Contact and Hybrid Laser in the Treatment of Benign Prostatic Hyperplasia

Comparison with Transurethral Resection of the Prostate

Doctoral dissertation

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Department of Surgery
University of Kuopio

ABSTRACT

Transurethral resection of the prostate (TURP) is the gold standard of treatment of benign prostatic hyperplasia (BPH). The search for equal efficacy but less morbidity has led to the development of so-called minimally invasive treatments of BPH.

In a prospective clinical study BPH patients with prostates < 40 ml were randomised to contact laser vaporization (CLV) (n=26) or TURP (n=26), and were followed up to four years. Patients with prostates ≥ 40 ml were randomised to hybrid laser (HL, combination of CLV and side-firing laser) treatment (n=21) or TURP (n=25) and were reviewed up to two years. Preoperatively all patients had bladder outlet obstruction (BOO).

The intraoperative blood loss was less (p<0.001), but the postoperative bladder drainage time was longer (p<0.001) in laser treatments compared with TURP.

In BPH patients with < 40 ml glands the improvement in median Danish Prostate Symptom Score (DanPSS, from 18 to 5 vs. from 18 to 4) and in maximal urinary flow rate (Qmax, from 8.3 ml/s to 14.3 ml/s vs. from 8.6 ml/s to 16.1 ml/s) was equal after CLV and TURP during four years of follow-up, respectively. However, the median PdetQmax at four years was higher in CLV group (38 cmH2O) than in TURP group (28 cmH2O) (p<0.01). The secondary operation rate was 4% for both treatments.

In the treatment of ≥ 40 ml prostates the mean Dan-PSS decreased in the HL group from 18.6 to 7.2 (p<0.01) and in TURP group from 22.8 to 3.4 (p<0.001), with no difference between the groups during the two-year follow up. The initial increase in mean Qmax at six months (5.9 ml/s in HL group and 12.4 ml/s in TURP group) was durable only in the TURP group at two years (1.8 ml/s vs. 13.4 ml/s) (p<0.001). At six months there were more urodynamically obstructed patients in the HL group (37%) compared with TURP group (10%) (p<0.05), and consequently, the mean PdetQmax was higher in HL patients (53 cmH2O) than in TURP patients (36 cmH2O, p<0.01). Secondary operation rate was 14.3% in the HL and 8.0% in the TURP arm.

Preoperatively the prevalence of erectile dysfunction (ED), ejaculatory dysfunction and discomfort/pain on ejaculation was 86%, 84% and 25%, respectively. The prevalence of ED increased 2% (ns) in laser group and decreased 7% in TURP group (ns) during the one year follow up, without differences between the groups. The laser treatments did not have any significant effect on ejaculation, but in the TURP group the absence of ejaculate was reported to increase from 10% to 71% (p<0.001). The reported discomfort/pain on ejaculation decreased in men in laser group from 22% to 7% (p<0.05) and in TURP group from 29% to 7% (p<0.01).

CLV is an option in the treatment of lower urinary tract symptom (LUTS) patients with a small or moderately enlarged obstructing benign prostate. In the treatment of patients with BPH and big prostates HL treatment is not recommended as a routine procedure. The prevalence of sexual dysfunction in LUTS patients is high even before treatment. Normal ejaculatory function is better maintained after Nd-YAG CLV or HL treatment than after TURP.

National Library of Medicine Classification: WJ 752, WJ 768

Medical Subject Headings: prostatic hyperplasia; lasers; laser surgery; transurethral resection of prostate; prostatectomy; bladder neck obstruction; neodymium; urodynamics; penile erection; ejaculation; comparative study; follow-up studies; treatment outcome; clinical trial; randomized controlled trial
To Henri
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Kuopio, April 2004

Kari Tuhkanen
**ABBREVIATIONS**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AUR</td>
<td>acute urinary retention</td>
</tr>
<tr>
<td>BOO</td>
<td>bladder outlet obstruction</td>
</tr>
<tr>
<td>BPH</td>
<td>benign prostatic hyperplasia</td>
</tr>
<tr>
<td>BPE</td>
<td>benign prostatic enlargement</td>
</tr>
<tr>
<td>CLV</td>
<td>contact laser vaporization</td>
</tr>
<tr>
<td>CPPS</td>
<td>chronic pelvic pain syndrome</td>
</tr>
<tr>
<td>DanPSS</td>
<td>Danish prostatic symptom score</td>
</tr>
<tr>
<td>DanPSS Sex</td>
<td>Danish prostatic symptom score sex</td>
</tr>
<tr>
<td>DRE</td>
<td>digital rectal examination</td>
</tr>
<tr>
<td>ED</td>
<td>erectile dysfunction</td>
</tr>
<tr>
<td>HE-TUMT</td>
<td>high-energy transurethral microwave thermotherapy</td>
</tr>
<tr>
<td>HL</td>
<td>hybrid laser</td>
</tr>
<tr>
<td>HoLEP</td>
<td>holmium laser enucleation of the prostate</td>
</tr>
<tr>
<td>Ho:YAG</td>
<td>holmium:yttrium aluminium garnet</td>
</tr>
<tr>
<td>Laser</td>
<td>light amplification by stimulated emission of radiation</td>
</tr>
<tr>
<td>LE-TUMT</td>
<td>low-energy transurethral microwave thermotherapy</td>
</tr>
<tr>
<td>HIFU</td>
<td>high-intensity focused ultrasound</td>
</tr>
<tr>
<td>ICS</td>
<td>International Continence Society</td>
</tr>
<tr>
<td>IIIF</td>
<td>international index of erectile function</td>
</tr>
<tr>
<td>ILC</td>
<td>interstitial laser coagulation</td>
</tr>
<tr>
<td>IPSS</td>
<td>international prostatic symptom score</td>
</tr>
<tr>
<td>KTP</td>
<td>potassium titanyl phosphate</td>
</tr>
<tr>
<td>LUTS</td>
<td>lower urinary tract symptoms</td>
</tr>
<tr>
<td>Nd:YAG</td>
<td>neodymium:yttrium aluminium garnet</td>
</tr>
<tr>
<td>PdetQmax</td>
<td>detrusor pressure at maximum urinary flow rate</td>
</tr>
<tr>
<td>PSA</td>
<td>prostate specific antigen</td>
</tr>
<tr>
<td>PVR</td>
<td>post-void residual urine</td>
</tr>
<tr>
<td>RCT</td>
<td>randomized controlled trial</td>
</tr>
<tr>
<td>Qmax</td>
<td>maximum urinary flow rate</td>
</tr>
<tr>
<td>QoL</td>
<td>quality of life</td>
</tr>
<tr>
<td>TRUS</td>
<td>transrectal ultrasound</td>
</tr>
<tr>
<td>TUEP</td>
<td>transurethral electrovaporization of the prostate</td>
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<tr>
<td>TUIP</td>
<td>transurethral incision of the prostate</td>
</tr>
<tr>
<td>TUMT</td>
<td>transurethral microwave thermotherapy</td>
</tr>
<tr>
<td>TUNA</td>
<td>transurethral needle ablation</td>
</tr>
<tr>
<td>TUR</td>
<td>transurethral resection</td>
</tr>
<tr>
<td>TURP</td>
<td>transurethral resection of the prostate</td>
</tr>
<tr>
<td>TZI</td>
<td>transition zone index</td>
</tr>
<tr>
<td>US</td>
<td>ultrasonography</td>
</tr>
<tr>
<td>VLAPE</td>
<td>visual laser ablation of the prostate</td>
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1. INTRODUCTION

Benign prostatic hyperplasia (BPH) is a common condition in aging men. BPH can be described as a clinical condition composed of three distinctive features: lower urinary tract symptoms (LUTS), prostate enlargement (BPE) and bladder outlet obstruction (BOO). These features exist independently with various degrees of overlap and define the clinical condition (Hald 1989, Abrams et al 1998). The absence of unifying definition of clinical BPH suitable for use in epidemiological studies is a major problem. Garraway and co-workers (1991) found that the prevalence rate of BPH defined as enlargement of the prostate gland ≥ (equivalent weight greater than) 20 g in the presence of lower urinary tract symptoms (LUTS) and/or a maximal urinary flow rate (Qmax) < (less than) 15 ml/s and without evidence of the prostate malignancy, was 253 per 1000 men in the community, rising from 138 per 1000 men aged 40-59 to 430 per 1000 men aged 60-69 years.

Sexual dysfunction is another common disorder of aging men. In Massachusetts Male Aging Study (Feldman et al 1994) 52% of men between age 40 and 70 years reported erectile dysfunction (ED). There is also growing evidence that sexual dysfunction, and urinary symptoms are closely associated with each other (Macfarlane et al 1996) and they both are identified as an important component of quality of life (QoL) in men (Calais Da Silva et al 1997).

