and MRI currently have no place in the routine imaging of the upper urinary tract in elderly men with LUTS.

7. Routine imaging of the urinary bladder cannot be recommended as a diagnostic test in the work-up of patients with LUTS. Ultrasound of the bladder, however, is a valuable diagnostic tool for the detection of bladder diverticula or bladder stones.

8. Routine imaging of the urethra is not recommended in the diagnostic work-up of patients with LUTS.

9. The method of choice for the determination of prostate volume is ultrasonography, preferably via the transrectal route. However, imaging of the prostate by transabdominal ultrasound and TRUS is optional.

10. Prostate size should be assessed when considering open prostatectomy and TUIP, and prior to finasteride therapy.

11. If the voided volume is less than 150 mL or Qmax is greater than 10 mL/s, pressure-flow studies should be considered before surgical intervention, particularly in elderly men.

12. Measurement of residual urine volume is a recommended test in the assessment of patients with LUTS suggestive of benign prostatic obstruction.

13 Endoscopy is recommended as a guideline at the time of surgical treatment to rule out other pathology and to assess the shape and size of the prostate, which may have an impact on the treatment modality chosen.

14. Pressure-flow studies should be considered for patients prior to surgical treatment in the following subgroups:
   * Younger men (e.g. < 50 years of age)
   * Elderly patients (i.e. > 80 years of age)
   * Post-void residual urine volume over 300 mL
   * Qmax more than 15 mL/s
   * Suspicion of neurogenic bladder dysfunction
   * After radical pelvic surgery
   * Previous unsuccessful invasive treatment.

4. TREATMENT

4.1 Watchful waiting

Many men with LUTS do not complain of high levels of bother and so are suitable for non-medical non-surgical management – a policy of care that has been called watchful waiting (WW). It is customary for this type of management to include the following components: education, reassurance, periodic monitoring and lifestyle advice. In many men it is regarded as the first tier in the therapeutic cascade and therefore the majority of men will be offered watchful waiting at some point. WW is a viable option to many men as few, if left untreated, will progress to acute urinary retention and complications such as renal insufficiency and stones (1,2). Similarly some men's symptoms may improve spontaneously whilst others remain stable for many years (3).

4.1.1 Patient selection

All men with LUTS should be formally assessed prior to starting any form of management in order to identify those with complications that may benefit from intervention therapy.

Men with mild to moderate uncomplicated LUTS (causing no serious health threat) who are not too bothered by their symptoms are suitable for a trial of WW. A large study comparing WW and TURP in men with moderate symptoms showed that those who had surgery had improved bladder function over the WW group (flow rates and post void residual volumes) with the best results being in those with high levels of bother. 36% crossed over to surgery in 5 years leaving 64% doing well in the WW group (4).

Approximately 85% of men will be stable on WW at 1 year, deteriorating progressively to 65% at 5 years (5,6). The reason why some men deteriorate with WW and others do not is not well understood; increasing symptom bothersomeness and post-void residual volumes appeared to be strongest predictors of failure.

4.1.2 Education, reassurance and periodic monitoring

Although there is little high quality evidence to support this (the studies have not been done) it seems rational to provide the following for men who are candidates for WW:

- Prostate, BPH and LUTS education with the help of written information
- Reassurance that LUTS does not progress in everyone. Reassurance that serious complications are unlikely to occur.
- Information about prostate cancer is nearly always required. Anxiety regarding prostate cancer can be the principal reason why a man consults his doctor about his urinary symptoms. Most men over 50 will note changes in their urinary function with or without high levels of bother. If these men harbour an anxiety about prostate cancer, this may focus their attention on specific symptoms and reinforce their fear. At least three high-quality studies have shown that men with LUTS are at no greater risk of prostate cancer than asymptomatic men of the same age (7–9). It is however not possible to guarantee against early undetectable prostate cancer.
- WW does not imply no activity; men should be periodically seen by either a urologist, general practitioner or specialist nurse. Symptom scores, symptom bothersomeness, flow rates and post-void residual volume measurements are useful in determining whether a patient's condition has deteriorated.

4.1.3 Lifestyle advice

Optimisation of WW can be achieved with lifestyle modifications. Minor changes in lifestyle and behaviour can have a beneficial effect on symptoms and may prevent deterioration requiring medical or surgical treatment.

Lifestyle advice should include:

- Reduction of fluid intake at specific times aimed at reducing urinary frequency when most inconvenient, for example at night or when going out in public. The recommended total daily fluid intake of 1500 mL should not be reduced.
- Avoidance or moderation of caffeine and alcohol which may have a diuretic and irritant effect, thereby increasing fluid output and enhancing frequency, urgency and nocturia.
- Use of relaxed and double-voiding techniques.
- Urethral stripping to prevent postmicturition dribble.
- Distraction techniques, such as penile squeeze, breathing exercises, perineal pressure and mental 'tricks' to take the mind off the bladder and toilet in the control of irritative symptoms.
- Bladder re-training, by which men are encouraged to 'hold on' when they have sensory urgency to increase their bladder capacity (to around 400 mL) and the time between voids.
- Reviewing a man's medication and optimising the time of administration or substituting drugs for others that have fewer urinary effects.
- Providing necessary assistance when there is impairment of dexterity, mobility or mental state.
- Treatment of constipation.

Again it must be stated that there is little high-quality evidence that provides reliable information on any of these lifestyle activities. Research in this area is required so that lifestyle advice to men with LUTS can be refined.

4.1.4 Conclusions

Men with mild to moderate LUTS with low levels of bother are suitable for WW. Reassurance, periodic monitoring and lifestyle modifications can be used to optimise WW. Further research in this area is required.

4.1.5 REFERENCES

1. **Ball AJ, Feneley RC, Abrams PH.**
   The natural history of untreated 'prostatism'. Br J Urol 1981; 53: 613-616.
2. **Kirby RS.**
   The natural history of benign prostatic hyperplasia: what have we learned in the last decade? Urology 2000; 56: 3-6.
3. **Isaacs JT.**
   Importance of the natural history of benign prostatic hyperplasia in the evaluation of pharmacologic intervention. Prostate 1990; 3 (Suppl): 1-7.
4. **Flanigan RC, Reda DJ, Wasson JH Anderson RJ, Bruskewitz RC.**
   5-year outcome of surgical resection and watchful waiting for men with moderately symptomatic BPH: a department of Veterans Affairs cooperative study. J Urol 1998; 160: 12-17.
5. **Wasson JH, Reda DJ, Bruskewitz RC, Elinson J, Keller AM, Henderson WG.**
   A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. The Veterans Affairs Cooperative Study Group on Transurethral Resection of the Prostate. New Engl J Med 1995; 332: 75-79.
6. **Netto NR, de Lima ML, Netto MR, D'Ancona CA.**
   Evaluation of patients with bladder outlet obstruction and mild international prostate symptom score followed up by watchful waiting. Urol 1999; 53: 314-316.
7. **Catalona WJ, Richie JP, Ahmann FR, Hudson MA, Scardino PT, Flanigan RC, deKernion JB, Ratliff TL, Kavoussi LR, Dalkin BL et al.**
   Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a multicentre clinical trial of 6,630 men. J Urol 1994; 15: 1283-1290.
8. **Mettlin C, Murphy GP, Babaian RJ.**
   American Cancer Society National Prostate Cancer Detection Project. The results of a five-year early prostate cancer detection intervention. Cancer 1996; 77: 150-159.
9. **Rietenberg JBW, Kranse R, Boeken Kruger AE et al.**
   Additional value of the AUA 7 symptoms score in prostate cancer (PC) detection. J Urol 1997; 157: 467.

4.2 Finasteride (type 2 5-alpha-reductase inhibitor)

4.2.1 Efficacy and clinical endpoints

Today, after the completion of many trials, there is no doubt that finasteride can reduce the size of the prostate gland by 20–30%. It improves symptom scores by approximately 15% and can also cause a moderate improvement in the urinary flow rate of 1.3-1.6 mL/s (1–3).

The efficacy of finasteride, however, was questioned by a study published in 1996 which showed that terazosin monotherapy and terazosin plus finasteride were more effective than finasteride monotherapy or placebo (4). Indeed, finasteride in this study was no more effective than placebo. A meta-analysis of six randomized clinical trials with finasteride was performed because the results of this study conflicted with those of all previous trials (5). The main conclusions of the meta-analysis were that baseline prostate volume was a key predictor of various treatment outcomes and that finasteride was more effective in prostates larger than 40 mL.

The Finasteride Urodynamics Study Group published the results of two studies verifying the above conclusion. In the first study, it was shown that improvement in pressure-flow parameters with finasteride was greater in men with large prostates than in those with smaller prostates (6). In the second study, a modest, but statistically significant, correlation between detrusor pressure and prostate size was found, supporting the hypothesis that prostate size is important in deciding between various medical treatment options for BPH (7). Another study by Lepor et al. again questioned the efficacy of finasteride in improving the patient's quality of life and claimed that baseline prostate volume was not a predictor of response to finasteride. However, the mean prostate volume of the patients included in this trial was less than 40 mL (8). During the 5th International Consultation on Benign Prostatic Hyperplasia that took place in Paris in 2000, all the available data on this medical treatment option were analyzed and the conclusion was that finasteride shows a modest magnitude of

benefit in men with enlarged prostates (9).

Various trials have concluded that finasteride significantly reduced acute urinary retention and the need for surgical treatment in men with BPH (10–12). In a major placebo controlled trial including 3040 men, finasteride-treated patients had significantly less bother, activity interference and worry due to urinary symptoms. Baseline PSA levels ≥ 1.4 ng/mL, or enlarged prostate glands, could predict the best long-term response to finasteride (13). Data from three multinational, multicentre, placebo-controlled finasteride trials, in 4,222 men, showed that patients with larger prostate volumes or higher PSA levels have an increased risk of developing acute urinary retention and therefore derive the greatest benefit from finasteride therapy (14). The long-term effects of finasteride have also been examined. The North American Finasteride Study Group reported that patients treated with finasteride maintained a reduction of prostate volume and an improvement in symptom score and maximal urinary flow rate over a period of 5 years (15). The PROWESS Study Group (16) also found that finasteride caused long-term symptomatic improvement and verified the results of other reports discussed above (11,12). The risk of developing acute urinary retention or of needing surgery was also found to be reduced (16). In addition, the Scandinavian Finasteride Study Group has verified an earlier observation that the maximum efficacy of finasteride action is obtained after 6 months, and has shown that this improvement could be maintained for at least 6 years (17).

4.2.2 Combination therapy

The combination of finasteride with an alpha-blocker has been examined in two clinical trials (4,18). No additional benefit from combining these two drugs was observed in either study. The lack of finasteride efficacy in these two trials may be due to smaller baseline prostate volumes. Recently it was shown that the apoptotic index in a combination treatment of terazosin plus finasteride was significantly higher than the index of terazosin or finasteride alone (19). In another study examining combination therapy, it was shown that patients with lower urinary tract symptoms and moderately enlarged prostates initially receiving combination therapy with finasteride and an alpha-blocker were likely to experience no significant symptom deterioration after discontinuing the alpha-blocker following 9 to 12 months of combination therapy (20).

4.2.3 Haematuria and finasteride

Another important benefit of finasteride in common clinical urological practice is that it can be used to treat haematuria associated with BPH. Various studies have confirmed this alternative for patients with haematuria due to BPH who, at the same time, had no significant obstruction or adenocarcinoma of the prostate (21,22).

4.2.4 Side-effects

These are mainly related to sexual function. Ejaculation disorders, impotence and decreased libido have been reported in 12% of patients receiving finasteride; these figures were higher than those observed for placebo. Such side-effects were considered ‘minimal’ by the World Health Organization (WHO) Experts Committee during the Fifth International Consultation on BPH in Paris in 2000, as they did not increase over time and did not cause many patients to discontinue their treatment.

Another conclusion from the PLESS study was that in both older and younger men with symptomatic BPH, finasteride had the same safety profile and no drug interactions of clinical importance were observed (23).

4.2.5 Effect on PSA

It is known that finasteride lowers serum PSA levels. Thus, the question of whether or not it masks the early detection of localized prostatic adenocarcinomas has been raised. It has been agreed that 12 months of finasteride, 5 mg/day, reduces serum PSA levels by 50%. Two major studies (24,25) verified earlier reports, and concluded that doubling the PSA level allowed appropriate interpretation of PSA values and that finasteride treatment did not mask the detection of prostatic adenocarcinomas. It was also shown, at the histopathological level, that finasteride did not cause problems in the diagnosis of cancer from needle specimens as cancer tissue remained unaltered (26).

The results of papers dealing with the impact of finasteride on free PSA level are confusing. In one paper, finasteride seemed to lower total and free PSA levels equally, so that the ratio of free PSA to total PSA remained unchanged (27). In another report, the percentage of free PSA did not change significantly (28).