During the past decade BPH has been established as an important clinical condition. Intense research has been performed on pathophysiological, diagnostic and therapeutic aspects. Transurethral resection of the prostate (TURP) has been used in the treatment of BPH for more than 70 years and is still considered the gold standard, since 80-90% of patients report a good outcome (Ala-Opas et al 1993, Wasson et al 1995). The efficacy of TURP is unquestionable, but it is associated with intraoperative and early postoperative morbidity in 13 – 25% of patients, most commonly associated with bleeding and failure to void (Mebust et al 1989, Borboroglu et al 1999). The re-operation rate after TURP is estimated to be 2% each year for reformed adenoma (Roos et al 1989). TURP causes retrograde ejaculation frequently (70%) and impotence in 5% - 40% (Roehrborn 1996, Holtgrewe and Valk 1964, Finkle and Prian 1966).
The basis for the development of less invasive treatment modalities for BPH has been the morbidity associated with TURP including its adverse effects on sexual activity (Mebust et al 1989). In most cases the treatment is focused on decreasing symptoms and improving QoL (Mebust et al 1989). However, the treatment should also be effective, with a lasting outcome and minimal morbidity. A variety of minimally invasive treatment modalities introduced are applying the heat to destroy the prostatic tissue. For the generation of heat, microwaves, radiofrequency, ultrasound and laser have been used as energy source (Larson et al 1998, Roehrborn et al 1998, Madersbacher et al 1994, Costello et al 1992). With the introduction of the side-firing neodymium:yttrium aluminium garned (Nd:YAG) laser in the early 1990s (Costello et al 1992) laser prostatectomy became a widely used minimally invasive treatment for BPH. However, prolonged postoperative catheterization time, lack of immediate effect, and severe postoperative dysuria decreased the early enthusiasm and prompted investigation of other laser energies and techniques that can result in an immediate reduction in prostatic volume, and relief of symptoms. In this respect the development of Nd:YAG contact laser vaporization (CLV) and HL (HL, combination of CLV and side-firing laser) methods could be respected as very promising treatments. Medical and minimally invasive treatment modalities have decreased the number of TURPs performed in the United States in the Medicare program by approximately half from 1987 to 1997 (Holtgrewe 2001, Wasson et al 2000).

The purpose of the present prospective randomized study was to evaluate the safety, the efficacy and the treatment related sexual dysfunction of two Nd:YAG laser treatment methods, CLV and HL treatments of the prostate, and compare these results with the traditional TURP in the management of BPH.
2. REVIEW OF THE LITERATURE

2.1. Anatomy of the prostate

The term “prostate” was originally derived from the Greek word prohistani (to stand in front of) and has been attributed to Herophilus of Alexandria, who used this expression in 335 B.C. to describe the organ located in front of the urinary bladder (Kirby 1995). Anatomically prostate is the shape of an inverted pyramid, in which the base is the superior surface adjacent to the bladder, while the apex is inferior. The prostate measures between 3 and 4 cm at its widest portion, and it is 4-6 cm long. Normal prostate weights about 20 g and lies behind the symphysis pubis in front of the rectum. The prostate surrounds the prostatic urethra, which runs through the prostate from base to apex. The prostate is perforated posteriorly by the ejaculatory ducts, which pass obliquely through the gland to empty into the verumontanum on the floor of the prostatic urethra just proximal to the striated external urinary sphincter. McNeal (1972) described a concept of zonal anatomy with four distinct regions of the prostate. According to this concept the fibromuscular region comprises 1/3 of the total gland) and the glandular portion of the prostate comprises 2/3 of the gland. The latter region is composed of a large peripheral zone and a small central zone, which together constitute about 95% of the glandular part of the gland. The rest of the glandular region (5-10%) is formed by the transition zone, located adjacent to the urethra at the verumontanum, and is composed of the periurethral glands. The transition zone is involved with BPH, whereas 70-80% of prostatic cancer occurs in the peripheral zone (McNeal 1969 and 1978). Nodular hyperplasia is a characteristic histological feature of BPH, consisting of an increased cell population and changes of the architecture in the ducts and acini.

2.2. Benign prostatic hyperplasia

2.2.1. Epidemiology

Autopsy studies of BPH have shown little suggestion of any racial or geographical trends in the prevalence of histologically defined BPH (Berry et al 1984). This in contrast to the wide variation seen in the prevalence of clinically diagnosed BPH (Guess 1992). Differences in BPH prevalence in different studies may be due either to differences in
definitions or to actual clinical difference between the study populations. There are studies with the same clinical BPH case definition applied to different populations, which show still an appreciable variation in prevalence of BPH (Homma et al 1997, Sagnier et al 1996).

Berry and co-workers (1984) observed in their meta-analysis of autopsy studies that none of the men younger than 30 was found to have histological BPH. The prevalence rose with age, peaking at 88% in men aged 80. It has been estimated that nearly all men develop histologically identifiable BPH with advancing age but only about 50% of these men develop macroscopic BPH as identified by autopsy or DRE (Berry et al 1984, Arrighi et al 1991, Guess et al 1990). In a population-based study carried out in Scotland the prevalence of BPH, defined as an enlargement of the prostate gland to ≥ 20 g in the presence of LUTS or Qmax < 15 ml/s and with no evidence of malignancy, was 253 per 1000 men (Garraway et al 1991). The prevalence rose from 138 per 1000 men aged 40-59 to 430 per 1000 men aged 60-69 years. Koskimäki and colleagues (1998) conducted a population-based cross-sectional survey in Finland and reported that the prevalence of at least one symptom of DanPSS questionnaire is 84% among 50-, 91% among 60- and 94% among 70-year-old men.

2.2.2. Etiology

The etiology of BPH is still poorly understood. Advanced age and the presence of functioning testes are required for the development of BPH. Men castrated before puberty do not develop BPH (Wu and Gu 1987, Wilson 1980). Men with a family history of an enlarged prostate diagnosed at a young age may be at increased risk of development of BPH (Roberts et al 1995). The recently observed association between PSA and future prostatic enlargement (Wright et al 2002) has raised speculation about the possible prostate growth promoting effect of PSA (Thompson and Leach 2002). Probably diet does not have any major influence on development of BPH (Chyou et al 1993).
2.2.3. Pathophysiology

There is no unifying definition of clinical BPH. This condition consists of three distinctive features: BPE, BOO and LUTS. These features exist independently with various degrees of overlap (Hald 1989, Abrams et al 1998) (Figure 1).

![Diagram](image)

Figure 1. The diagram shows the three basic features of clinical BPH: lower urinary tract symptoms (LUTS), benign prostatic enlargement (BPE) and bladder outlet obstruction (BOO).

The normal prostate weighs 20 ± 6 gm in men 21 to 30 years old (Berry et al 1984). This weight remains essentially constant with increasing age unless BPH develops. Histologically BPH is characterized by abnormal patterns of proliferation and atrophy within the epithelium and stroma of the prostate. BPH originates in the periurethral glands and transitional zones of the prostate. The transition zone is normally the smallest glandular part in young men. In patients with BPH the size of peripheral zone, central zone, and the non-glandular zone of the prostate remain relatively constant. In contrast, the transition zone varies in size and determines the volume of the entire prostate (McNeal 1978, Rifkin et al 1990). Proliferation of the prostatic tissue with aging may lead to prostate hypertrophy, which can cause obstruction of urine outflow from the bladder, manifested by LUTS. In most cases BPH decreases only the QoL of the patient, but in some cases serious complications, such as acute urinary retention (AUR), urinary tract infection, bladder stones and upper urinary tract deterioration with renal insufficiency may develop (Thorpe and Neal 2003).
2.2.4. Natural history

Forty percent of men older than 60 years experience LUTS associated with BPH, but only 50% of them seek medical or surgical attention (Garraway et al 1991, Koskimäki et al 1998). In North America and western and northern Europe the mortality rate from BPH has fallen very low, for instance in Denmark only 66 deaths due to BPH was observed in 1990 (Boyle et al 1996). In the randomly selected longitudinal study of men 40 to 79 years old from Olmsted County, it has been shown that with age prostate volume steadily increases (Rhodes et al 1999), urinary flow decreases and severity of urinary symptoms slowly progress (Jacobsen et al 1996), and furthermore a 60 year old man was calculated to have a 23% probability of experiencing an episode of AUR if he survives an additional 20 years. Increased risk of AUR was associated with LUTS, depressed maximal urinary flow rate (Qmax), enlarged prostates and older age (Jacobsen et al 1997). However, only a modest correlation among symptoms, prostate size and urinary flow rate on unselected men has been found (Girman et al 1995).

The prediction of the individual evolution of clinical BPH is difficult. Isaacs (1990) showed in a meta-analysis that 16% of men with BPH had no change in symptoms, and 38% had fewer symptoms during a follow up ranging from 2.6 to 5 years. In a randomized trial comparing medical treatment to placebo in the treatment of BPH the risk for AUR in placebo group was 7%, and 10% needed operative treatment at four years (McConnel et al 1998). Correlation between PSA value and increased risk of prostate enlargement has been observed in LUTS patients (McConnel et al 1998) and also in unselected men (Wright et al 2002). Serum PSA is one predictor of the natural history of BPH. Men with higher PSA levels have a higher risk of future growth of the prostate, symptom and flow rate deterioration, AUR and BPH-related surgery (Roehrborn et al 1999, 2000, 2001). Total symptom score and storage subscore have also been reported to predict the need of prostatic surgery in LUTS patients (Roehrborn et al 2002).
2.3. Evaluation of benign prostatic hyperplasia

2.3.1. Patient history and questionnaires

2.3.1.1. Voiding symptoms

Traditionally LUTS associated with BPH have been separated into symptoms related to bladder filling (such as frequency, urgency, nocturia, urge incontinence, nocturnal incontinence, small voided volume) and emptying (such as weak stream, hesitancy, straining, intermittency, terminal dribbling, prolonged voiding, retention and overflow incontinence) (Abrams 1994). In addition to BPH, LUTS can be caused by a variety of other reasons including hypocontractility, overactivity or instability of the detrusor muscle, prostatic carcinoma or chronic pelvic pain syndrome (CPPS). Several symptom score questionnaires have been developed and validated to provide a quantitative assessment of overall severity of the symptoms associated with BPH. Questionnaires are not disease-specific for BPH and are not able to diagnose BOO (de la Rosette et al 1998), but are used to compare different patients and studies. Questionnaires are particularly useful for monitoring the severity of the symptoms of individual patients and evaluating therapeutic outcome. Among several scoring systems the International Prostate Symptom Score questionnaire (IPSS), initially developed and validated as the American Urological Association Symptom Index (AUASI) (Barry et al 1992), is the most widely used instrument in clinical practice and research to evaluate LUTS. IPPS includes seven questions measuring the frequencies of symptoms associated with BPH and one question measuring the impact of symptoms on QoL.

For a more detailed measurement of impact of LUTS on QoL a disease-specific BPH Impact Index (BII) questionnaire (Barry et al 1995) is commonly used. The Finnish Guidelines for Evaluation and Treatment of BPH (Tammela et al 1999) recommends the Danish Prostate Symptom Score questionnaire (DanPSS, Appendix 1), which associates each symptom with the amount of bother caused by that symptom alone. The questionnaire is therefore considered to provide a better guide to the treatment of patients and their QoL than other symptom score scales (Hald et al 1991). The scoring system is based on 12 questions exploring the known symptoms of BPH related to micturition and
urine storage problems. Each question is divided into two parts. The first part explores the existence of a given symptom and its intensity in terms of either severity or frequency (the symptom score). This part of question may score from 0 to 3. The second of the two-part question evaluates the degree of influence of the symptom on the patient's daily life (the bother score), also rated from 0 to 3. The symptom score is multiplied by bother score, giving a value ranging from 0 to 9 for each question. The total score, i.e. the sum of the products of the symptom score and bother score of the twelve voiding-related questions can be at most 108 (12 x 9). The 12 questions can be divided into three parts consisting of four questions concerning voiding symptoms, four questions concerning filling symptoms and four other questions (pain during voiding, dribbling after voiding and urinary leakage). Based on the total amount of points in the questionnaire symptom score can be arbitrarily categorized as mild (from 0 to 7), moderate (from 8 to 18) and severe (more than 18) (Tammela et al 1999).

2.3.1.2. Sexual dysfunction

Recent studies have shown that sexual dysfunction and LUTS are associated with each other (Rosen et al 2002, Macfarlane et al 1996) and both are important components of QoL in men (Calais Da Silva et al 1997). This aspect has increased the importance of analysis of sexual function as part of the interview. It is now generally accepted that the assessment of sexual function must be undertaken in clinical practice and in research (Tubaro et al 2003). For the evaluation of sexual dysfunction several self-administered questionnaires have been developed, of which the International Index of Erectile Function (IIEF) (Rosen et al 1997) is most widely accepted at the moment. At the time we started the present study, Danish Prostate Symptom Score Sex (DanPSS Sex) questionnaire was available (Hald et al 1991), which includes three items about sexual function: erectile stiffness, quantity of ejaculate and pain or discomfort during ejaculation. From all items, the level of the symptom severity (range from 0 to 3) as well as the degree of bother or distress caused by that symptom (range from 0 to 3) is recorded. International Continence Society (ICS) sex questionnaire is also commonly used in the evaluation sexual impact of BPH treatments (Donovan et al 1996). This questionnaire includes basically same questions as DanPSS sex and in addition one item concerning whether sex life is spoiled by urinary symptoms.
2.3.2. Physical examination

It is recommended to perform a digital rectal examination (DRE), focused neurological examination and palpation of lower abdomen for patients with LUTS suggestive of BPH. The purpose of a DRE is to estimate the size of the prostate, to detect areas suspicious for malignancy, and to identify any pathology in the anal canal and the lower rectum. Determination of prostate size by DRE is subjective, and there is no uniform widely accepted grading system. DRE underestimate prostate size by 25% to 55% for men with a prostate volume over 40 ml because only posterior part of the gland can be palpated (Ohe et al 1988, Roehrborn et al 1997). Because the size does not correlate with symptom severity or the degree of outflow obstruction (Girman et al 1995, Andersen et al 1979), size alone should not influence the decision of treatment. On the other hand, the estimation of volume of the gland is relevant when selecting the most appropriate medical or surgical therapy for the individual. Clinical examination is also important to rule out other underlying diseases such as prostate and rectal malignancy or neurological problems that may cause the presenting symptoms. It has been estimated that the probability of a man with a suspicious DRE actually having prostatic carcinoma is roughly one out of three (Chodak et al 1988). Tenderness of the gland may indicate underlying prostate inflammation or infection. Neurological examination should include assessment of the anal sphincter tone and a rough assessment of motor and sensory function of the lower extremities. Occasionally a chronic urinary retention can be diagnosed by abdominal palpation and percussion.

2.3.3. Laboratory tests

The PSA concentration is dependent upon the patient’s age and the volume of the prostate (Oesterling et al 1993a). It has been estimated that an increase in prostate volume of 1 ml produces on average a corresponding 4% increase in the serum PSA concentration (Collins et al 1993). Prostate volume is strongly related with free and total PSA, which both can predict the prostate volume measured by transrectal ultrasound (TRUS) ± 20% accuracy in more than 90% of the patients (Morote et al 2000). A significant increase in PSA levels may be observed with urinary retention, instrumentation, infections, and in other prostatic diseases such as prostatitis and infarction (Oesterling et al 1993b, Yamamoto et al 1993).
In men with LUTS the main importance of serum PSA testing is in the detection of prostatic carcinoma. Increased volume of prostatic epithelium in BPH causes overlap in the PSA levels between BPH patients and those with early prostatic carcinoma. Discrimination between BPH and carcinoma can be improved by measuring the ratio of free to total PSA, as the proportion of PSA that is bound to alpha-1-antichymotrypsin is significantly higher in men with cancer (Stenman et al 1991). The total PSA values between 3 and 10 with the ratio of free to total PSA less than 0.15 means elevated probability of prostate cancer (Woodrum et al 1998). Serum PSA has been shown to predict AUR, LUTS and flow rate deterioration, need for surgery and prostate growth in men with BPH (Roehrborn et al 1999, McConnel et al 1998). PSA level helps in choosing the medical treatment for a LUTS patient, because the outcome of finasteride treatment depends on prostate volume and PSA level (Boyle et al 1996, 1997).

Serum creatinine measurement is commonly recommended for patients with LUTS as a guideline test of renal function. Elevated values should prompt the use of appropriate imaging studies (Koyanagi et al 1998). Surgically treated BPH patients with renal insufficiency have increased risk of postoperative complications (Mebust et al 1989) and elevated mortality rate (Melchior et al 1974b).

The urinalysis must be done for all LUTS patients, either by using a dipstick test or examining the spun sediment. It is necessary to rule out urinary tract infection, because it causes similar symptoms as BPH. On the other hand, it must be kept in mind that BPH is a common reason for urinary tract infections in elderly men. In 4-5% of men with microscopic hematuria, further investigations have revealed another benign disease or urological cancer (Mohr et al 1986).

2.3.4. Voiding diary

A frequency volume chart gives objective evidence of frequency, nocturia, voided urine volume and the pattern of urine production. Urinary frequency, voided volumes and episodes of incontinence are recorded in addition to fluid intake during a 48-hour period. The day time should be separated from the night time. The voiding diary is very simple and informative method of assessing patients with LUTS suggestive of BPH (Abrams and Klevmark 1996). Nocturia is one of the commonest presenting symptoms in men with
BPH, but the mechanism is poorly understood. Frequency volume chart gives valuable information about patient’s drinking habits and will help to identify patients with excessive fluid intake and nocturnal polyuria (Nakamura et al 1996). Increased nocturnal urine production may also be associated with low nocturnal level of plasma vasopressin (Mathiesen et al 1996), or with disordered fluid balance secondary to subclinical cardiac failure.