4.2.6 GI198745 (types 1 and 2, 5-alpha-reductase inhibitor)

It is known that finasteride suppresses dihydrotestosterone (DHT) by about 70% in the serum and by 90% in the prostate. The remaining DHT is the result of type 1 5-alpha-reductase activity. GI198745 is a new drug that has the ability to suppress both type 1 and 2 isoenzymes. A phase II study including 399 patients showed that GI198745 can cause greater suppression of DHT than finasteride (29). Clinical phase III studies in order to evaluate the true impact of GI198745 are underway.

4.2.7 Phytotherapeutic agents

The use of alternative treatment for BPH with phytotherapeutic agents has been popular in Europe for many years and has recently spread substantially in the USA (30). These agents are composed of various plant extracts and it is always difficult to identify which component has the major biological activity (31). During the Fifth International Consultation on BPH all the available data on phytotherapy were analyzed. Only a few studies were found to have the statistical power and proper follow-up period to prove the clinical efficacy of these agents (31).

A meta-analysis of 18 randomized, controlled trials involving 2,939 men was performed and concluded that Serenoa repens produced similar improvements in symptoms and urinary flow to finasteride, with fewer side-effects (33). Recent trials have shown that some benefit from these agents might exist but further randomized trials are needed (33–36).

4.2.8 Conclusions

1. It has been shown in numerous randomized, placebo-controlled clinical trials that finasteride is capable of reducing prostate volume and improving symptom scores and flow rates. Maximum benefits are seen at a mean period of 6 months.

2. Men with small prostates (< 40 mL) are less likely to benefit from finasteride.

3. Finasteride can alter the natural history of symptomatic BPH by influencing prostatectomy and acute urinary retention rates. The costs of such protocols, however, should be further evaluated.

4. The long-term (up to 6 years) effects of finasteride are substantial.

5. The combination of finasteride with an alpha-blocker is of no benefit according to the data currently available.

6. Side-effects of finasteride are minimal.

7. Finasteride treatment does not mask the detection of prostate carcinoma. By doubling PSA serum levels, an accurate estimation can be expected.

8. The mode of action of phytotherapeutic agents is unknown. Their biological effect is unclear, although a few randomized clinical trials already show encouraging results.

4.2.9 REFERENCES

1. **Andersen JT, Ekman P, Wolf H, Beisland HO, Johansson JE, Kontturi M, Lehtonen T, Tveter K.** Can finasteride reverse the progress of benign prostatic hyperplasia? A two year placebo-controlled study. The Scandinavian BPH study group. Urology 1995; 46: 631-637.
2. **Gormley GJ, Stoner E, Bruskewitz RC, Imperato-McGinley J, Walsh PC, McConnell JD, Andriole GL, Geller J, Bracken BR, Tenover JS, et al.** The effect of finasteride in men with benign prostatic hyperplasia. The Finasteride Study Group. N Engl J Med 1992; 327: 1185-1191.
3. **Nickel JC, Fradet Y, Boake RC, Pommerville PJ, Perreault JP, Afridi SK, Elhilali MM.** Efficacy and safety of finasteride therapy for benign prostatic hyperplasia: results of a 2-year randomised controlled trial (the PROSPECT Study). Can Med Assoc J 1996; 155: 1251-1259.
4. **Lepor H, Williford WO, Barry MJ, Brawer MK, Dixon CM, Gormley G, Haakenson C, Machi M, Narayan P, Padley RJ.** The efficacy of terazosin, finasteride, or both in benign prostatic hyperplasia. Veterans Affairs Cooperative Studies, Benign Prostatic Hyperplasia Study Group. N Engl J Med 1996; 335: 533-539.
5. **Boyle P, Gould AL, Roehrborn CG.** Prostate volume predicts the outcome of treatment of benign prostatic hyperplasia with finasteride: meta-analysis of randomized clinical trials. Urology 1996; 48: 398-405.
6. **Abrams P, Schafer W, Tamela TL, Barrett DM. Hedlund H, Rolema HJ, Matos-Ferreira A, Nording J, Bruskewitz R, Andersen JT, Hald T, Miller P, Kirby R, Mustonen S, Cannon A, Jacobsen CA, Gormley GJ, Malice MP, Bach MA.** Improvement of pressure flow parameters with finasteride is greater in men with large prostates. Finasteride Urodynamics Study Group. J Urol 1999; 161: 1515-1517.
7. **Tammela TL, Schafer W, Barrett DM, Abrams P, Hedlund H, Rollema HJ, Matos-Ferreira A,**

Nordling J, Bruskewitz R, Miller P, Kirby R, Andersen JT, Jacobsen C, Gormley GJ, Malice MP, Bach MA.
Repeated pressure-flow studies in the evaluation of bladder outlet obstruction due to benign prostatic enlargement. Finasteride Urodynamics Study Group. Neurol Urodyn 1999; 18: 17-24.

8. **Lepor H, Williford WO, Barry MJ, Haakenson C, Jones K.**
The impact of medical therapy on bother due to symptoms, quality of life and global outcome, and factors predicting response. Veterans Affairs Cooperative Studies Benign Prostatic Hyperplasia Study Group. J Urol 1998; 160; 1358-1367.

9. **Bartsch G, Mc Connell JD, Mahler C et al.**
Endocrine treatment of Benign Prostatic Hyperplasia In: Chatelain C et al. (eds). Proceedings of the Fifth International Consultation on BPH, Paris, June 2000. Health Publications: Plymouth, 2001, pp. 423-457.

10. **Andersen JT, Nickel JC, Marshall VR, Schulman CC, Boyle P.**
Finasteride significantly reduces acute urinary retention and need for surgery in patients with symptomatic benign prostatic hyperplasia. Urology 1997; 49: 839-845.

11. **McConnell JD, Bruskewitz R, Walsh P, Andriole G, Lieber M, Holtgrewe HL, Albertsen P, Roehrborn CG, Nickel JC, Wang DZ, Taylor AM, Waldstreicher J.**
The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostatic hyperplasia. Finasteride Long-term Efficacy and Safety Study Group.
N Engl J Med 1998; 338: 557-563.

12. **Roehrborn CG, Bruskewitz R, Nickel GC, Glickman S, Cox C, Anderson R, Kandzari S, Herlihy R, Kornitzer G, Brown BT, Holtgrewe HL, Taylor A, Wang D, Waldstreicher J.**
Urinary retention in patients with BPH treated with finasteride or placebo over 4 years. Characterization of patients and ultimate outcomes. The PLESS Study Group. Eur Urol 2000; 37: 528-536.

13. **Bruskewitz R, Girman CJ, Fowler J, Rigby O.F, Sullivan M, Bracken R.B. Fusilier H.A, Kozlowski D, Kantor S.D, Johnson E.L, Wang D.Z, Waldstreicher J.**
Effect of finasteride on bother and other health-related quality of life aspects associated with benign prostatic hyperplasia. PLESS Study Group. Proscar Long-term Efficacy and Safety Study.
Urology 1999; 4: 670-678.

14. **Marberger MJ, Andersen JT, Nickel JC, Malice MP, Gabriel M, Pappas F, Meehan A, Stoner E, Waldstreicher J.**
Prostate volume and serum prostate-specific antigen as predictors of acute urinary retention. Combined experience from three large multinational placebo-controlled trials. Eur Urology 2000; 38: 563-568.

15. **Hudson PB, Boake R, Trachtenberg J, Romas NA, Rosenblatt S, Narayan P, Geller J, Lieber MM, Elhilali M, Norman R, Patterson L, Perreault JP, Malek GH, Bruskewitz RC, Roy JB, Ko A, Jacobsen CA, Stoner E.**
Efficacy of finasteride is maintained in patients with benign prostatic hyperplasia treated for 5 years. The North American Finasteride Study Group. Urology 1999; 53: 690-695.

16. **Marberger MJ.**
Long term effects of finasteride in patients with benign prostatic hyperplasia: a double-blind, placebo-controlled multicenter study. PROWESS Study Group. Urology 1998; 51: 677-686.

17. **Ekman P.**
Maximum efficacy of finasteride is obtained within 6 months and maintained over 6 years. Follow-up of the Scandinavian Open-extension Study. The Scandinavian Finasteride Study Group.
Eur Urol 1998; 33: 312-317.

18. **Debruyne FM, Jardin A, Colloi D, Resel L, Witjes WP, Delauche-Cavallier MC, McCarthy C, Geffriaud-Ricouard C.**
Sustained-release alfuzosin, finasteride and the combination of both in the treatment of BPH. European ALFIN Study Group. Eur Urol 1998; 34: 169-175.

19. **Glassman DT, Chon JK, Borkowski A, Jacobs SC, Kyprianou N.**
Combined effect of terazosin and finasteride on apoptosis, cell proliferation, and transforming growth factor-beta expression in benign prostatic hyperplasia. Prostate 2001; 46: 45-51.

20. **Baldwin KC, Ginsberg PC, Roehrborn CG, Harkaway RC.**
Discontinuation of alpha-blockade after initial treatment with finasteride and doxazosin in men with lower urinary tract symptoms and clinical evidence of benign prostatic hyperplasia. Urology 2001; 58: 203-209.

21. **Foley SJ, Soloman LZ, Wedderburn AW, Kashif KM, Summerton D, Basketter V, Holmes SA.**
A prospective study of the natural history of hematuria associated with benign prostatic hyperplasia and the effect of finasteride. J Urol 2000; 163: 496-498.

22. **Foley SJ, Soloman LZ, Wedderburn AW, Kashif KM, Summerton D, Basketter V, Holmes SA.**
A prospective study of the natural history of hematuria associated with benign prostatic hyperplasia and the effect of finasteride. J Urol 2000; 164: 1670-1671.

23. **Kaplan SA, Holtgrewe HL, Bruskewitz R, Saltzman B, Mobley D, Narayan P, Lund RH, Weiner S, Wells G, Cook TJ, Meehan A, Waldstreicher J.**
Comparison of the efficacy and safety of finasteride in older versus younger men with benign prostatic hyperplasia. Urology 2001; 57: 1073-1077.

24. **Oesterling JE, Roy J, Agha A, Shown T, Krarup T, Johansen T, Lagerkvist M, Gormley G, Bach M, Waldstreicher J.**
Biologic variability of prostate specific antigen and its usefulness as a marker for prostate cancer: effects of finasteride. The Finasteride PSA Study Group. Urology 1997; 50: 13-18.

25. **Andriole GL, Guess HA, Epstein JL, Wise H, Kadmon D, Crawford ED, Hudson P, Jackson CL, Romas NA, Patterson L, Cook TJ, Waldstreicher J.**
Treatment with finasteride preserves usefulness of prostate specific antigen in the detection of prostate cancer: results of a randomized, double-blind, placebo-controlled clinical trial. PLESS Study Group. Proscar Long-term Efficacy and Safety Study. Urology 1998; 52: 195-201.

26. **Yang XJ, Lecksell K, Short K, Gottesman J, Peterson L, Bannow J, Schellhammer PF, Fitch WP, Hodge GB, Parra R, Rouse S, Waldstreicher J, Epstein JI.**
Does long-term finasteride therapy affect the histologic features of benign prostatic tissue and prostate cancer on needle biopsy? PLESS Study Group. Proscar Long-term Efficacy and Safety Study. Urology 1999; 53: 696-700.

27. **Keetch DW, Andriole GL, Ratliff TL, Catalona WJ.**
Comparison of percent free prostate specific antigen levels in men with benign prostatic hyperplasia treated with finasteride, terazosin or watchful waiting. Urology 1997; 50: 901-905.

28. **Pannek J, Marks LS, Pearson JD, Rittenhouse HG, Chan DW, Shery ED, Gormley GJ, Subong EN, Kelley CA, Stoner E, Partin AW.**
Influence of finasteride on free and total serum prostate specific antigen levels in men with benign prostatic hyperplasia. J Urol 1998; 159: 449-453.

29. **Clark R, Hermann D, Gabriel H, Wilson T, Morril B, Hobbs S.**
Effective suppression of dihydrotestosterone (DHT) by GI 198745, a novel, dual 5-alpha reductase inhibitor. J Urol 1999; 161: 1037.

30. **Lowe FC, Fagelman E.**
Phytotherapy in the treatment of benign prostatic hyperplasia: an update. Urology 1999; 53: 671-678.

31. **Dreikorn K, Lowe F, Borkowski A, et al.**
Other medical therapies. In: Chatelain et al. (eds). Proceedings of the Fifth International Consultation on BPH, Paris, June 2000. Health Publications: Plymouth, 2001, pp. 481-511.

32. **Wilt T, Ishani A, Stark G, Macdonald R, Lau J, Mulrow C.**
Saw palmetto extracts for treatment of benign hyperplasia: a systematic review. JAMA 1998; 280: 1604-1609.

33. **Wilt T, Ishani A, MacDonald R, Stark G, Mulrow C, Lau J.**
Beta-sitosterols for benign prostatic hyperplasia. Cochrane Database Syst Rev 2000, CD001043.

34. **Wilt T, Mac Donald R, Ishani A, Rutks I, Stark G.**
Cernilton for benign prostatic hyperplasia. Cochrane Database Syst Rev 2000, CD001042.