### 2.3.5. Prostate imaging

Enlargement of the prostate without other signs of BPH is not considered to be an indication for treatment. Recent data suggest that the size of the prostate gland may predict which patients with LUTS will develop progressive symptoms and complications (Jacobsen et al 1997). Prostate size and anatomy may help to select patients for specific treatment options. Patients with median lobe enlargement are not usually considered to be candidates for TUIP and TUMT. Response to certain types of BPH therapy, especially finasteride, depends on prostate volume (Boyle et al 1996). Knowledge of prostate volume is widely accepted for surgical planning prior to open surgery, TURP or TUIP. TUIP is recommended only for patients with prostate volume less than 30 – 50 ml and open surgery is considered an option to TURP for treatment of patients with prostates bigger than 100 ml (Orandi 1990, Riehmann et al 1995, Bruskewitz et al 1998). Ultrasonography (US), computerized tomography (CT) and magnetic resonance imaging (MRI) have been used for the imaging of the prostate.

Total prostatic volume can be measured by US either transabdominally or transrectally. Transabdominal US cannot visualize the zonal anatomy of the prostate and the measurement of prostate size is less accurate compared with transrectal US (TRUS) (Styles et al 1988). Prostatic volume determined by TRUS differs also depending on the formula and method used (Nathan et al 1996). Step-section planimetry is the most accurate method of determining prostate volume by TRUS, but this technique is not clinically practical (Watanabe et al 1974). A more easy method is to use prolate ellipse formula (Litrup et al 1991, Myschetzky et al 1991). With this method, the prostate gland is approximated to a prolate ellipsoid body with the same width, height and length and volume is calculated according to the following formula: height x width x length x π/6
(about 0.52). A single plane ellipsoid US measurement of prostate volume is done by measuring the area of the screen-traced maximal circumference in the transaxial plane and using formula \(8 \times \text{ellipsoid area} \times \frac{2}{3} \times \pi \times \text{ellipsoid width}\). In BPH it is typically the transition zone that begins to enlarge and determines the size of the prostate (Rifkin et al 1990). The additional information gained by measurement of the transition zone or transition zone index (TZI, ratio between transition zone volume and total prostate volume) is controversial (Kaplan et al 1995, Lepor et al 1997, Witjes et al 1997, Choi et al 2002).

MRI and CT are also accurate methods in evaluating prostate size, but their routine use cannot be justified because of the high costs (al-Rimawi et al 1994, Resnick et al 1997, Badiozamani et al 1999).

2.3.6. Urodynamic studies

2.3.6.1. Urinary flow

Urinary flow rate measurement is a simple and non-invasive method yielding parameters of average flow rate, maximum flow rate (Qmax), voided urine volume, voiding time, time to maximum flow, and a graphic of the urinary flow pattern. Qmax is the most widely used of these parameters in screening of BOO with LUTS patients and also in assessment of outcome after BPH treatment. Qmax depends on both the driving pressure and the resistance in the urethra. Consequently, Qmax at any level may or may not be associated with obstruction (Poulsen et al 1994). Normal values of Qmax in uroflowmetry are age-dependent. In Olmsted County Study Qmax decreased 2 ml/s per decade of life in men aged 40 to 79 years (Girman et al 1995). There is little or no correlation between the various symptoms of BPH and either the pressure-flow study or Qmax (de la Rosette et al 1998). A decreased flow rate does not distinguish between BOO and decreased bladder contractility, although BOO is more common at a lower Qmax. The majority of men (88%) with Qmax less than 10 ml/s have been found to be urodynamically obstructed, whereas only 30% of men with Qmax >15 ml/s were obstructed (Abrams 1995, Poulsen et al 1994). Logically, these findings led to a classification that defines obstruction as Qmax < 10 ml/s and no obstruction as Qmax > 15 ml/s, with equivocal results between. The outcome of TURP is better for patients with a preoperative Qmax less than 15 ml/s
compared with those with higher preoperative Qmax values (Abrams 1977, Jensen et al 1988).

There is a learning effect with repeated flow rate measurements in elderly men, and furthermore single flow rates in the same patient have a significant variability (Barry et al 1995, Reynard et al 1996). Qmax depends on the volume voided, but the relationship between volume and flow is not linear (Girman et al 1993). No agreement exists about the highest and lowest admissible volume voided that may permit accurate interpretation of the flow rate measurement. The Fourth International Consultation on BPH recommended to obtain at least two flow rate recordings, each ideally with a voided volume of >150 ml, to improve the validity of the test prior to making a treatment decision (Denis et al 1998). Up to 20% of curves show artefacts, particularly spikes, and machine thereby prints a false reading of Qmax (Jorgensen et al 1993). Flow curves should be visually checked. As a rule, any rapid change in the flow rate lasting less than two seconds is nonphysiological, and such artefacts should be disregarded.

2.3.6.2. Post-void residual urine

Post-void residual urine (PVR) is defined as the volume of fluid remaining in the bladder immediately following the completion of micturition (Abrams et al 1988). Preferably PVR is measured by ultrasound imaging the bladder transabdominally in a transverse and longitudinal orientation and using either three diameter (length, height, width), or the surface area in the transverse image and the length obtained from the longitudinal image, to estimate the bladder volume by utilizing the volume formula for a spherical or ellipsoid body. Residual urine can also be measured by catheterization. The clinical significance of a single residual urine measurement is unknown. PVR varies widely in the same patient on repeated measurements (Birch et al 1988, Bruskewitz et al 1982). Voiding in unfamiliar surroundings or voiding on command with overfilled bladder may lead to unrepresentative results (Griffiths 1973). Among healthy men with normal function PVR is small (<12 ml) (Di Marc et al 1963). A PVR greater than 50-100 ml is arbitrarily considered to be abnormal. An elevated PVR is associated with prostatic obstruction, but the relationship is not particularly strong (Ball 1981). An increase in PVR is a sign of bladder decompensation rather than obstruction. PVR is frequently found in elderly people without
urethral obstruction or BPE (Griffiths et al 1992). Presumably the causes of PVR are multifactorial, with obstruction being just one of the factors. Consequently, the presence or absence of BOO cannot be deduced from the volume of residual urine. The events that determine how incomplete emptying leads to AUR, low pressure chronic retention, or high pressure chronic retention with renal impairment are not understood. Unless chronic retention is diagnosed, PVR does not offer any substantial insight into a patient's clinical condition and cannot predict urodynamic or symptomatic outcome after surgery (Neal et al 1989).

2.3.6.3. Pressure-flow study

Obstruction develops partly due to the anatomical presence of the enlarged prostate (mechanical or static obstruction) and the tonus exerted by the smooth muscle in the prostate and in the bladder neck (dynamic obstruction). The increased urethral resistance prevents the detrusor muscle from rapidly expelling urine, which in turn gives rise to a high driving pressure (Griffiths 1980). The pressure-flow study is the only reliable method to assess BOO. Pressure-flow study records intravesical pressure during voiding and urinary flow rate at the same time. Measurement of the intravesical pressure requires introduction of the recording device either transurethrally or suprapubically into the bladder. Furthermore, a recording device needs to be placed into the rectum to subtract intra-abdominal pressure from the intravesical pressure. Urodynamic criteria for BOO are not absolute, and there is no generally accepted definition of obstruction. A mathematical model of the Abrams and Griffiths nomogram allows classification of pressure-flow voiding pattern data into obstructed, unobstructed or equivocal (Abrams and Griffiths 1979). The Qmax and the corresponding detrusor pressure (the detrusor pressure at maximum flow, PdetQmax) are plotted on a nomogram to determine whether voiding pattern is obstructed, unobstructed or equivocal. In the Abrams and Griffiths nomogram the voiding pattern falling into equivocal area can be further classified as obstructed or unobstructed by supplementary rules. Schäfer (1993) described a relationship between the detrusor pressure and flow rate and termed the passive urethral resistance relation, providing seven grades of obstruction ranging from not obstructed (grade 0) to severely obstructed (grade VI). The International Continence Society recommended a new provisional standard method for diagnosing of urethral obstruction, with some changes compared with the Abrams and Griffiths nomogram (Griffiths et al 1997). The provisional
nomogram defines obstruction as follows: If $(P_{det}Q_{max} - 2 \times Q_{max}) > 40$, the pressure-flow study is obstructed; If $(P_{det}Q_{max} - 2 \times Q_{max}) < 20$, the pressure-flow is unobstructed; Otherwise, the study is equivocal. In Abrams and Griffiths nomogram equivocal area is larger and patients with low pressure and low flow are classified equivocal, while in the provisional nomogram they are classified unobstructed.