35. **Wilt TJ, Ishani A, Rutks I, MacDonald R.**
Phytotherapy for benign prostatic hyperplasia. Public Health Nutr 2000; 3: 459-472.

36. **Sokeland J.**
Combined sabal and urtica extract compared with finasteride in men with benign prostatic hyperplasia: analysis of prostate volume and therapeutic outcome. BJU Int 2000; 86: 439-442.

4.3 Alpha-blockers

Over the past 10 years, the prescribing of alpha-blockers has steadily increased. This increase has been driven partly by patients wishing to achieve symptomatic relief without undergoing surgical treatments and partly by the marketing of these drugs by pharmaceutical companies. In view of the very real placebo effect seen in the treatment of patients with LUTS secondary to BPH, this review will focus on the results of randomized, prospective, placebo-controlled clinical studies.

4.3.1 Uroselectivity

Alpha-blockers were first introduced into clinical practice for the treatment of LUTS secondary to BPH in 1978, following experimental work demonstrating the predominance of adrenoceptors in human prostate smooth muscle (1).

Initially, the non-selective alpha-blocker, phenoxybenzamine, was investigated. However, the side-effect profile, due to its unselective nature, was unacceptable to patients (2,3). Subsequently, alpha1-adrenoceptors were identified and selective, better-tolerated, alpha-blockers were developed. A large number of alpha1-

selective, alpha-blockers are available (alfuzosin, doxazosin, indoramin, prazosin, terazosin). Broadly speaking, they all have a similar efficacy and side-effect profile.

4.3.2 Mechanism of action

Alpha-blockers are thought to act by reducing the dynamic element of prostatic obstruction by antagonizing the adrenergic receptors responsible for smooth muscle tone within the prostate and bladder neck. This is implied from in-vitro experiments and the predominant distribution of alpha1-receptors within the prostate and bladder neck. However, the exact contributions of alpha1-receptor subtypes and the potential central effects in vivo remain unclear. Urodynamic studies measuring voiding pressures do not reveal any significant relief of obstruction, although flow rates do improve with these agents relative to placebo.

4.3.3 Pharmacokinetics

Alpha-blockers are taken orally and the dosage depends on the half-life of the relevant drug. Tamsulosin, terazosin and doxazosin have the advantage of being long-acting, once-daily preparations.

4.3.4 Assessment

It is not unreasonable to offer a trial of alpha-blockers to all men with uncomplicated LUTS. The optimal duration of the trial of therapy has been debated. Symptoms can improve within 48 hours. An I-PSS assessment requires at least one month of therapy. There is no justification in prolonging therapy beyond one month in men who do not respond. One-third of men will not experience significant symptom reduction. Currently there is no method of predicting which men will show a response (4).

4.3.5 Clinical efficacy

The interpretation of existing literature regarding the efficacy of alpha-blocker therapy is clouded by the wide discrepancy in methodology and reporting of clinical studies. Because of this, secondary publications that have compared outcomes between these studies have been useful (5–7). Djavan and Marberger's meta-analysis estimated that overall symptoms improved by 30–40% and that flow rates improved by 16–25%, compared with placebo (6). Predicting response for any individual is more difficult and therefore a trial of therapy is required. The various types of alpha-blockers cannot be distinguished by their ability to relieve symptoms or improve flow.

4.3.6 Durability

Good data on long-term efficacy and the effect on natural history are currently not available. Long-term studies tend to be open-label extensions or increasingly 'real life practice' studies which do not conform to an experimental design. Nevertheless, in this context these types of design are informative.

Patients may choose to stop taking medication for a number of reasons. Studies have concentrated on two important reasons, namely, the occurrence of adverse effects and lack of efficacy (8). In general, the symptom status of men did not predict whether they were likely to stop therapy. Drop-outs occurred at the same rate, irrespective of whether symptoms were moderate or severe. The rate of drop-out in men on alpha-blockers appears to be between 0.01 and 1.6 per month. There is no evidence that efficacy diminishes with time.

4.3.7 Adverse effects

The most commonly reported side-effects with alpha-blocker therapy are headaches, dizziness, postural hypotension, asthenia, drowsiness, nasal congestion and retrograde ejaculation (6). In general, the rate of side-effects in studies looking at tamsulosin and alfuzosin were equivalent to placebo (4–10%). Tamsulosin resulted in less orthostatic hypotension than alfuzosin under test conditions. Whether this translates to a reduction in clinical side-effects remains to be seen.

4.3.8 Combination therapy

Two major studies have looked at the benefits of combining an alpha-blocker with a 5-alpha-reductase inhibitor in patients with clinical BPH (9,10). Neither the Veterans study nor the ALFIN study showed any benefit from combining both drugs, and in both studies the alpha-blocker proved more effective than the 5-alpha-reductase inhibitor.

4.3.9 Acute urinary retention

Early trials comparing alpha-blockers to placebo showed an increased likelihood of a successful trial, without catheter, following an episode of acute urinary retention. As a result, a large number of urologists have adopted this practice. The effect seems to be independent of the type of alpha-blocker studied. Two trials have looked at alfuzosin (11), and one at terazosin (12).

None of these trials continued therapy beyond the period of catheterization. Most men experience re-retention within the first two months (13). Studies are underway which address the question of whether men do benefit from alpha-blockade in the six months following acute urinary retention.

4.3.10 Conclusions

- Alpha-blocker therapy can result in a rapid improvement in symptoms by a factor of 20–50% and an improvement in the flow rate of 20–30%. These changes have been shown to be significant in randomized, placebo-controlled studies.
- Long-term data are limited but suggest that the benefits of treatment are sustained. If a patient does not experience an improvement in symptoms after an 8-week trial, treatment should be discontinued.
- Patients should be informed about the side-effects of alpha-blocker therapy and the need for long-term use.
- There does not appear to be a role for alpha-blockers in combination therapy with 5-alpha-reductase inhibitors.
- There is no difference between different alpha-blockers in terms of efficacy. Although the side-effect profiles for some drugs are reported to be more favourable, supportive data are weak.

4.3.11 REFERENCES

1. **Caine M, Raz S, Zeigler M.**
   Adrenergic and cholinergic receptors in the human prostate, prostatic capsule and bladder neck. Br J Urol 1975; 47: 193-202.
2. **Caine M, Perlberg S, Meretyk S.**
   A placebo controlled double blind study of the effect of phenoxybenzamine in benign prostatic obstruction. Br J Urol 1978; 50: 551-554.
3. **Abrams PH, Shah PJ, Stone AR, Choa RG.**
   Bladder outflow obstruction treated with phenoxybenzamine. Br J Urol 1982; 54: 527-530.
4. **Witjes WP, Rosier PF, Caris CT, Debruyne FM, de la Rosette JJMCH.**
   Urodynamic and clinical effects of terazosin in symptomatic patients with and without bladder outlet obstruction. A stratified analysis. Urology 1997; 49: 197-206.
5. **Chapple CR, Andersson KF, Bono VA et al.**
   a-blockers clinical results. In: Denis L, Griffiths K, Khoury S et al. (eds). Proceedings of the Fourth International Consultation on BPH, Paris, July 1997. Health Publications: Plymouth, 1998, pp. 610-632.
6. **Djavan B, Marberger M.**
   Meta-analysis on the efficacy and tolerability of alpha1-adrenoceptor antagonists in patients with lower urinary tract symptoms suggestive of benign prostatic obstruction. Eur Urol. 1999;36(1):1-13.
7. **Debruyne FMJ.**
   Alpha blockers: are all created equal? Urology. 2000 Nov 1;56(5 Suppl 1):20-2. Review.
8. **Luckacs B, McCarthy C, Grange JC.**
   Long-term quality of life in patients with benign prostatic hypertrophy: preliminary results of a cohort survey of 7093 patients treated with alpha-1 adrenergic blocker, alfuzosin. QOL BPH Study Group in General Practice. Eur Urol 1993; 24 (Suppl 1): 34–40.
9. **Lepor H.**
   Long-term evaluation of tamsulosin in benign prostatic hyperplasia: placebo-controlled, double-blind extension of phase III trial. Tamsulosin Investigator Group. Urology 1998; 51: 901-906.
10. **Debruyne FMJ, Jardin A, Colloi D, Resel L, Witjes WP, Delauche-Cavallier MC, McCarthy C, Geffriaud-Ricouard C.**
    Sustained-release alfuzosin, finasteride and the combination of both in the treatment of benign prostatic hyperplasia. European ALFIN Study Group. Eur Urol 1998; 34: 169-175.
11. **McNeil SA, Daruwala PD, Mitchel I-D, Shearer MG, Hargreave TB.**
    Sustained-release alfuzosin andtrial without catheter after acure urinary retention: a prospective placebo-controlled. BJU Int. 1998;84(6):622-7.
12. **Chan PSF, Wong WS, Chan LW, Cheng CW.**
    Can terazosin (alpha blocker) relieve acute urinary retention and obviate the need for an indwelling urethral catheter? Br J Urol 1996;77 suppl.1:A26, p27.

13. **McNeill SA, Hargreave TB, Gallagher H, Daruwala PD, Mitchell I-DC, Rizvi S.**
Long term follow-up following presentation with first episode of acute urinary retention.
J. Urol 2000;163(4):307.

4.4 Surgical management

Transurethral resection of the prostate (TURP), transurethral incision of the prostate (TUIP) and open prostatectomy are the conventional surgical options for the treatment of symptomatic BPH. Transurethral vaporisation (TUVP), an electrosurgical modification of the TURP-technique, is also included in this review. A single randomized controlled trial is available for open prostatectomy, while TURP, TUIP and TUVP have been subjected to a number of randomized controlled trials.

4.4.1 Indications for surgery

The most frequent indication for surgical management is bothersome LUTS refractory to medical management (1,2). The following complications of BPH/BPE are considered strong indications for surgery:

- Refractory urinary retention
- Recurrent urinary tract infection
- Recurrent haematuria refractory to medical treatment (finasteride)
- Renal insufficiency
- Bladder stones.

Increased post-void residual volume may be used as an indication for surgery. However, there is a great intra-individual variability and an upper limit requiring intervention has not been defined. Variables that most likely predict the outcome of prostatectomy are severity of LUTS and degree of bother (3,4).

4.4.2 Choice of surgical treatment

Nine randomized controlled trials compared TUIP to TURP. They showed similar improvements of LUTS in patients with small prostates (< 20–30 mL) and no middle lobe (5,6). TUIP has several advantages over TURP, such as a lower incidence of complications, minimal risk of bleeding and blood transfusion, decreased risk of retrograde ejaculation and shorter operating time or hospital stay (5). TURP comprises 95% of all surgical procedures and is the treatment of choice for prostates sized between 30 mL and 80–100 mL. Intra- and postoperative complications are correlated with the size of the prostate and the length of the procedure (2). Open surgery is the treatment of choice for large glands (> 80–100 mL), associated complications such as large bladder stones, or if resection of bladder diverticula is indicated (7,8). TUVP is considered an alternative to TUIP and TURP, particularly for patients with bleeding disorders and a small prostate (6).

4.4.3 Perioperative antibiotics

A known urinary tract infection should be treated before surgery (9,10). The routine use of prophylactic antibiotics remains controversial. However, antibiotics are recommended in patients on catheterization prior to surgery.

4.4.4 Treatment outcome

LUTS

All four surgical procedures result in an improvement of LUTS, exceeding 70% with open prostatectomy leading to slightly superior results (4–8). Mean improvement of LUTS in the 29 randomized controlled trials with a TURP-arm was 71% (range: 66–76%) (6). In the nine randomized controlled trials comparing TURP to TUIP, both procedures resulted in a similar improvement in symptoms after 12 months (5). The four randomized controlled trials comparing TURP to TUVP also revealed a similar improvement in LUTS(6).

Uroflowmetry

The mean increase of Qmax following TURP is 115% (range: 80–150%) based on a meta-analysis of 29 randomized controlled trials (6); in absolute terms +9.7 mL/s (range: 8.6–11.2 mL/s (6). Following TUIP, the Qmax increase is slightly lower (+100%; range: 27–112%); in absolute terms +7.8 mL/s (range: 4–11.6 mL/s) as compared to TURP (5,6). Following TUVP, the Qmax increased by 155% (range: 128–182%) in the four randomized controlled trials available (6). The highest Qmax improvement (+175%) in seen after open prostatectomy (absolute numbers: 8.2–22.6 mL/s) (7,8,11).

Post-void residual volume

All four surgical procedures allow a reduction of the post-void residual volume of more than 50%: –65% after open prostatectomy; –60% after TUVP; –60% after TURP; and –55% after TUIP (5–8, 11).

4.4.5 Complications

Intra-/peri-operative

Mortality following prostatectomy has decreased significantly within the past two decades and is less than < 0.25% in contemporary series (6,12).

The risk of a TUR-syndrome (fluid intoxication, serum Na+ < 130 nmol/L) is in the range of 2%. Risk factors for the development of the TUR-syndrome are excessive bleeding with opening of venous sinuses, prolonged operation time, large glands and past or present smoking (13).