The use of pressure-flow studies in clinical practice is controversial because it is an invasive and expensive procedure. The most important issue remains whether accurate diagnosis of BOO leads to sufficiently better treatment choice and outcome (McConnel 1994). Several studies have confirmed that subjective and objective outcome after TURP is better for those patients with confirmed BOO prior to operation compared with those who are non-obstructed (Abrams and Griffiths 1979, Rolleman et al 1991, Neal et al 1989). Abrams and Griffiths (1979) found that selection of LUTS patients based on the pressure-flow study reduced the symptomatic failure rate of TURP from 28 to 12%. More than 25% of TURP patients are estimated to be urodynamically unobstructed (Rolleman et al 1991). The presence and severity of symptoms associated with BPH do not correlate with urodynamic results (de la Rosette et al 1998) and as many as one third of men undergoing urodynamics for LUTS are not obstructed (Gerber 1996). The Fourth International Consultation on BPH recommended pressure-flow studies in LUTS patients with BPH who are young (<50 years), have flow rates >12-15 ml/s, have neurological disorders, or have poor a symptomatic outcome after surgical treatment (Koyanagi et al 1998).

2.3.7. Other investigations

Urethrocystoscopy is not routinely recommended for LUTS patients suggestive of BPH because its invasiveness and high costs. Patients with BPH may develop certain signs visible by endoscopy indicating the presence of obstruction such as narrowing and elongation of the prostatic urethra and bladder neck, muscular trabeculation and formation of diverticula in the bladder wall or formation of bladder stones. Normal urethrocystoscopic findings do not exclude BOO and severely trabeculated bladder wall does not indicate urodynamic obstruction (El Din et al 1996). Hematuria with or without LUTS is an indication for urethrocystoscopy to rule out the possible bladder cancer.
Imaging of the upper urinary tract is not necessary in otherwise healthy LUTS patients with suggested uncomplicated BPH. On US one may expect to find upper urinary tract dilatation or loss of renal parenchyma associated with BOO. Significant upper urinary tract dilatation is rarely found by US in BPH patients with normal serum creatinine and PVR less than 150 ml (Koch et al 1996). Indications for upper urinary tract US imaging for LUTS include hematuria, urinary retention, history of urolithiasis, history of urinary tract surgery and renal insufficiency (Koyanagi et al 1998).
2.4. OPERATIVE TREATMENT

2.4.1. Open prostatectomy

Open prostatectomy done either transvesically (Feyer 1900) or retropubically (Millin 1945) is probably the option of choice for prostates of 100 ml or larger, particularly when associated with big bladder stones, functionally significant bladder diverticula or severe ankylosis of the hips. Open prostatectomy is considered the most efficient treatment for relieving symptoms and improving urodynamic parameters (Bosch 1997), but it is also the most invasive and morbid procedure. Open prostatectomy provides flow rates that are as good as those of a healthy young population (Frimodt-Møller 1975), and open prostatectomy and TURP achieve voiding dynamics that are better than those of the normal same-aged population (Andersen et al 1978). In a recent prospective study of 32 consecutive transvesical prostatectomies for BPH with big glands, short-term improvement in clinical outcome parameters was excellent (Tubaro et al 2001). The total complication rate was 31.3% consisting of urinary tract infection 13%, wound infection 3%, temporary stress incontinence and bladder neck contracture 6%. Historically open prostatectomy has been associated with potentially dangerous intraoperative hemorrhage. In a recent survey of 1800 open prostatectomies in southern Europe severe bleeding occurred in 12% of the operations (Serretta et al 2002). In a large retrospective study in three countries the cumulative re-operation rate was 12-15.5% after TURP and 1.8-4.5% after open prostatectomy during the mean eight-year follow up of operations done between 1963 and 1978 (Roos et al 1989).

2.4.2. Transurethral resection of the prostate

The initial technique of TURP was first described by Nesbit in 1943. Prostatic tissue is resected slice by slice from the bladder neck to the level of verumontanum. The development of Hopkins rod lens wide-angle system significantly improved visualization for endoscopic surgery (Hopkins 1976). Iglesias and associates (1975) introduced the constant flow resectoscope, which allowed a continuous resection, shorter operation time, clearer vision and low intraprostatic fossa pressure with decreased fluid absorption. Use of “iso-osmotic” irrigation fluid during the procedure has reduced the risk of transurethral resection (TUR) syndrome. Meatotomy or urethrotomy is recommended if the meatus or
urethra is too tight to negotiate the resectoscope sheet (D'Ancona et al 1990). Videoresection is nowadays a common practice, which has made the procedure more convenient for the urologist. Prophylactic antibiotics have been found to decrease infection complications associated with TURP (Lukkarinen et al 1996, Sholz et al 1998, Viitanen et al 1998). Advances in resection technique and perioperative care have shortened the postoperative hospital stay without affecting adversely to the quality of care (Harrison et al 1995). In selected cases TURP can be done on a day-case bases in patients with mild to moderate BPE and no coexisting medical illness (Chander et al 2003, Klimberg et al 1994).

The recent introduction of medical and minimally invasive treatment modalities have reduced the number of TURPs. In USA the TURP rate was reduced by approximately half from 1987 to 1997 among Medicare beneficiaries (Holtgrewe 2001, Wasson et al 2000). Operative treatment is considered imperative for BPH patients with deterioration of renal function due to BPO, acute refractory urinary retention, recurrent urinary tract infections due to BPO, recurrent gross hematuria due to BPE, bladder stones due to BPO or large bladder diverticula (Denis et al 1998). The operation should also be offered for patients with severe symptoms or failed conservative treatment.

TURP is still considered the standard surgical treatment for BPH against which all other invasive treatments must be compared, because 80–92% of TURP treated patients are reporting a good outcome (Ala-Opas et al 1993, Wasson et al 1995). After the introduction of symptom score questionnaires associated with BPH, it has been possible to evaluate symptomatic improvement of treatments more precisely. The reported average improvement of symptoms and Qmax after TURP is 68% and 105% (Gajewski 2000). Urodynamically obstructed patients have better symptomatic outcome compared with unobstructed patients (Abrams 1995). Meyhoff and Nordling (1986) have reported that PdetQmax decreased from 75 to 40 cmH2O after TURP. In a large retrospective study from 1980s (Mebust et al 1989) mortality rate after TURP was 0.2%, intraoperative complication rate 6.9%, and immediate postoperative morbidity 18%. The most common complications during the operation were bleeding requiring transfusion (2.5%), dilutional hyponatremia (2.0%), and myocardial arrhythmia (1.1%). Postoperatively most common complications were failure to void (6.5%), bleeding requiring transfusion (3.9%) and clot
retention (3.3%). In a more recent retrospective study (Borboroglu et al 1999) the perioperative and postoperative complication rate after TURP done in the 1990s was significantly lower than those in earlier series. The intraoperative, immediate postoperative and late postoperative complication rate was 2.5%, 10.8% and 8.5%, respectively. There was no perioperative mortality, and blood transfusion rate was only 0.4%. Late complications were urinary tract infection (4.0%), bladder neck contracture (2.1%), urethral stricture (1.0%), and late postoperative bleeding (1.3%). The risk for stress urinary incontinence after TURP is about 1% (Wasson et al 1995). The annual re-operation rate for reformed adenoma after TURP is 2% (Roos et al 1989). Prostatic carcinoma is diagnosed from the electoresected chips in 6.3-22% of the patients (Borboroglu et al 1999, Mebus et al 1989).

2.4.3. Transurethral incision of the prostate

The technique of TUIP has been originally described already in the 19th century, although the first significant series of TUIP have been published not until 1980's (Orandi 1985 and 1987, Hellström et al 1986). Surgical technique of TUIP is relatively simple. The incision with a specially designed knife with cutting current is made through the bladder neck and along the length of the prostatic urethra to the level of the verumontanum unilaterally or bilaterally gradually deepening down to the point where fine filaments of the external capsule are seen. TUIP is quicker and technically easier than TURP, and has been done in selected cases under local anesthesia as an outpatient procedure (Hugosson et al 1993, Irani et al 1996). In a prospective randomized trial Hellström and associates (1986) reported a good symptomatic outcome and similar postoperative flow rates after TUIP and TURP in the treatment of BPH with a small prostate. PdetQmax decreased more in the TURP group than in the TUIP group, however. Yang and colleagues (2001) reported a meta-analysis of nine randomized controlled trials comparing TUIP and TURP. They found that the improvement in symptoms was equivalent 12 months postoperatively, but TURP resulted in 4.1 ml/s greater improvement of Qmax than TUIP. In contrast, TUIP was associated with lower incidence of complications, fewer blood transfusions, decreased risk of retrograde ejaculation and a shorter operative time and hospital stay. Because of these advantages some authors have suggested that TUIP is the treatment of choice for prostates up to 30 g (Orandi 1990, Irani et al 1996). There is no clear cut-off point for prostate size that leads to good results after TUIP, but it is usually recommended for
prostates with resectable tissue less than 20-30 g and no median lobe enlargement. However, in a recent randomized, controlled trial of 85 men with prostate volumes from 20 to 40 g TURP was found to produce better objective long term results and fewer secondary operations than TUIP (Johnson et al 1998).

2.4.4. Minimally invasive treatments

2.4.4.1. General

The past fifteen years have brought various new procedures for the treatment of BPH, usually referred to as minimally invasive treatments, which aim at good efficacy with lower morbidity than TURP. These applications use various energy sources (such as laser, microwave, ultrasound and radio frequency) to heat prostatic tissue and cause coagulation or vaporization. Coagulation is the process of causing molecular breakdown of organic compounds in temperatures between 45°C and 100°C (Leib et al 1986), whereas temperatures above 100°C are capable of producing tissue and water vaporization. The intended effect of minimally invasive treatments is thermoablation of the obstructing tissue. Heat of sufficient magnitude and duration causes cell death. Heating of the prostate may cause also periurethral prostatic tissue denervation (Brehmer et al 2000). The field of minimally invasive treatments is evolving rapidly. Some procedures have not stood the test of time, and new technologies have been introduced.

2.4.4.2. Laser in the treatment of benign prostatic hyperplasia

2.4.4.2.1. Laser energy

Atoms exit with their electrons in a low-energy configuration known as "ground level". Electrons may, however, be forced into a higher energy level by the application of external energy. This is an unstable situation, and excited electrons spontaneously revert to their original energy state giving off energy, some as photons of light. An example of spontaneous emission is the household electric light bulb. Laser (LASER=Light Amplification by Stimulated Emission of Radiation) light was first developed in the 1960s (Johnson 1961). Laser light is of one wavelength, unidirectional, and in phase. The heating effect of laser in the prostate causes either coagulation or vaporization of the tissue,
depending on the induced temperature. Neodymium:yttrium-aluminium-garnet (Nd:YAG), potassium titanyl phosphate (KTP), diode and holmium:YAG (Ho:YAG) have been used as a lasing medium with respective wavelengths of 1064 nm, 532 nm, 800-1000 nm and 2140 nm. Typically shorter wavelengths are absorbed by proteins but longer wavelengths produced by Ho:YAG laser are absorbed by water and cause its vaporization. In addition to wavelength the type of laser tissue interaction is dependent on many factors such as irradiation time and power, delivery fiber, tissue and technique variables (Nau et al 2000).

2.4.4.2.2. Visual laser ablation of the prostate

In 1991 Johnson and Levinson reported the use of a right-angle delivery system coupled to the Nd:YAG laser to produce a widespread necrosis within the canine prostate. The first clinical experiences in the treatment of BPH were published in the following year by Costello and co-workers (1992), demonstrating a significant subjective and objective response with minimal hemorrhage and limited complications. These results were later confirmed (Kabalin et al 1996, Te Slaa et al 1996). This technique is called “non-contact coagulation”, also commonly referred to as the free-beam, “right-angle fiber technique” or visual laser ablation of the prostate (VLAP). In this approach, the Nd:YAG laser energy is used to photocoagulate the prostate tissue to induce coagulation necrosis. Nd:YAG laser penetrates a variable depth into the tissue, depending on the power and duration of the exposure, typically 10 to 12 mm (Kabalin and Gill 1994). This results in thermal coagulation necrosis and delayed sloughing of the prostate for a variable period of time, usually several weeks to months after the procedure. However, comparative studies of TURP and VLAP have shown the advantage of TURP in improving symptoms and urinary measures (Anson et al 1995, Jung et al 1996). The most common complication of VLAP is irritative urinary symptoms lasting for several weeks and requiring prolonged catheterization time (Schatzl et al 2000, Te Slaa et al 1996, Anson et al 1995). Bioabsorbable stents have been suggested to overcome this postoperative problem (Petas et al 1997). In a randomized study the secondary operation rate after VLAP was found to be more than double that of TURP during a five-year follow up (McAllister et al 2000).
2.4.4.2.3. Contact laser vaporization of the prostate

The technique of CLV was first introduced by Daughtry and Rodan in 1992. Contact laser tips used to vaporize tissue are made of synthetic sapphire with a special coating that absorbs laser energy and become very hot. This allows cutting and vaporization with an otherwise coagulating wavelength of Nd:YAG laser. Contact laser tip is applied to the luminal surface of the gland and pushed in the direction of the bladder neck continuing the vaporization of the tissue until the prostatic lumen is judged to be adequate (Gomella et al 1995). With the contact laser method the tissue is removed primarily at the time of the procedure by vaporization which offers the patient shorter catheterization time and more rapid resolution of symptoms compared with VLAP. There is immediate loss of tissue with minimal penetration of the laser beam beyond the point of vaporization. Large glands remain cumbersome and tedious to handle with this technique. CLV is therefore better applicable for small or moderately enlarged prostates (Gomella et al 1995, Watson 1995). In selected patients CLV is possible to carry out as a day-case operation (Keoghane et al 1995). There is only one small randomized clinical trial comparing VLAP and CLV, which found that both treatments offered the same improvement with minimal morbidity after two years (Bryan et al 2000). In a double-blind randomized controlled trial of CLV and TURP both showed equal efficacy in the short and long term (Keoghane et al 1996a, Keoghane et al 2000). In another randomized trial comparing CLV, TURP and transurethral electrovaporization of the prostate (TUEP) there were no difference in the improvement of urodynamic and uroflowmetry parameters six months after treatment (Van Melick et al 2002). CLV caused less intraoperative bleeding (Keoghane et al 1996a), but it was more expensive than TURP (Keoghane et al 1996c). The re-operation rate after CLV varies from 4.8% to 18% during 2 - 5 years of follow up (Keoghane et al 2000, Floratos et al 2000, Bryan et al 2000).

2.4.4.2.4. Hybrid laser treatment

In hybrid laser (HL) treatment VLAP is combined with laser vaporization of the prostatic urethra and bladder neck to promote immediate postoperative voiding. Different techniques of opening the bladder neck and prostatic urethra have been used: bladder neck
incision by a KTP laser (Langley et al 1997, Chahal et al 2000), and bladder neck incisions and vaporization of the median lobe and lateral prostatotomies if needed by KTP laser (Carter et al 1999a). Performing a KTP bladder neck incision in conjunction with VLAP has been reported to enhance the outcome, with early catheter removal and improved flow rates and symptoms (Langley et al 1997). HL treatment has also been shown to be equivalent to TURP in its effect on improvements in QoL, symptom scores and Qmax at one year (Carter et al 1999a, 1999b). The most common postoperative complications are dysuria and urinary tract infections (Langley et al 1997, Carter et al 1999a).

2.4.4.2.5. Interstitial laser coagulation

Interstitial laser coagulation (ILC) by diode or Nd:YAG laser involves the placement of light guides directly into the prostatic adenoma during cystoscopy (Muschter and Hofstetter 1995, Muschter et al 1996) to cause circumferential coagulation around the diffusing fiber tip. This technique is fast and easy to learn and can be done as an outpatient procedure. It is supposed that preserved epithelium of the prostatic urethra might reduce postoperative irritative symptoms commonly associated with VLAP. Muschter and co-workers (1996) treated 112 BPH patient by ILC (diode) and during the six-month follow up AUA symptom score decreased from 20.9 to 7.9 and Qmax increased from 8.0 ml/s to 14.2 ml/s. The results are quite similar to those with side-fire laser coagulation of the prostate, and there is a similar prolonged period of postoperative catheter drainage (Muschter and Hofstetter 1995). Biodegradable stents have been reported to ensure early postoperative voiding in the case of temporary obstruction caused by prostatic edema (Laaksovirta et al 2002, Petas et al 2000). In a study evaluating the cost-effectiveness of BPH treatments ILC was found to be inferior to TURP and TUMT in the short term (Norby et al 2002). In a randomized trial ILC patients had slightly inferior Qmax, but the symptom score and QoL were similar after a two-year follow up compared with TURP (Kursh et al 2003). A high re-treatment rate (41%) after ILC has been reported after a three-year follow up (Floratos et al 2000).
2.4.4.2.6. Holmium:YAG and KTP laser treatments

The Ho:YAG laser has been considered to be a potential candidate for the treatment of BPH because of its precise cutting abilities, immediate relief of symptoms and good level of hemostasis (Johnson et al 1992). Since vaporization and cutting are the predominant tissue effects, it has been used for bladder neck incision (Johnson et al 1992) and enlargement of the prostatic urethra by removing pieces of prostatic tissue (holmium laser resection of the prostate) (Le Duc and Gilling 1999, Volpe et al 2001). Prostate lobes can also be enucleated intact and morcellated in the bladder to enable transurethral removal of the tissue (holmium laser enucleation of the prostate or HoLEP) (Fraundorffer and Gilling 1998). It takes more time to remove prostatic tissue by HoLEP than by TURP, but catheterization time and hospital stay are shorter (Tan et al 2003). Holmium laser resection of the prostate causes similar clinical outcome in AUA symptom score, Qmax and QoL score compared with TURP at the two-year follow up (Gilling et al 2000). In the treatment of big prostates (40 to 200 grams) Tan and co-workers (2003) reported HoLEP to be superior to TURP for relieving BOO in men with BPH and to be equivalent to TURP in relieving LUTS and improving Qmax at 12 months of follow up.