The estimated need for blood transfusion following TURP is in the range of 2–5%. Slightly higher percentages have been reported following open prostatectomy (6,8,11). The risk of bleeding following TUIP and TUVP is negligible (5,6).

Long-term complications

Incontinence: Median probability for developing stress incontinence ranges is 1.8% following TUIP, 2.2% following TURP, and up to 10% following open prostatectomy (5–8,11). Limited information on this issue is available for TUVP; one randomized controlled trial reported an incontinence rate of 5% (14).

Bladder neck contracture and urethral stricture: The risk of developing an urethral stricture is 2.6% after open prostatectomy, 3.8% after TURP and 1.7% after TUIP (5–8,11). The risk of bladder neck contracture is 1.8% after open surgery, 4% after TURP and 0.4% after TUIP (5–8,11). The respective figures for TUVP are in the range of TURP.

Sexual function: Retrograde ejaculation results from the destruction of the bladder neck and is reported in 80% after open prostatectomy, 65–70% after TURP and 40% after TUIP (5–8,11). There is a long-standing controversy on the impact of prostatectomy, particularly TURP, on erectile function. The only randomized controlled trial that compared TURP to a 'wait and see' policy reported identical rates of erectile dysfunction in both arms (4). In the 29 randomized controlled trials recently reviewed, the incidence of erectile dysfunction following TURP was 6.5% (95% CI: 0.2–12.7%) (6). The frequently reported rise of erectile dysfunction after TURP is therefore most likely not a direct consequence of TURP but rather caused by confounding factors, such as age.

4.4.6 Long-term outcome

Retreatment rate

Favourable long-term outcome is common after open prostatectomy, TURP and TUIP. A secondary prostatic operation is reported at a constant rate of approximately 1–2% per year (5–8,11). Few data are available on the long-term outcome following TUVP

Long-term risk of mortality

The possibility of an increased long-term risk of mortality after TURP compared to open surgery has been raised by Roos et al. (15). These findings have not been replicated by others (12,16,17).

4.4.7 Conclusions and recommendations

Surgery should be considered for those men:

- who are moderately/severely bothered by LUTS, yet who do not improve after non-surgical (including pharmacological) treatment
- with bothersome LUTS, who not want medical treatment but who request active intervention
- with a strong indication for surgery.
- Surgical prostatectomy (open, TURP, TUIP, TUVP) results in significant subjective and objective improvements superior to medical or minimally invasive treatment. All four surgical procedures have been evaluated in randomized controlled trials.
- TUIP is the surgical therapy of choice for men with prostates < 30 mL and no middle lobes.

4.4.8 REFERENCES

1. **Borboroglu PG, Kane CJ, Ward JF, Roberts JL, Sands JP.**
   Immediate and postoperative complications of transurethral prostatectomy in the 1990s.
   J Urol 1999; 162: 1307-1310.
2. **Pickard R, Emberton M, Neal DE.**
   The management of men with acute urinary retention. National Prostatectomy Audit Steering Group.
   Br J Urol 1998; 81: 712-720.

3. **Bruskewitz RC, Reda DJ, Wasson JH, Barrett L, Phelan M.**
Testing to predict outcome after transurethral resection of the prostate. J Urol 1997; 157: 1304-1308.
4. **Wasson JH, Reda DJ, Bruskewitz RC, Elinson J, Keller AM, Henderson WG.**
A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. The Veterans Affairs Cooperative Study Group on Transurethral Resection of the Prostate. New Engl J Med 1995; 332: 75-79.
5. **Yang Q, Peters TJ, Donovan JL, Wilt TJ, Abrams P.**
Transurethral incision compared with transurethral resection of the prostate for bladder outlet obstruction: a systematic review and meta-analysis of randomised controlled trials. J Urol 2001; 165: 1526-1532.
6. **Madersbacher S, Marberger M.**
Is transurethral resection of the prostate still justified? Br J Urol 1999; 83: 227-237.
7. **Tubaro A, Carter S, Hind A, Vicentini C, Miano L.**
A prospective study of the safety and efficacy of suprapubic transvesical prostatectomy in patients with benign prostatic hyperplasia. J Urol 2001; 166: 172-176.
8. **Mearini E, Marzi M, Mearini L, Zucchi A, Porena M.**
Open prostatectomy in benign prostatic hyperplasia: 10-year experience in Italy.
Eur Urol 1998; 34: 480-485.
9. **Elmalik EM, Ibrahim AI, Gahli AM, Saad MS, Bahar YM.**
Risk factors in prostatectomy bleeding: preoperative urinary tract infection is the only reversible factor.
Eur Urol 2000; 37: 199-204.
10. **Scholz M, Luftenegger W, Harmuth H, Wolf D, Holtl W.**
Single-dose antibiotic prophylaxis in transurethral resection of the prostate: a prospective randomized trial. Br J Urol 1998; 81: 827-829.
11. **Roehrborn CG.**
Standard surgical interventions TUIP/TURP/OPSU. In: Kirby R et al. (eds). Textbook of Benign Prostatic Hyperplasia. Oxford: Isis Medical Media, 1996, pp. 341-375.
12. **Holman CDJ, Wisniewski ZS, Semmens JB, Rouse IL, Bass AJ.**
Mortality and prostate cancer risk in 19 598 men after surgery for benign prostatic hyperplasia.
BJU Int 1999; 84: 37-42.
13. **Hahn RG.**
Smoking increases the risk of large scale fluid absorption during transurethral prostatic resection.
J Urol 2001; 166: 162-165.
14. **Gallucci M, Puppo P, Perachino M, Fortunato P, Muto G, Breda G, Mandressi A, Comeri G, Boccafoschi C, Francesca F, Guazzieri S, Pappagallo GL.**
Transurethral electrovaporization of the prostate vs. transurethral resection. Resection of a multicentric, randomised clinical study on 150 patients. Eur Urol 1998; 33: 359-364.
15. **Roos NP, Wennberg JE, Malenka DJ, Fisher ES, McPherson K, Andersen TF, Cohen MM, Ramsey E.**
Mortality and reoperation after open and transurethral resection of the prostate for benign prostatic hyperplasia. N Engl J Med 1989; 320: 1120-1124.
16. **Hahn RG, Farahmand BY, Hallin A, Hammar N, Persson PG.**
Incidence of acute myocardial infarction and cause-specific mortality after transurethral treatments of prostatic hypertrophy. Urology 2000; 55: 236-240.
17. **Shalev M, Richter S, Kessler O, Shpitz B, Fredman B, Nissenkorn I.**
Long-term incidence of acute myocardial infarction after open and transurethral resection of the prostate for benign prostatic hyperplasia. J Urol 1999; 161: 491-493.

4.5 Lasers

The use of lasers to treat BPH has been contemplated since 1986 but was anecdotal until the early 1990s (1,2), when Shanberg et al. (3) reported the use of the Nd:YAG laser to perform prostatectomy in 10 patients with BPH, resulting in marked improvement in their voiding symptoms. With the development of the right-angle fibre and the refinement of both equipment and technique, the results of many studies have been published. However, as far as durability is concerned, long-term follow-up results are only available from initial studies.

4.5.1 Laser types

Four types of laser have been used to treat the prostate: Nd:YAG, Holmium:YAG, KTP:YAG and diode. Energy can be delivered through a bare fibre, right-angle fibre or interstitial fibre. The use of contact lasers using a bare fibre has been abandoned. In addition, energy levels can be varied to achieve coagulation or vaporization. The difference between coagulation and vaporization is that coagulation causes little vaporization and depends on temperature changes to achieve permanent tissue damage. There is also secondary tissue slough, which is

associated with tissue oedema. Vaporization depends upon temperature changes of over 100°C, which cause the tissue to be dehydrated (4,5). This effect decreases forward scatter into tissue and may cause less tissue oedema. Interstitial treatments depend on inserting the fibre into the prostatic tissue and the use of coagulation techniques (6).

4.5.2 Right-angle fibres

From 1991 onward, reports describing a TRUS-guided, side-firing Nd:YAG laser instrument (the TULIP™ device) for BPH therapy appeared in the urological literature (7,8). These, and other, reports documented the fact that prostatic tissue ablation could be achieved using the Nd:YAG laser. In subsequent years, the TULIP™ device was abandoned and other authors experimented with even greater prostatic tissue ablation using a much simpler side-firing Nd:YAG laser delivery system. This consisted of a gold-plated mirror affixed to the distal end of a standard, flexible, silica-glass, laser transmission fibre (Urolase™ fibre) (9).

Operative technique

Side-firing laser prostatectomy is performed using Nd:YAG laser light at 1064 nm and relatively high power settings (typically between 40 and 80 W), delivered via an optical fibre equipped with a distal reflecting mechanism. This fibre fits through standard cystoscopes and all laser applications are performed transurethrally under the direct visual control of the surgeon. The operation may be performed under general or regional anaesthesia, or under local peri-prostatic block as described by Leach et al. (10). The operating time is approximately 45 minutes or less. Optimal tissue ablation is achieved using long-duration (60–90 seconds) Nd:YAG laser applications to fixed spots along the prostatic urethra. These laser applications are repeated systematically and with considerable overlap until all visible obstructing prostatic tissue has been coagulated (11).

Outcome, morbidity, durability and limitations

There have been many studies comparing side-fire laser to TURP. If randomized studies are considered, the results are quite similar, showing an equivalent improvement in symptom scores and increases in uroflow rates in both groups, although they are higher in the TURP arms (12–17).

An improvement in voiding produced by side-firing Nd:YAG laser prostatectomy has been extensively documented in the urological literature. Kabalin et al. (18) reported that 85% of men undergoing laser prostatectomy could expect at least a 50% improvement in either prostate symptom score or peak urinary flow rate. As far as complex urodynamic evaluation is concerned, several studies have demonstrated the ability of side-firing laser prostatectomy to produce a significant improvement in bladder outflow obstruction. Results of pressure-flow studies have been reported by several authors (8,19–21). These authors reported that 78.6–95% of men undergoing laser treatment were rendered unobstructed at 3- or 6-months of post-operative follow-up.

Catheter irrigation is generally not required and blood loss is statistically lower with Nd:YAG laser coagulation than with TURP because of the excellent haemostasis produced. Both the US and UK multicentre trials documented dramatic differences in serious treatment-related complications, favouring laser prostatectomy as a much safer procedure than TURP (12,13). Disadvantages are the delayed time to normal voiding and severe dysuria (8,12,22).

In a single-institution, randomized, prospective evaluation, Costello et al. (14) found equivalent voiding outcomes for the two procedures, but again documented differences in morbidity between these operations. During the 3-year post-operative follow-up, serious treatment-related complications occurred in 11.8% of laser prostatectomy patients and 35.1% of TURP patients. No study has reported any occurrence of impotence or sustained incontinence. Retrograde ejaculation has been reported in up to 22% of patients. With regard to durability, the observed retreatment rates following laser prostatectomy – approximately 2% per year of follow-up – seem comparable to documented reoperation rates after TURP (18).

Conversely, an Italian retrospective study of 36 patients submitted to side-fire Nd:YAG laser prostatectomy with a minimum follow-up of 5 years reported striking results (23). All patients had undergone pressure-flow studies at 3 months after laser treatment: 32 previously obstructed patients were unobstructed. After 5 years, 43.8% of these patients underwent TURP because of recurring obstruction. Such a retreatment rate is definitely greater than that observed after TURP and even after TUIP. These data therefore suggest caution in giving indications to laser treatment, particularly in patients who are candidates for TURP or TUIP. In fact, these techniques, TURP and TUIP, offer better long-term results and comparable (if not superior) efficacy than laser prostatectomy. Further long-term follow-up studies are needed.

The major limitation of the laser technique compared with conventional TURP is the lack of immediate effect and requirement for urinary catheter drainage for several post-operative days. Some patients may require catheterization for 3–4 weeks or more (24). Even after catheter removal, an improvement in voiding occurs only gradually, and most patients do not notice significant benefits until approximately 3–4 weeks post-operatively.

The best results are obtained if the weight of the gland is below 50–60 g; in larger glands significant

amounts of obstructive prostatic tissue can be left behind (17). Moreover, men with chronic urinary tract infections and chronic bacterial prostatitis are not good candidates for Nd:YAG laser coagulation of the prostate (18) because of the possibility of infection of the necrotic tissue that remains in situ for several weeks after the operation; emergent TURP has been reported to solve this problem (8).

4.5.3 ILC

ILC as a therapy for BPH was first mentioned by Hofstetter in 1991 (25). Since then, several variations and technical and procedural developments have been introduced and tested in clinical trials (26). The objective of ILC of BPH is to achieve marked volume reduction and to decrease urethral obstruction and symptoms. Coagulation necrosis is generated within the adenoma, sparing its urethral surface. As the applicator can be inserted as deeply and as often as necessary, it is possible to coagulate any amount of tissue at any desired location. Post-procedure, the intraprostatic lesions result in secondary atrophy and regression of the prostate lobes rather than sloughing of necrotic tissue (27).

Operative technique

Fibres employed for ILC must emit laser radiation at a relatively low power density. The most commonly used fibres are ITT Light Guide™, Dornier, and the Diffusor-Tip™, Indigo. Nd:YAG lasers or diode lasers are used for ILC. ILC can be carried out using the transurethral approach, with local, regional or systemic anaesthesia. The laser fibre is introduced from a cystoscope within the urethra. The total number of fibre placements is dictated by the total prostate volume and configuration. As a general guideline, one or two placements are used for each estimated 5–10 cm^3 of prostate volume. In general, the sites for fibre placement are chosen according to where the bulk of hyperplastic tissue is found (26).

Outcome, morbidity, durability and limitations

Studies were performed to compare the results with ILC with those of other laser techniques, primarily TURP. The results of several studies indicated the effectiveness of ILC in treating BPH with regard to symptoms, obstruction and enlargement. All studies reported marked improvements in symptom score, peak flow rate, residual urine volume and prostate volume (26–31). Urodynamic parameters were also measured before and after ILC treatment (32,33). Pressure-flow studies demonstrated a sufficient decrease of the intravesical pressure, urethral opening pressure and urethral resistance.

Prospective and randomized studies were also performed to compare the results achieved with ILC with those of other laser techniques (33) and TURP (30,34,35). Muschter et al. reported on a series of 97 patients with severely symptomatic BPH; 48 patients received ILC and 49 underwent TURP (34). Within 12 months, there were no statistical differences between groups for all the considered parameters. However, four ILC patients (8.3%) were considered to be treatment failures and underwent TURP.

As for morbidity, there is a temporary increase of obstruction after ILC, which can result in urinary retention and temporary irritative symptoms, such as urgency (25). Post-operative irritative symptoms have been observed in 5–15% of patients (28,31,34). Post-operative catheterization was required for an average of up to 18 days, although the catheter was removed within 10 days in more than 70% of cases. No study has reported any occurrence of impotence or sustained incontinence, though retrograde ejaculation was occasionally reported, with an incidence ranging from 0–11.9%. Urethral strictures or bladder neck strictures are not common, and have been reported in approximately 5% of patients.

The retreatment rate is up to 15.4% with a maximum follow-up of 12 months; although as follow-up becomes longer, the retreatment rate is expected to be higher. Currently, the results of only one long-term follow-up study are available (36). In 394 patients followed for up to 3 years, the retreatment rate was 3.1% per year in the first year, rising to 9.6% thereafter (36).

ILC can be performed in small prostates and also seems to be suitable to debulk larger prostates or to treat highly obstructed patients (26). This procedure can be seen as a true alternative to TURP in selected patients with some advantages, such as almost no serious morbidity, and certain disadvantages, such as the need for longer post-operative catheterization and the lack of tissue for biopsy. However, further comparative randomized studies with longer follow-up are needed to assess the durability of this procedure.

4.5.4 Holmium laser resection of the prostate (HoLRP)

The Holmium laser (2140 nm) is a pulsed, solid-state laser that has been used in urology for a variety of endourological applications in soft tissues and for the disintegration of urinary calculi (37). Prostatectomy using this energy source is a relatively new technique with the first patient reports appearing in 1995 (37,38). The Ho:YAG wavelength is strongly absorbed by water and the zone of coagulation necrosis in tissue is limited to 3–4 mm, sufficient to obtain adequate haemostasis (38). The peak power achieved results in intense tissue vaporization and in precise and efficient cutting ability in the prostatic tissue.

Operative technique

Instrumentation for this technique includes a 550-µm end-firing quartz fibre and an 80-W Ho:YAG laser. A continuous flow resectoscope is required with a working element; normal saline is used as the irrigant. The basic principle of the technique consists of retrograde enucleation of the prostate and fragmentation of the enucleated tissue to allow its elimination through the operating channel of the resectoscope (38,39).

Outcome, morbidity, durability and limitations

As this technique is relatively new, only a few studies with a short follow-up have been published to date. Gilling et al. (40) presented the results of a prospective, randomized trial comparing TURP with HoLRP; so far, 120 patients with urodynamic obstruction have been enrolled with prostates less than 100 g in size (Schafer grade 2). Preliminary analysis has revealed a longer mean resection time (42.1 vs. 25.8 minutes; $p < 0.0001$) for HoLRP patients, but a shorter mean catheter time (20.0 vs. 37.2 hours; $p < 0.0001$) and length of hospital stay (26.4 vs. 47.4 hours; $p < 0.0001$). Symptomatic and urodynamic improvement were equivalent in the two groups.

Comparative studies of Nd:YAG versus prostatectomy have been conducted, clearly demonstrating that HoLRP is associated with significantly shorter catheter time and a lower incidence of post-operative dysuria (41). Unfortunately, the longest available follow-up is only 12 months, which has confirmed the short-term durability of the procedure (36).

Post-operative dysuria is the most common complication, with an incidence of approximately 10% (38,40,42). No major complication has been described; however, the technique is a surgical procedure that requires significant endoscopic skill and cannot be considered easy to learn. Conversely, there are no specific limitations to the procedure; the size of the prostate that can be treated depends on the experience and patience of the urologist, although the presence of a prostate gland over 100 mL is a relative contraindication in urologists' early experience (38). Patients on anticoagulant medication and those with urinary retention can be safely treated (43). Retrograde ejaculation occurs in 75–80% of patients; no post-operative impotence has been reported (38).

4.5.5 Conclusions

Laser prostatectomy should be advised for patients who are:

- Receiving anticoagulant medication
- Unfit for TURP (side-fire or ILC)
- Wanting to maintain ejaculation (side-fire or ILC).

4.5.6 REFERENCES

1. **Kandel LB, Harrison LH, McCullough DL.**
   Transurethral laser prostatectomy: Creation of a technique for using the Neodymium-Yttrium-Aluminium-Garnet (YAG) laser in the canine model. J Urol 1986; 133: 110A.
2. **Johnson DE, Levinson AK, Greskovich FJ.**
   Transurethral laser prostatectomy using a right-angle delivery system. SPIE Proceedings 1991; 1421: 36.
3. **Shanberg AM, Tansey LA, Baghdassarian R.**
   The use of the neodymium YAG laser in prostatotomy. J Urol 1985; 133: 331A.
4. **Stein BS.**
   Laser-tissue interaction. In: Smith JA et al. (eds). Lasers in Urologic Surgery. St Louis, USA: Mosby, 1994, p. 10.
5. **Johnson DE, Price RE, Cromeens DM.**
   Pathologic changes occurring in the prostate following transurethral laser prostatectomy. Lasers Surg Med 1992; 12: 254-263.
6. **Muschter R, Hofstetter A, Hessel S.**
   Interstitial laser prostatectomy - experimental and first clinical results. J Urol 1992; 147: 346A.
7. **Assimos DG, McCullough DL, Woodruff RD et al.**
   Canine transurethral laser-induced prostatectomy. J Endourol 1991; 5: 145-149.
8. **Puppo P, Perachino M, Ricciotti G, Scannapieco G.**
   Transurethral ultrasound-guided laser-induced prostatectomy: objective and subjective assessment of its efficacy for treating benign prostatic hyperplasia. Eur Urol 1994; 25: 220-225.
9. **Costello AJ, Bowsher WG, Bolton DM, Braslis KG, Burt J.**
   Laser ablation of the prostate in patients with benign prostatic hypertrophy. Br J Urol 1992; 69: 603-608.
10. **Leach GE, Sirls L, Ganabathi, Roskamp D, Dmochowski R.**
    Outpatient visual laser-assisted prostatectomy under local anesthesia. Urology 1994; 43: 149-153.

11. **Muschter R, Perlmutter AP.**
The optimisation of laser prostatectomy. II. Other lasing techniques. Urology 1994; 44: 856–461.
12. **Cowles RS, Kabalin JN, Childs S, Lepor H, Dixon C, Stein B, Zabbo A.**
A prospective randomized comparison of transurethral resection to visual laser ablation of the prostate for the treatment of benign prostatic hyperplasia. Urology 1995; 46: 155-160.
13. **Anson K, Nawrocki J, Buckley J, Fowler C, Kirby R, Lawrence W, Paterson P, Watson G.**
A multicenter, randomized, prospective study of endoscopic laser ablation versus transurethral resection of the prostate. Urology 1995; 46: 305-310.
14. **Costello AJ, Crowe HR, Asopa R.**
Long-terms results of randomized laser prostatectomy vs. TURP: modification of laser prostatectomy technique with biodegradable stent insertion. J Urol 1996; 155: 316A.
15. **Oswald M, Schmidlin F, Jichilinski P et al.**
Combination of thermocoagulation and vaporisation using a Nd:YAG/KTP laser versus TURP in BPH treatment: preliminary results of a multicenter prospective randomized study. J Urol 1997; 157: 42A.
16. **Kabalin JN.**
Neodymium: YAG laser coagulation prostatectomy for patients in urinary retention.
J Endourol 1997; 11: 207-209.
17. **Costello AJ, Kabalin JN.**
Side-firing neodymium:YAG laser prostatectomy. Eur Urol 1999; 35: 138-146.
18. **Kabalin JN, Bite G, Doll S.**
Neodymium:YAG laser coagulation prostatectomy: 3 years of experience with 227 patients.
J Urol 1996; 155: 181-185.
19. **Te Slaa E, De Wildt MJ, Rosier PF, Wijkstra H, Debruyne FM, de la Rosette JJ.**
Urodynamic assessment in the laser treatment of benign prostatic enlargement.
Br J Urol 1995; 76: 604-610.
20. **Cannon A, De Wildt M, Abrams PH, De la Rosette JJ.**
Urodynamics and laser prostatectomy. World J Urol 1995; 13: 134-136.
21. **Choe JM, Sirls LT.**
High-energy visual laser ablation of the prostate in men with urinary retention: pressure flow analysis.
Urology 1996; 48: 584-588.
22. **Stein BS, Altwein JE, Bruschter R et al.**
Laser prostatectomy. In: Denis L, Griffiths K, Khoury S et al. (eds). Proceedings of the Fourth International Consultation on BPH, Paris, July 1997. Health Publications: Plymouth, 1998, pp. 529-540.
23. **Perachino M, Puppo P.**
Prostatectomia laser con metodica side-fire: risultati a distanza di 5 anni.
Acta Urol Ital 1998; 12 (Suppl 1): 44.
24. **Kabalin JN, Bite G.**
Laser prostatectomy performed with right angle firing neodymium: YAG laser fiber at 40 watt power settings. Urology (letter) 1997; 158: 1923.
25. **Hofstetter A.**
Interstitielle Thermokoagulation (ITK) von Prostatatumoren. Lasermedizin 1991; 7: 179-180.
26. **Muschter R, Whitfield H.**
Interstitial laser therapy of benign prostatic hyperplasia. Eur Urol 1999; 35: 147-154.
27. **Muschter R, Hofstetter A.**
Technique and results of interstitial laser coagulation. World J Urol 1995; 13: 109-114.
28. **Bhatta KM, Perlmutter A, Cho G et al.**
A new technique of subsurface and interstitial laser therapy using a diode laser (wavelength = 1000 nm) and a catheter delivery device. J Urol 1996; 155: 310A.
29. **Schettini M, Diana M, Fortunato P et al.**
Results of interstitial laser coagulation of the prostate. J. Endourol 1996; 10 (Suppl 1): S191.
30. **Whitfield HN.**
A randomized prospective multicenter study evaluating the efficacy of interstitial laser coagulation.
J Urol 1996; 155: 318A.
31. **Fay R, Chan SL, Kahn R et al.**
Initial results of a randomized trial comparing interstitial laser coagulation therapy to transurethral resection of the prostate. J Urol 1997; 157 (Suppl 1): 41.
32. **Henkel TO, Greschner M, Luppold T, Alken P.**
Transurethral and transperineal interstitial laser therapy of BPH. In: Muller G et al. (eds). Laser-induced Interstitial Thermotherapy. Bellingham: SPIE Press, 1995, pp. 416-423.
33. **Horninger W, Janetschek G, Watson G, Reissigl A, Strasser H, Bartsch G.**

Are contact laser, interstitial laser, and transurethral ultrasound-guided laser-induced prostatectomy superior to transurethral prostatectomy? Prostate 1997; 31: 255-263.

34. **Muschter R, Sroka R, Perlmutter AP et al.**
High power interstitial laser coagulation of benign prostatic hyperplasia.
J Endourol 1996; 10 (Suppl 1): S197.

35. **Whitfield HN.**
The use of an interstitial diode laser (Indigo) in laser prostatectomy. A randomized, controlled, prospective study. J Endourol 1995; 9 (Suppl 1): S149.

36. **Muschter R, Hofstetter A, de la Rosette JJ.**
Thermocoagulation au laser de l'adenome de la prostate par voie interstitielle.
Ann Urol (Paris) 1997; 31: 27-37.