The 532 nm wavelength of KTP laser provides an intermediate level of vaporization and coagulation. Penetration of the laser effect reaches only half the depth produced by Nd:YAG laser light. Higher energy per unit tissue volume can produce increased vaporization and this property of KTP laser has been used in hybrid techniques (Langley et al 1997, Chahal et al 2000, Carter et al 1999a). The high-power (60-80W) KTP laser vaporizes tissue with minimal coagulation of the underlying structures. Immediate removal of the obstructing tissue and minimal intraoperative bleeding enable short catheterization time (Malek et al 2000, Hai and Malek 2003). After one to two years of follow up a decrease in AUA symptom score between 82% and 89% and an increase in Qmax between 278% and 198% have been reported (Malek et al 2000, Hai and Malek 2003).
2.4.3. Transurethral needle ablation of the prostate

Transurethral needle ablation (TUNA) uses low radiofrequency waves (465 kHz) intended to heat and destroy the obstructing prostatic tissue, while leaving the urethra and the rest of the prostate intact (Heaton 1995). Energy is administered through two 18-gauge needles at the tip of a TUNA catheter. Energy delivery is monitored using an automatic software program. The machine also has a urethral cooling system to prevent urethral heat injury and to avoid prolonged postoperative edema and retention. TUNA can be done on a day-case basis and under combined topical and regional anesthesia (Issa and Oesterling 1996). TUNA is usually recommended only for patients with prostate volume less than 50 – 60 ml and predominantly lateral lobe enlargement (Naslund 1997). Complications are rare, except for transient urinary retention lasting usually less than a week, mild degree of transient macroscopic hematuria and irritative voiding symptoms (Roehrborn et al 1998). In a combined analysis of over 500 patients in ten series there was an improvement in the symptom score of 58% and in peak urinary flow rate from 60% to 80% at one year (Issa and Oesterling 2000). Some series report lower improvement (from 30% to 33%) in peak urinary flow (Ramon et al 1997, Chapple et al 1999) and a significant re-operation rate of 20% during two years (Schatzl et al 2000). In a randomized study comparing TUNA and TURP the increase in Qmax was higher in TURP group 18 months after treatment whereas there were no differences regarding improvements in the IPSS and QoL score (Cimente et al 2003).

2.4.4. Transurethral microwave thermotherapy

Transurethral microwave thermotherapy (TUMT) is also a technique of heat destruction of the prostate, based upon microwave heat energy. The procedure involves placement of the microwave antenna in the prostatic urethra and is provided by a urethral cooling system. The complete treatment unit is controlled by software. Urethral and rectal temperatures are monitored by sensors, and threshold limits prevent any risk of heat injuries of urethra and rectum. Furthermore, there is one device with direct treatment feedback using intraprostatic temperature measurements (ProstaLund®) (Larson et al 2003).
The main advantage of TUMT is that the treatment can be carried out in an outpatient setting under local anesthesia. Patients with a distinct median lobe of the prostate should not be treated by TUMT because of difficulties in catheter placement. Modest results of the original low-energy TUMT (LE-TUMT) (Ogden et al 1993) led to the development of high-energy TUMT (HE-TUMT) with improved efficacy (Goldfarb et al 1995). In a review article Djavan and Marberger (2001) reported an improvement of 43 – 70% in the symptom score and 19 – 59% in Qmax in randomized controlled trials of microwave treatment in BPH patients. The symptomatic improvement is equal to TURP, but the urodynamic results are inferior. TUMT is a safe treatment with few complications except for transitory urinary retention, especially after HE-TUMT (Djavan et al 1999). In a randomized trial of HE-TUMT and TURP Floratos and associates (2000) reported a decrease in IPSS from 20 to 12 and an increase in Qmax from 9.2 ml/s to 11.9 ml/s in the HE-TUMT group during a three-year follow up. The corresponding figures in TURP group were from 20 to 3 and from 7.8 ml/s to 24.7 ml/s. In this study the re-treatment rate was 19.8% after HE-TUMT and 12.9% after TURP.

2.4.4.5. Other minimally invasive treatments

Transurethral electrovaporization of the prostate (TUEP) uses electrosurgical principles and techniques to remove adenoma tissue transurethrally and to make a cavity in the prostate similar to TURP (Kaplan and Te 1995, Naraya et al 1996). The adenoma is vaporized usually with a roller electrode using high power setting of cutting current. Also modified electrovaporative loops have been developed, which have basically a thicker wider band than standard loops, but the technique of standard loop resection is not altered drastically (Perlmutter 1997). In relatively small studies with a short-term follow up TURP and TUEP have shown a similar improvement in symptom score and Qmax (Kaplan and Te 1998, Shokeir et al 1997). These studies suggest that the main advantages of TUEP compared with TURP are good intraoperative hemostasis and lack of bleeding or fluid absorption and a shorter postoperative catheterization period and hospital stay.

In the treatment of BPH stents are used to mechanically relieve the obstruction from the surrounding prostatic tissue. They may be broadly classified as permanent or temporary. Biodegradable or bioabsorbable stents are particularly attractive alternatives for the patient requiring temporary relief of obstruction (Petas et al 1997, Petas et al 2000, Laaksovirta et
al 2002). To date, permanent stents have been mostly used for BPH patients with urinary retention or poor general condition. A majority of patients have been able to void after placement of the stent (Oesterling 1994). Prostatic stents are associated with complications such as encrustation, occlusive re-growth, perineal pain and discomfort on urination (Anjum et al 1997).

High-intensity focused ultrasound (HIFU) is a method of causing heat-induced prostatic destruction using ultrasound energy transrectally without the need for intra-urethral manipulation. Treatment area is precisely targeted by US. Treatment is usually carried out under general or spinal anesthesia and in some cases under iv-sedation (Madersbacher et al 1994). Complications of the treatment include hematospermia (13%), mild to moderate hematuria (9%), AUR (4 %), perineal pain 11%) and epididymitis (9%) (Sullivan et al 1999). During a four-year follow-up, the symptom score decreased by a half, but Qmax increased only marginally (12%) (Madersbacher et al 2000). Furthermore, the secondary TURP rate was as high as 44%.

Injection of absolute ethanol into the prostate results in coagulative necrosis of the tissue (Zvara et al 1999). In the treatment of 15 BPH patients Ditriolio and co-workers (2002) reported a significant improvement in the symptom score and Qmax and a decrease in prostate volume with minimal morbidity.

Intraprostatic injection of botulinium toxin, which blocks acetylcholine release at the neuromuscular junction and in autonomic neurons, into the rat prostate has been documented to induce selective denervation and subsequent atrophy of the gland (Doggweiler et al 1998). The first human experiences of this treatment have recently been published, with good tolerability and improvement of symptoms during a short-term follow up (Maria et al 2003).

Water-induced thermotherapy (WIT) is a very simple and inexpensive treatment that can be administered in an outpatient setting. The prostatic tissue is heated by a catheter balloon inflated by hot water. An international multicenter trial demonstrated significant alleviation of LUTS and an increase in Qmax (Muschter et al 2000). The same hot liquid
principle with a slightly different technique (fast liquid ablation system for hyperplasia) in the treatment of BPH has been published by Corica and colleagues (2003).

2.4.5. Sexual function after operative treatment of benign prostatic hyperplasia

The impact of TURP on erectile function is controversial. Earlier retrospective studies suggested a high rate of impotence after TURP, up to 40% (Finkle and Prian 1966). Many of the more recent studies with prospective design have found no adverse impact of TURP on erectile function (Wasson et al 1995, Kunelius et al 1998, Brookes et al 2002, Leliefeldt et al 2002). A retrospective meta-analysis of patients who underwent surgical treatment for BPH revealed the incidence of ED of 13.6%, 15.6% and 4.6%, and the incidence of retrograde ejaculation of 70.4%, 65.0 to 80.8 and 38.3% after TURP, open prostatectomy and TUIP, respectively (Roehrborn 1996). Richman and co-workers (1995) in their randomized, prospective study of TUIP or TURP for 120 BPH patients with small glands reported the retrograde ejaculation rate of 35% in TUIP group and 68% in TURP group. The better chance of maintaining normal ejaculation favours TUIP over TURP in younger and sexually active men who require operative treatment for BPH.