37. **Le Duc A, Gilling PJ.**
Holmium laser resection of the prostate. Eur Urol 1999; 35: 155-160.

38. **Gilling PJ, Cass CB, Malcolm AR, Fraundorfer MR.**
Combination Holmium and Nd: YAG laser ablation of the prostate: initial clinical experience.
J Endourol 1995; 9: 151-153.

39. **Chun SS, Razvi HA, Denstedt JD.**
Laser prostatectomy with the holmium:YAG laser. Tech Urol 1995; 1(4): 217-221.

40. **Gilling PJ, Fraundorfer MR, Kabalin JB.**
Holmium: YAG laser resection of the prostate (HoLRP) versus transurethral electrocautery resection of the prostate (TURP): a prospective randomized, urodynamic-based clinical trial. J Urol 1997; 157: 149A.

41. **Gilling PJ, Cass CB, Malcolm A, Cresswell M, Fraundorfer MR, Kabalin JN.**
Holmium laser resection of the prostate (HoLRP) versus neodymium: YAG visual laser ablation of the prostate (VLAP): a randomized prospective comparison of two techniques for laser prostatectomy.
Urology 1998; 51: 573-577.

42. **Le Duc A, Anidjar M, Teillac P, Desgrandchamps F.**
The Holmium YAG laser in the transurethral resection of prostate. Br J Urol 1997; 80 (Suppl 2): A773.

43. **Kabalin JN, Mackey MJ, Cresswell MD, Fraundorfer MR, Gilling PJ.**
Holmium: YAG laser resection of the prostate (HoLRP) for patients in urinary retention.
J Endourol 1997; 11: 291-293.

4.6 Transrectal high-intensity focused ultrasound (HIFU)

4.6.1 Assessment

No specific diagnostic work-up prior to transrectal HIFU therapy is necessary. However, the following parameters should be obtained:

- I-PSS, including quality of life
- Free uroflowmetry, including post-void residual urine volume
- Serum PSA
- TRUS
- Pressure-flow study advisable.

4.6.2 Procedure

A beam of ultrasound can be brought to a tight focus at a selected depth within the body, thus producing a region of high energy density within which tissue can be destroyed without damage to the overlying or intervening structures (1–3). If the site-intensity is set below the tissue cavitation threshold, the predominant therapeutic effect is the induction of heat. This technique is known as high-intensity focused ultrasound (HIFU). The source for HIFU is a piezoceramic transducer, which has the property of changing its thickness in response to an applied voltage (1–3). Theoretically the prostate can be ablated by HIFU via a transabdominal or transrectal route. In clinical use, however, only transrectal HIFU devices are applied for the indication of BPH.

Clinical data are only available for one device, the Sonablate® (1–4). This system uses the same 4.0 MHz transrectal transducer for imaging and therapy. The focal length (2.5–4.0 cm) is dependent upon the crystal used. The site intensity can be varied from 1.260 to 2.200 W/cm^2. Within the HIFU beam focus, an ellipsoidal tissue volume approximately 2 mm in diameter and 10 mm in length is destroyed (1–3). In order to create a clinically useful volume of necrosis, a multiplicity of laterally or axially displaced individual lesions is generated by physical movement of the sound-head. The histological effect of transrectal HIFU therapy using the Sonablate® on the canine and human prostate has been studied in detail (1–3,5,6).

4.6.3 Morbidity/complications

In general, transrectal HIFU is well-tolerated but requires general anaesthesia or heavy intravenous sedation.

The most prominent side-effect is prolonged urinary retention, lasting for 3–6 days. Haematospermia for 4–6 weeks is observed in up to 80% of sexually active men, and patients frequently discharge two to three drops of blood prior to micturition for several weeks. Urinary tract infection occurs in around 7% of patients. No cases of urethral strictures, incontinence or the need for blood transfusion have been reported in the literature.

Two severe complications have been reported. In one patient, perforation of the descending colon approximately 50–60 cm above the treatment zone occurred. It was caused by inadvertent overfilling to 500 mL and subsequent rupture of the condom that covered the ultrasound probe. This complication led to reconstruction of the filling apparatus and the probe such that the problem can now be reliably avoided. The second severe complication was a thermolesion of the rectum requiring surgical intervention. This was most likely caused by using an inappropriately high-site intensity exceeding 2.300 W/cm2. As a consequence, the maximum site intensity was set at 2.000 W/cm^2.

4.6.4 Outcome

In June 1992, an international Phase II clinical trial was initiated to evaluate the safety and efficacy of transrectal HIFU therapy for patients with LUTS due to BPH. To date, several hundred patients have been treated with the Sonablate® at various sites. In the initial US series, Bihrle et al. (7) reported on experience with 15 patients and a follow-up of 90 days. The Qmax increased from 9.3 mL/s to 14.0 mL/s and the post-void residual urine volume decreased from 154 mL to 123 mL (7). Ebert et al. (8) treated 35 patients, eight of whom had urinary retention. The Qmax increased from 7.6 mL/s to 15.2 mL/s after 3 months. Within the same time period, the post-void residual urine volume decreased from 182 mL to 50 mL and the I-PSS from 17.9 to 7.1. The initial report of the study included 50 patients, 20 of whom were followed up for 12 months (5). The Qmax increased from 8.9 (± 4.1) to 12.4 (± 5.6) mL/s (6 months, n = 33) and 13.1 (± 6.5) mL/s (12 months, n = 20). In the same time period, the post-void residual urine volume decreased from 131 (± 120) mL to 48 (± 41) mL at 6 months and to 35 (± 30) mL at 12 months. The AUA symptom score reduced from 24.5 (± 4.7) to 13.4 (± 4.7) at 6 months and to 10.8 (± 2.5) at 12 months (5). Several other sites have confirmed these data (9–11).

4.6.5 Urodynamics

The urodynamic effect of transrectal HIFU therapy has been studied by Madersbacher et al. (12). Thirty patients underwent urodynamic investigations (pressure–flow study) before and after a mean of 4.5 months following HIFU therapy. Pre-operatively, 80% of patients were obstructed and a further 20% were in the intermediate zone according to the Abrams–Griffith nomogram. After therapy, a statistically significant decrease in maximum detrusor pressure, detrusor pressure at Qmax and linear passive urethral resistance relation was observed. After HIFU, half of the patients were in the equivocal zone and 13% were clearly unobstructed, yet 37% were still obstructed according to the Abrams–Griffith nomogram. The authors concluded that the capability of transrectal HIFU to reduce bladder outlet obstruction was moderate (12). As a consequence, transrectal HIFU should not be considered for severely obstructed patients or those with an absolute indication for surgery.

4.6.6 Quality of life and sexual function

There are no reliable data on quality of life after transrectal HIFU except from a study by Schatzl et al. (13), who studied in detail the early post-operative morbidity of several less invasive procedures. Similarly, there is little data on sexual function. Haematospermia lasting for a maximum of 4–6 weeks is seen in the majority of sexually active patients. Retrograde ejaculation and erectile dysfunction can be safely avoided, although some patients report a decreased ejaculate volume.

4.6.7 Durability

The long-term outcome of 80 patients with a follow-up of up to 4 years and a minimum follow-up of 2 years has been studied (14). The mean follow-up of the study population (excluding patients who crossed over to TURP due to insufficient therapeutic response) was 41.3 months (range: 13–48 months). Thirty-five men (43.8%) underwent TURP due to an insufficient therapeutic response during the 4-year study period. The retreatment-free period was significantly longer for patients with a pre-treatment average flow rate of more than 5 mL/s ($p = 0.05$) and lower grades of urodynamically documented bladder outlet obstruction ($p = 0.03$) (14). A similar trend, which did not reach statistical significance, was noted for individuals with a higher Qmax and lower post-void residual urine volume.

4.6.8 Patient selection

The fact that only a handful of clinical studies with a limited number of patients have been published, hinders a reliable statement concerning patient selection, yet a few selection criteria have been identified. Patients with one or more of the following criteria are unsuitable for transrectal HIFU therapy:

- Prostates with dense calcifications (possibility of tissue cavitation)
- Large prostates (> 75 mL)

- Rectum to bladder neck distance over 40 mm
- Large middle lobes
- Higher grades of bladder outlet obstruction (BOO) – (higher treatment failure rate)
- Absolute indication for surgery.

4.6.9 Conclusions

Transrectal HIFU therapy is the only technique that provides non-invasive tissue ablation; however, general anaesthesia or at least heavy intravenous sedation is required. Improvement of urinary symptoms is in the range 50–60% and Qmax increases by a mean of 40–50%. Long-term efficacy is limited, with a treatment failure rate of approximately 10% per year. No data are yet available from randomized, controlled trials.

4.6.10 REFERENCES

1. **Madersbacher S, Marberger M.**
   Applications of high energy focused ultrasound in urology. Curr Opinion Urol 1995; 5: 147-149.
2. **Madersbacher S, Marberger M.**
   Therapeutic applications of ultrasound in urology. In: Marberger M (ed). Application of Newer Forms of Therapeutic Energy in Urology. Oxford: Isis Medical Media, 1995, pp. 115-136.
3. **Madersbacher S, Marberger M.**
   High-intensity focused ultrasound for prostatic tissue ablation. Curr Opinion Urol 1996; 6: 28-32.
4. **Madersbacher S, Djavan B, Marberger M.**
   Minimally invasive therapy in BPH. Curr Opinion Urol 1998; 8: 17-26.
5. **Madersbacher S, Kratzik C, Susani M, Marberger M.**
   Tissue ablation in benign prostatic hyperplasia with high intensity focused ultrasound. J Urol 1994; 152: 1956-1961.
6. **Madersbacher S, Pedevilla M, Vingers L, Susani M, Marberger M.**
   Effect of high-intensity focused ultrasound on human prostate cancer in vivo. Cancer Res 1995; 55: 3346-3351.
7. **Bihrle R, Foster RS, Sanghvi NT, Donohue JP, Hood JP.**
   High intensity focused ultrasound for the treatment of benign prostatic hyperplasia: early United States clinical experience. J Urol 1994; 151: 1271-1275.
8. **Ebert T, Graefen M, Miller S, Saddeler D, Schmitz-Drager B, Ackermann R.**
   High-intensity focused ultrasound (HIFU) in the treatment of benign prostatic hyperplasia (BPH). Keio J Med 1995; 44: 146-149.
9. **Mulligan ED, Lynch TH, Mulvin D, Greene D, Smith JM, Fitzpatrick JM.**
   High-intensity focused ultrasound in the treatment of benign prostatic hyperplasia. Br J Urol 1997; 79: 177-180.
10. **Nakamura K, Baba S, Saito S et al.**
    High-intensity focused ultrasound energy for benign prostatic hyperplasia: clinical response at 6 months to treatment using Sonablate 200™. J Endourol 1997; 11: 197-201.
11. **Sullivan LD, McLoughlin MG, Goldenberg LG et al.**
    Early experience with high-intensity focused ultrasound for the treatment of benign prostatic hyperplasia. Br J Urol 1997; 79: 172-176.
12. **Madersbacher S, Klingler CH, Schatzl G et al.**
    The urodynamic impact of transrectal high intensity focused ultrasound on bladder outflow obstruction. Eur Urol 1996; 30: 437-445.
13. **Schatzl G, Madersbacher S, Lang T, Marberger M.**
    The early postoperative morbidity of transurethral resection of the prostate and of four minimally invasive treatment alternatives. J Urol 1997; 158: 105-111.
14. **Madersbacher S, Schatzl G, Djavan B, Stulnig T, Marberger M.**
    The long-term outcome of transrectal high intensity focused ultrasound therapy for benign prostatic hyperplasia. Eur Urol 2000; 37: 687-694.

4.7 TUNA®

4.7.1 Assessment

No specific diagnostic work-up prior to TUNA®, is necessary.

4.7.2 Procedure

The TUNA® device delivers low-level, radio-frequency energy to the prostate via needles inserted transurethrally (1).

4.7.3 Morbidity/complications

TUNA® is usually performed as an out-patient procedure under local anaesthesia, although intravenous sedation is required in some patients (1). Post-operative urinary retention is seen in 13.3–41.6% of patients and lasts for a mean of 1–3 days; within 1 week, 90–95% of patients are catheter-free (1). Irritative voiding symptoms lasting up to 4–6 weeks are frequently present (2). Continence status is not affected.

4.7.4 Outcome

Several non-randomized clinical trials have documented the clinical efficacy of this procedure with a fairly consistent outcome (3–7). Worldwide, approximately 650 patients have been studied in strict clinical trials. The symptomatic improvement reported ranged from 40–70%. These data are statistically significantly better than at baseline and surpass the expected placebo effect. Improvements in Qmax vary widely from 26–121% in non-retention patients. There is no convincing evidence that prostate size is significantly reduced following TUNA® (7–9).

4.7.5 Randomized clinical trials

TUNA® has been compared with TURP in one trial (8) with 12-month follow-up data. In both treatment arms, there was a significant decrease in AUA symptom score and bother score, although improvements were slightly higher in the TURP arm. Improvement in Qmax was significantly higher after TURP than after TUNA®. Adverse events, such as bleeding, dysuria, erectile dysfunction, urinary tract infection or strictures, were more frequent in the TURP arm.

4.7.6 Impact on bladder outflow obstruction

The impact of TUNA® on bladder outflow obstruction as assessed by pressure-flow studies was determined in seven clinical studies (7–13). In all studies, a statistically significant decrease in maximum detrusor pressure or detrusor pressure at Qmax was demonstrable, yet a number of patients remained in the obstructed range after TUNA® therapy.

4.7.7 Durability

Several authors have reported on the long-term efficacy of the TUNA® procedure. Within 1 year, positive results can be translated into percentages ranging from 5–42% (1). Schulman et al. (14) recently presented 3-year follow-up data on 49 patients after TUNA®. Improvement in Qmax exceeding 50% was seen in 53% of patients after 36 months. Ten patients (20%) underwent TURP because of an insufficient therapeutic response (1). Long-term follow-up data exceeding this time period are not yet available.

4.7.8 Patient selection

Few selection criteria have been identified. TUNA® is not suitable for patients with prostate volumes exceeding 75 mL or isolated bladder neck obstruction

4.7.9 Conclusions

TUNA, is a simple and safe technique and can be performed under local anaesthesia in a significant number of patients. It results in an improvement of urinary symptoms in the range 50–60% and Qmax increases by a mean of 50–70%. Clinical efficacy has been proven in only one randomized controlled trial, and there is limited evidence of long-term efficacy.

4.7.10 REFERENCES

1. **Chapple CR, Issa MM, Woo H.**
   Transurethral needle ablation (TUNA). A critical review of radiofrequency thermal therapy in the management of benign prostatic hyperplasia. Eur Urol 1999; 35: 119-128.
2. **Schatzl G, Madersbacher S, Lang T, Marberger M.**
   The early postoperative morbidity of transurethral resection of the prostate and of four minimally invasive treatment alternatives. J Urol 1997; 158: 105-111.
3. **Giennakopoulos X, Grammeniatis E, Gartzios A, Pappas G.**
   Transurethral needle ablation (TUNA) of the prostate: preliminary results using the new generation TUNA III catheter on patients with symptomatic BPH controlled by a series of 50 patients using TUNA II

device. Eur Urol 1996; 30: 986-992.

4. **Ramon J, Lynch TH, Eardley I, Ekman P, Frick J, Jungwirth A, Pillai M, Wiklund P, Goldwasser B, Fitzpatrick JM.**
Transurethral needle ablation of the prostate for the treatment of benign prostatic hyperplasia: a collaborative multicentre study. Br J Urol 1997; 80: 128-134.

5. **Roehrborn CG, Issa MM, Bruskewitz RC, Naslund MJ, Oesterling JE, Perez-Marrero R, Shumaker BP, Narayan P.**
Transurethral needle ablation for benign prostatic hyperplasia: 12-month results of a prospective, multicenter US study. Urology 1998; 51: 415-421.

6. **Schulman CC, Zlotta AR.**
Transurethral needle ablation (TUNA) of the prostate: clinical experience with two years' follow-up in patients with benign prostatic hyperplasia (BPH). J Urol 1997; 157: 98-102.

7. **Minardi D, Garafolo F, Yehia M, Cristalli AF, Giammarco L, Galosi AB, Muzzonigro G.**
Pressure-flow studies in men with benign prostatic hypertrophy before and after treatment with transurethral needle ablation. Urol Int 2001; 66: 89-93.

8. **Bruskewitz R, Issa MM, Roehrborn CG, Naslund MJ, Perez-Marrero R, Shumaker BP, Oesterling JE.**
A prospective randomized 1-year clinical trial comparing transurethral needle ablation to transurethral resection of the prostate for the treatment of symptomatic benign prostatic hyperplasia.
J Urol 1998; 159: 1588-1594.

9. **Rosario DJ, Woo H, Potts KL, Cutinha PE, Hastie KJ, Chapple CR.**
Safety and efficacy of transurethral needle ablation of the prostate for symptomatic outlet obstruction.
Br J Urol 1997; 80: 579-586.

10. **Issa MM.**
Transurethral needle ablation of the prostate: report of initial United States experience.
J Urol 1996; 156: 413-419.

11. **Millard RJ, Harewood LM, Tamaddon K.**
A study of the efficacy and safety of transurethral needle ablation (TUNA®) treatment for benign prostatic hyperplasia. Neurourol Urodyn 1996; 15: 619-629.

12. **Campo B, Bergamaschi F, Corrada P, Ordesi G.**
Transurethral needle ablation (TUNA) of the prostate: a clinical and urodynamic evaluation.
Urology 1997; 49: 847-850.

13. **Steele GS, Sleep DJ.**
Transurethral needle ablation of the prostate: a urodynamic based study with 2-year follow-up.
J Urol 1997; 158: 1834-1838.

14. **Schulman CC, Zlotta AR.**
Transurethral needle ablation (TUNA™) of the prostate: clinical experience with three years follow-up in patients with benign prostatic hyperplasia (BPH). Eur Urol 1998; 33 (Suppl 1): 148.

4.8 TUMT

4.8.1 Assessment

Diagnostic endoscopy is essential because it is important to identify the presence of an isolated enlarged middle lobe or an insufficient length of the prostatic urethra.

4.8.2 Procedure

TUMT is a registered trademark of Technomed Medical Systems (France), a company considered to be the pioneer of microwave thermotherapy. To date, tens of thousands of patients worldwide have been treated with the Prostatron® device. Other thermotherapy devices have also been developed: Prostcare® (Brucker, France); ProstaLund® (Lund Systems, Sweden); and Targis® (Urologix, USA). On a conceptional basis, they are all similar in delivering microwave energy to the prostate with some type of feedback system. The majority of data in the literature on thermotherapy has been based on the Prostatron® device. Initial experience focused on low-energy protocols, but subsequently higher energy levels were used to improve treatment outcomes and response rates.

4.8.3 The microwave thermotherapy principle

Microwave thermotherapy devices consist of a treatment module that contains the microwave generator with a temperature measurement system and a cooling system. A treatment catheter is connected to the module and inserted into the prostatic urethra. The main difference between the devices available is the design of the urethral applicator. Apart from differences in the construction of the catheter, the characteristics of the applicators differ, significantly affecting the heating profile (1,2). The similarity in catheter construction consists

of the presence of a microwave antenna positioned in the tip of the catheter just below the balloon. Fluid channels surrounding the catheter provide urethral cooling. Also incorporated in the catheter are one or more temperature sensors that differ in the way in which they measure temperature.

4.8.4 Morbidity

Morbidity following TUMT is an important issue. Low-energy TUMT is well-tolerated by patients. Most patients experience perineal discomfort and urinary urgency for several days after treatment, but not usually for longer. Occasionally, haematuria is noticed. No tissue sloughing occurs and urinary retention is expected in up to 25% of patients (2–6). In these cases, a catheter may be necessary for an average of 7 days.

High-energy treatment is also well-tolerated, although pain medication needs to be administered to most patients prior to or during therapy. In contrast to the low-energy protocol, urinary retention is usual in patients treated with high-energy TUMT; the average catheterization time is 2 weeks. Only two papers mention erectile dysfunction following thermotherapy (incidence 0.8–5%) (7,8). For patients treated with low-energy protocols, the retrograde ejaculation rate ranges from 0–11%, while for high-energy protocols, this figure increases up to 44%.

Outcome: objective, subjective and urodynamics

Low-energy protocols: The standard operating software for the Prostatron® is version 2.0, and remarkably similar clinical results have been reported worldwide from several centres (2–4, 7, 9–13). The clinical efficacy of TUMT has been confirmed in several randomized, SHAM-(placebo) controlled studies (4, 5, 14, 15). Symptomatic improvement is significant, with a decrease in Madsen symptom score from around 13 to 4. Changes in objective parameters are less pronounced. The mean increase in Qmax is 3–4 mL/s, representing a mean improvement of approximately 35% over baseline. These improvements are noted from 6 weeks and persist over a period of 5 years (16, 17).

A randomized study comparing TUMT with TURP was performed by Dahlstrand et al. (3). This study showed significant improvement after both TUMT and TURP in symptom score, Qmax, post-void residual urine volume and grade of bladder outlet obstruction. Although the decrease in symptom score was more pronounced after TURP (92%) than after TUMT (78%).

High-energy protocol: The first reports on the application of high-energy levels using Prostasoft® 2.5 were published by de la Rosette et al. (18) and Devonec et al. (19) and demonstrated clinically significant improvements. More recently, the European BPH Study Group performed a multicentre study of 116 patients using high-energy TUMT (20). In this study, the mean Madsen score improved from 13.6 at baseline to 5.5 at 26 weeks. Qmax improved from 9.6 mL/s at baseline to 14.1 mL/s at 26 weeks of follow-up. These objective and subjective improvements were sustained at 52 weeks.

At 3-months of follow-up TRUS identified a prostatic cavity in almost 40% of patients. There appeared to be a good correlation between the presence of a cavity and uroflowmetry improvement (21). The best candidates for this treatment protocol appeared to be patients with moderate-to-severe bladder outlet obstruction, as measured by pressure-flow studies, and those with larger prostates (22).

One-year follow-up results of a prospective randomized study comparing high-energy TUMT with TURP were reported recently (23). After TURP and thermotherapy, there was a significant improvement in all clinical parameters. At 1 year of follow-up, the symptomatic improvement was 78% in the TURP group versus 68% in the TUMT group, with improvements in free flow being 100% and 69%, respectively. Both groups had showed significant relief of bladder outlet symptoms. No serious complications occurred in either group, but one patient in each group required another treatment. It was concluded that satisfactory results were obtained after both treatments, with improvements observed following high-energy TUMT being in the same range as those seen after TURP.

4.8.5 High-intensity-dose protocol

Although the results following high-energy TUMT are good, changes to the Prostasoft® software have recently been reported. It was concluded from clinical experience that a shorter duration of treatment did not alter efficacy or decrease morbidity (22). On a conceptual basis, the so-called Prostasoft® 3.5 protocol differed significantly from former protocols. Firstly, the principle of stepwise energy increments was abandoned and the treatment was initiated at an 80 W energy level. Secondly, the urethral temperature feedback system was also abandoned. Energy delivery is now guided by the rectal temperature sensor via a feedback loop. Third, the cooling temperature starts at a lower value (8°C) and is also linked to rectal temperature. Finally, the total treatment duration is shortened to only 30 minutes. This Prostasoft® 3.5 protocol can therefore be considered to be high-intensity-dose TUMT.

Pace et al. (24) found in 56 patients, at six months, a decrease in IPSS from 18.1 to 5.1, an increase in maximum flow from 9.1 mL/s to 17.8 mL/s and cavities within the prostatic tissue of 54 of the 56 patients (95%). De La Rosette et al. (26) found in 167 patients, at 12 months, a decrease in IPSS from 19.2 to 7.9 and an

increase in maximum flow rate from 8.9 to 16.4.

4.8.6 Durability

Several studies using low-energy thermotherapy report on surgical retreatment rates for up to 1 year of 11% (25) and 10% (20). On the other hand, Van Cauwelaert et al. (11) reported only low retreatment rates with significant subjective and objective improvements. Recently Tsai et al. (27) reported a 5-year retreatment rate in 45 patients of 84.4% with medication (46.7%) or endoscopic surgery (37.7%), while Daehlin et al. (28) found a retreatment rate after 5 years in 71 patients of 68%.

When applying higher energy levels, the outcome seems improved and may eventually result in a more durable response. In a study by de la Rosette et al. (5,18) additional TURP was performed in only three out of 116 patients. De Wildt et al. (29) confirmed these findings, documenting five surgical interventions at 1-year follow-up in 85 patients treated.

4.8.7 Patient selection

As the morbidity is relatively low and the treatment can be performed without anaesthesia, patients in poor health are particularly good candidates for thermotherapy. In particular, such patients with retention can benefit from this treatment. Good results with regard to catheter release have been obtained, with a success rate of 72% after 6 months in 29 patients (30). In a larger study of 200 patients, with a follow up of 2 years in 155 patients, only 7% failed to respond (31).

4.8.8 Conclusions

- High-energy TUMT produces significant subjective and objective improvement, with sustained and durable long-term results.
- Morbidity after TUMT consists mainly of the need for catheter drainage after treatment due to urinary retention.
- High-energy TUMT is associated with improved objective results compared with low-energy TUMT, but with increased morbidity.

4.8.9 REFERENCES

1. **Bolmsjo M, Wagrell L, Hallin A, Eliasson T, Erlandsson BE, Mattiasson A.**
   The heat is on – but how? A comparison of TUMT devices. Br J Urol 1996; 78: 564-572.
2. **Blute ML, Tomera KM, Hellerstein DK, McKiel CF, Lynch JH, Regan JB, Sankey NE.**
   Transurethral microwave thermotherapy for management of benign prostatic hyperplasia: results of the United States Prostatron Cooperative Study. J Urol 1993; 150: 1591-1596.
3. **Dahlstrand C, Walden M, Deirsson G, Pettersson S.**
   Transurethral microwave thermotherapy versus transurethral resection for symptomatic benign prostatic obstruction: a prospective randomized study with a 2-year follow-up. Br J Urol 1995; 76: 614-618.
4. **Ogden CW, Reddy P, Johnson H, Ramsay JW, Carter SS.**
   Sham versus transurethral microwave thermotherapy in patients with symptoms of benign prostatic bladder outflow obstruction. Lancet 1993; 341: 14-17.
5. **De la Rosette JJMCH, de Wildt MJAM, Alivizatos G, Froeling FM, Debruyne FM.**
   Transurethral microwave thermotherapy (TUMT) in benign prostatic hyperplasia: placebo versus TUMT. Urology 1994; 44: 58-63.
6. **Servadio C.**
   Ten years of clinical experience in transurethral hyperthermia to the prostate. In: Fitzpatrick JM (ed.) Non Surgical Treatment of BPH. SIU report 3. Edinburgh: Churchill-Livingstone, 1992, pp. 175-186.
7. **Rodrigues Netto N, Claro JD, Cortado PL.**
   Ejaculatory dysfunction after transurethral microwave thermotherapy for treatment of benign prostatic hyperplasia. J Endourol 1994; 8: 217–219.
8. **Francisca EA, d'Ancona FC, Hendriks JC, Kiemeney LA, Debruyne FM, de la Rosette JJ.**
   Quality of life assessment in patients treated with lower energy thermotherapy (Prostasoft 2.0): results of a randomized transurethral microwave thermotherapy versus sham study. J Urol 1997; 158: 1839-1844.
9. **Marteinsson VT, Due J.**
   Transurethral microwave thermotherapy for uncomplicated benign prostatic hyperplasia.
   Scand J Nephrol 1994; 28: 83-89.
10. **Kirby RS, Williams G, Witherow R, Milroy EJ, Philip T.**
    The Prostatron transurethral microwave device in the treatment of bladder outflow obstruction due to benign prostatic hyperplasia. Br J Urol 1993; 72: 190-194.

11. **Van Cauwelaert RR, Castillo OC, Aquirre CA, Azocar GH, Medina FI.**
Transurethral microwave thermotherapy for the treatment of benign prostatic hyperplasia: preliminary experience. Eur Urol 1993; 23: 282-284.

12. **Terai A, Arai Y, Onishi H, Oishi K, Takeuchi H, Yoshida O.**
Transurethral microwave thermotherapy for benign prostatic hyperplasia: clinical results after a 1-year follow-up. Int J Urol 1995; 2: 24-28.

13. **Devonec M, Tomera K, Perrin P.**
Review: transurethral microwave thermotherapy in benign prostatic hyperplasia.
J Endourol 1993; 7: 255-259.

14. **Devonec M, Houdelette P, Colombeau P et al.**
A multicenter study of SHAM versus thermotherapy in benign prostatic hypertrophy.
J Urol 1994; 151: 415A.

15. **Blute ML, Patterson DE, Segura JW, Tomera KM, Hellerstein DK.**
Transurethral microwave thermotherapy vs. SHAM: a prospective double-blind randomized study.
J Endourol. 1996 Dec;10(6):565-73.

16. **De Wildt MJ, d'Ancona FC, Hubregtse M, Carter SS, Debruyne FM, de la Rosette JJ.**
Three year follow-up of patients treated with lower energy thermotherapy (Prostasoft version 2.0).
J Urol 1996; 156: 1959-1963.

17. **Keijzers GB, Francisca EA, d'Ancona FCH, Kiemeney LA, Debruyne FM, de la Rosette JJ.**
Long-term results of lower energy transurethral microwave thermotherapy. J Urol 1998; 159: 1966-1972.

18. **De la Rosette JJ, de Wildt MJ, Hofner K, Carter SS, Debruyne FM, Tubaro A.**
High energy thermotherapy in the treatment of benign prostatic hyperplasia: results of the European Benign Prostatic Hyperplasia Study Group. J Urol 1996; 156: 97-102.

19. **Devonec M, Carter SS, Tubaro A et al.**
Microwave thermotherapy. Curr Opinion Urol 1995; 5: 3-9.

20. **De Wildt MJ, Tubaro A, Hofner K, Carter SS. Debruyne FM, Tubaro A.**
Responders and non-responders to transurethral microwave thermotherapy: a multicenter retrospective analysis. J Urol 1995; 154: 1775-1778.

21. **De la Rosette JJMCH, de Wildt MJAM, Hofner K, Carter SS, de la Rosette JJ, Devonec M.**
Pressure/flow study analyses in patients treated with high-energy thermotherapy (Prostasoft 2.5).
J Urol 1996; 156: 1428-1433.

22. **De la Rosette JJ, d'Ancona FC, Francisca EA et al.**
Clinical results of strategies to reduce morbidity in high energy transurethral microwave thermotherapy (HE-TUMT). (Congress report). AFU, 1997.

23. **D'Ancona FC, Francisca EA, Witjes WP, Welling L, Debruyne FM, de la Rosette JJ.**
High energy thermotherapy versus transurethral resection in the treatment of benign prostatic hyperplasia (BPH): results of a prospective randomized study with 1-year follow-up. J Urol 1997; 158: 120-125.

24. **Pace G, Selvaggio O, Palumbo F, Selvaggi FP.**
Initial experience with a new transurethral microwave thermotherapy treatment protocol '30-minute TUMT'. Eur Urol 2001; 39: 405-411.

25. **Carter SStC, Ogden CW, Patel A.**
Long term results of transurethral microwave thermotherapy for benign prostatic obstruction. In: Guliani L et al. (eds). Urology 1992. Bologna, 1992, pp. 257-261.

26. **de la Rossette JJ, Laguna MP, Pace G, Kortmann BB, Selvaggio O, Debruyne FM, Selvaggio FP.**
Efficacy and safety of the new high-energy 30-minute transurethral microwave thermotherapy: results of 1-year follow-up in a multicenter study. Tech Urol 2000; 6: 271-275.

27. **Tsai YS, Lin JS, Tong YC, Tzai TS, Yang WH, Chang CC, Cheng HL, Lin YM, Jou YC.**
Transurethral microwave thermotherapy for symptomatic benign prostatic hyperplasia: long-term durability with Prostcare. Eur Urol 2001; 39: 688-62.

28. **Daehlin L, Frugard J.**
Transurethral microwave therapy in the management of lower urinary tract symptoms from benign prostatic obstruction: follow-up after five years. Scand J Urol Nephrol 2000; 34: 304-308.

29. **De Wildt MJ, Debruyne FM, de la Rosette JJ.**
High-energy transurethral microwave thermotherapy: a thermoablative treatment for benign prostatic obstruction. Urology 1996; 48: 416-423.

30. **Djavan B, Wammack R, Ghawidel K, Alavi S, Hasenzagel C, Dobronski P, Stoklosa A, Jakubcky T, Borkowski A, Marberger M.**
Microwave thermotherapy in patients with chronic urinary retention. Tech Urol 2000; 6: 278-281.

31. **Naqvi SA, Rizvi SA, Hasan AS.**
High-energy microwave thermotherapy in patients in urinary retention. J Endourol 2000; 14: 677-681.

4.9 RECOMMENDATIONS FOR TREATMENT

1. The WW policy should be recommended to patients with mild symptoms that have minimal or no impact on their quality of life.

2. Finasteride is an acceptable treatment option for patients with bothersome LUTS and an enlarged prostate (> 40 ml) and can be used when there is no absolute indication for surgical treatment.

3. Alpha-blocker therapy is a treatment option for patients with bothersome LUTS, irrespective of prostate volume, who do not have an absolute indication for surgical treatment.

4. Surgical management (TURP, TUIP, open prostatectomy) is recommended as first-line treatment for patients with (an absolute indication for treatment of) LUTS.

5. Significant post-operative morbidity, disappointing long-term data and higher costs have resulted in a substantial decline in the clinical use of side-fire and ILC. It is not recommended as a first-line surgical treatment for patients with LUTS, but may have a role in the treatment of high-risk patient subgroups.

6. HoLRP is a promising new technique with outcomes in the same range as those of TURP.

7. Transrectal HIFU therapy is currently not recommended as a therapeutic option for elderly men with LUTS and is considered an investigational therapy.

8. Due to the significant treatment failure rate, TUNA, is not recommended as a first-line therapy for patients with LUTS.

9. TUMT should be reserved for patients who prefer to avoid surgery or who no longer respond favourably to medication.

10. Patients with mainly symptomatic BPH without signs of bladder outlet obstruction are the best candidates for low-energy TUMT protocols.

11. Patients with higher degrees of obstruction and larger prostates are better candidates for high energy TUMT

5. FOLLOW-UP

All patients who receive treatment require follow-up, which will depend on the type of treatment modality undertaken. Patients who subsequently develop chronic retention will require evaluation of their upper tract by serum creatinine measurement and/or renal ultrasound. These patients may be candidates for urodynamic assessment and surgical treatment.

5.1 Watchful Waiting (WW)

Patients who elect to persue a ww policy should be reviewed at 6 months and then annually, provided there is no deterioration of symptoms or development of absolute indications for surgical treatment. The following are recommended:

- I-PSS
- Uro-flowmetry and post-void residual urine volume.

5.2 Alpha-blocker therapy

Patients should be reviewed after the first 6 weeks of therapy in order to determine their response. If patients gain symptomatic relief in the absence of troublesome side-effects, alpha-blocker therapy may be continued. Patients should be reviewed at 6 months and then annually, provided there is no deterioration of symptoms or development of absolute indications for surgical treatment. The following are recommended:

- I-PSS
- Uro-flowmetry and post-void residual urine volume.

5.3 5-alpha-reductase inhibitors

Patients should be reviewed after 12 weeks and at 6 months to determine their response. Subsequent review is as for alpha-blocker therapy. The following are recommended:

- I-PSS
- Uro-flowmetry and post-void residual urine volume.

5.4 Surgical management

Following surgical treatment, patients may be seen within 6 weeks to discuss the histological findings and to identify early post-operative morbidity. Long-term follow-up should be scheduled at 3 months to determine the final outcome. Patients who fail treatment should have urodynamic studies with pressure-flow analysis. Assessment includes:

- I-PSS: recommended
- Uro-flowmetry and post-void residual urine volume: recommended
- Urine culture: optional
- Histology: mandatory.

5.5 Alternative therapies

Long-term follow-up is recommended because of concerns about the efficacy and durability of alternative therapies. The intervals for follow-up will depend on the treatment modality employed. The following time schedule is appropriate for the majority of minimally invasive therapies: within 6 weeks, at 3 months, at 6 months, and then annually. Assessment includes:

- I-PSS: recommended
- Uroflowmetry and post-void residual urine volume: recommended
- Urine culture: optional
- Histology where available: mandatory.

6. ABBREVIATIONS USED IN THE TEXT

AHCPR:	Agency for Health Care Policy and Research
ALFIN study:	European multicenter double-blind study to assess the efficacy and safety of Alfuzosin (5 mg twice daily) versus finasteride (5mg once daily) and the combination of both in patients with symptomatic BPH
AUA:	American Urological Association
BOO:	bladder outlet obstruction
BPE:	benign prostatic enlargement
BPH:	benign prostatic hyperplasia
BUN:	blood urea/nitrogen
CT:	computed tomography
DAN-PSS:	Danish Prostate Symptom Score
dL/dt 40:	velocity of detrusor contraction at 40 mL volume
DHT	dihydrotestosterone
DRE:	digital rectal examination
HE-TUMT:	high-energy thermotherapy
HIFU:	high-intensity focused ultrasound
HoLRP:	Holmium laser resection of the prostate
ICS:	International Continence Society
I-PSS:	I-Prostate Symptom Score
ILC:	interstitial laser coagulation
IVP:	intravenous pyelography
IVU:	intravenous urography
LOCM:	low-osmolar contrast material
LinPURR:	Linear Passive Urethral Resistance Relation
LUTS:	lower urinary tract symptoms
MRI:	magnetic resonance imaging
PCAR:	presumed circle area ratio
PLESS:	proscar Long-term efficacy and safety stud
PPV:	predictive positive value
PQSF:	Prostate weight, Quality of life, Symptoms, Maximum flow rate
PSA:	prostate-specific antigen
Qav:	average flow
Qmax:	maximum flow
Qm90:	mean flow for middle 90% of voided volume
ROC:	Receiver Operating Characteristics
VLAP:	visual laser ablation
Tdesc:	time from Qmax until 95% of volume voided
TRUS:	transrectal ultrasonography
TUIP:	transurethral incision of the prostate
TUMT:	transurethral microwave therapy
TUNA®:	transurethral needle ablation
TURP:	transurethral resection of the prostate
TUVP:	transurethral electrovaporization
URA:	Urethral Resistance Index
VLAP:	visual laser ablation
WW:	watchful waiting (deferred treatment)