The data on sexual dysfunction after minimally invasive procedures are scanty and not always reported (Kassabian 2003). Most of the published data indicate that minimally invasive treatments have no or minimal impact on erectile function. Many studies report VLAP and ILC not to have adverse effect on erectile function (Kabalin et al 1995, Muschter and Hofstetter 1995, Kollmorgen et al 1996, Kursh et al 2003). In a prospective non-randomized study a mild to moderate decrease in erectile function was noted in 26.5%, 18.2%, 18.4% and 20.0% of TURP, TUMT, ILC and TUNA patients, respectively, but there was no significant difference between pretreatment and posttreatment ED scores in any group (Araki et al 2000). Loss of ejaculation or a severe decrease in ejaculate was reported by 48.6%, 28.1%, 21.6% and 24.3% of the patients, respectively. The incidence of ejaculation loss after VLAP ranges between 16% and 27% (Kabalin et al 1995, Kollmorgen et al 1996). In a prospective randomized study comparing CLV and TURP the postoperative impotence rates were 4% and 3%, respectively (Keoghane et al 1996b). A 35% retrograde ejaculation rate after CLV has also been reported (Watson 1995). Contrary to other studies Chahal and co-workers (2000) found a significant interference with sexual function after HL treatment. In that study 33% of preoperatively sexually active patients
claimed significant change in the strength of erections, and 79% had a significant decrease in their ejaculate. The authors could not explain the reason for the high incidence of sexual dysfunction after HL treatment.
3. AIMS OF THE STUDY

TURP is regarded as the gold standard of intervention for BPH. However, TURP is associated with a considerable morbidity in the treatment of a benign disease. The present study was undertaken to evaluate the safety, the efficacy and the treatment related sexual dysfunction of two Nd:YAG laser treatment methods (CLV and HL treatment) and to compare these results with the traditional TURP in the management of BPH. More specifically, the aims of this study were:

1. To compare the perioperative morbidity and short-term results of Nd:YAG CLV and TURP in the treatment of BPH patients with small or moderately enlarged prostates (I).
2. To compare the perioperative morbidity and short-term outcome of HL treatment, i.e., the combination of Nd-YAG VLAP and Nd-YAG CLV with TURP in the treatment of BPH patients with high volume prostate (II).
3. To compare the long-term outcome of HL treatment and TURP in the management of BPH with big prostates (III).
4. To compare the long-term effects of CLV and TURP in the treatment of BPH patients with small and moderately enlarged glands (IV).
5. To assess the effect of Nd:YAG laser treatment and TURP on sexual function (V).
4. PATIENTS AND METHODS

4.1. Patients and study design

The studies were carried out at the Department of Surgery, Urological Unit, Kuopio University Hospital in the years 1994 – 2003. The study protocol was approved by the ethical committee of Kuopio University Hospital. Patients with LUTS suggestive of BPH who were referred to the outpatient urology clinic of Kuopio University Hospital underwent normal evaluation including DanPSS, DanPSS Sex, urine analysis, serum creatinine, serum PSA, uroflowmetry, PVR, DRE and TRUS. If the operative treatment was indicated after investigations and discussion with the patient, a pressure-flow study was performed. Inclusion criteria for the study were LUTS suggestive of BPH, BOO confirmed by pressure-flow studies, and a written consent. Patients with prostate carcinoma, urethral stricture, neurogenic bladder dysfunction, previous prostate operation, prostate volume >100 ml or PVR >350 ml were excluded. Between September 1994 and January 1998 ninety eight patients were randomized to Nd:YAG laser treatment or TURP. Patients with prostate glands smaller than 40 ml measured by TRUS were allocated to CLV (I, n=25; IV and V, n=26) or TURP (I, n=25; IV and V, n=26) and patients with prostate volume between 40 ml and 100 ml were randomized to HL treatment (II, III and V, n=21) or TURP (II, n=24; III and V, n=25).

All interventions were performed under spinal anesthesia by the same experienced operator (K.T.). All patients received prophylactically 250 mg ciprofloxacin orally in the previous evening and on the morning of the operation. Serum sodium, potassium and hemoglobin were measured before and one hour after the operation. Used Nd:YAG energy and irrigation fluid volume were recorded and removed prostate chips were weighed. Operative blood loss was estimated from the hemoglobin concentration of the irrigant effluent by a Haemocue photometer. Operative time, perioperative complications, postoperative catheterization time and hospital stay were recorded.

Patients were reassessed at three, sex, 12, 24 and 48 months. Preoperatively and at each follow-up visit DanPSS and DanPSS Sex questionnaires were filled out by the patients, urine analysis and culture, serum creatinine and PSA were analysed, and Qmax, average
urinary flow rate and PVR were recorded. In addition, the DRE was performed at each visit. Urethroscopy was performed at 6 month’s visit to assess the possible postoperative urethral stricture and to estimate the width of the prostatic urethra and bladder neck. A pressure-flow study and TRUS were done at the 6 month (CLV v. TURP and HL vs. TURP) and 4 year visits (CLV vs. TURP). In patients with cancer suspicion due to abnormal prostate palpation finding, abnormalities in TRUS examination or elevated serum PSA level, TRUS guided biopsies were taken from the prostate. Prostate cancer patients were excluded from the study. Patients were followed for four years.

4.2. Urinary symptoms (I – V)

Urinary symptoms were evaluated by the DanPSS questionnaire completed by the patient at each visits. The symptom score of each question was multiplied by the corresponding bother score, and the total sum of the scores of 12 questions was recorded.

4.3. Sexual function (I, II, V)

At each visit patients completed DanPSS Sex questionnaire (Appendix 2). The analysis of preoperative prevalence of sexual dysfunction in LUTS patients was based on the DanPSS Sex questionnaire and this was compared with one year data to estimate impact of Nd:YAG laser and TURP on sexual function (Hald et al 1991). The questionnaire includes three items about sexual function: erectile stiffness, volume of ejaculate and pain or discomfort during ejaculation. From all items, the level of the symptom severity (range from 0 to 3) as well as the degree of bother or distress caused by that symptom (range from 0 to 3) was recorded.

4.4. Uroflowmetry and post-void residual volume (I – IV)

The urinary flow rate was measured in the outpatient clinic by uroflowmetry (Urodyne 1000, Type 22 G 02, Dantec Medical, Denmark). Minimal accepted urinary volume for measurement of Qmax was 120 ml. Electronically obtained peak flow values were also checked manually by K.T. from the flow curves. Trained urological nurse measured PVR by transabdominal US using formula width x height x length divided by two.
4.5. **Pressure-flow studies (I, II, IV)**

Pressure-flow studies were done by an experienced nurse using a urodynamic device (Menuec, Dantec Medical, Denmark). A 4.5 Fr transurethral pressure catheter was used. The pressure-flow plots were analysed by a urologist (K.T.). Patients with results falling in the equivocal area of the Abrams and Griffiths (1979) nomogram were regarded as obstructed if their minimum voiding detrusor pressure was > 40 cm H2O or the mean slope of their detrusor pressure / urinary flow plot was >2 cm H2O per ml/s (I, II, IV). During the study period, the International Continence Society published a provisional nomogram (Griffiths et al 1997), which defines obstruction as follows: If \((P_{\text{detQmax}} - 2 \times Q_{\text{max}}) > 40\), the pressure-flow study is obstructed; If \((P_{\text{detQmax}} - 2 \times Q_{\text{max}}) < 20\), the pressure-flow is unobstructed (IV).

4.6. **Transrectal ultrasound of the prostate (I – IV)**

A urologist measured prostate volume in the out-patient clinic by TRUS using an ultrasound scanner (Ultrasound Scanner, Type 1846, Brüel&Kjaer, Denmark) with sector transducer (Sector Transducer, Type 8538, Brüel & Kjaer, Denmark) in the transverse orientation with an automatic ellipsoid formula. This single plane ellipsoid US measurement of prostate volume is done by measuring the area of the screen-traced maximal circumference in the transverse plane and marking the most lateral points of this area (width). The computer automatically calculates prostate volume using formula \(8 \times \text{ellipsoid area} \times 2/3 \times \pi \times \text{ellipsoid width}\).

4.7. **Transurethral resection of the prostate (I – V)**

Traditional video monitored TURP was performed by a 28 Fr Wolf® resectoscope under spinal anesthesia and glycine solution was used as irrigant. Afterwards a 24 Fr urethral catheter was placed routinely for as long as needed for the urine to clear up.
4.8. Contact laser vaporization of the prostate (I, IV, V)

In the CLV, the prostatic urethra was vaporized with an Nd:YAG laser (SLT Contact Laser, CL 60, Surgical Laser Technologies, Pennsylvania, USA) at a power setting of 40 W with an SLT MTRL 10 contact probe placed through a 25 Fr Storz cystoscope with single instrument port using in a 30-degree wide-angle optic lens. In this technique laser energy is delivered through a conducting fiber to a synthetic sapphire tip which absorbs energy and becomes very hot, causing vaporization of the tissue with penetration of less than 1 mm. No tissue effect is caused unless the tip is placed in contact with the tissue. The contact tip was placed repeatedly just above the level of the verumontanum, the laser was fired and the tip was pushed gently against the prostatic adenoma towards the bladder neck, which created furrows of vaporized tissue. The vaporization of the tissue was continued until the prostatic urethral lumen was judged to be adequately wide, much as in standard electrosurgical TURP. At the beginning of the operation a 15 Fr suprapubic catheter was introduced and was allowed to drain freely to ensure an uninterrupted flow of saline irrigant during the laser treatment. At the end of the procedure a 20 Fr urethral catheter was inserted for one day. The suprapubic catheter remained until the patient was able to urinate and the measured PVR was less than 150 ml.

4.9. Hybrid laser treatment of the prostate (II, III, V)

At the beginning of the operation A 15 Fr suprapubic catheter was introduced to allow free drainage of continuous flow of saline irrigant during the treatment. The HL treatment was started by urethro cystoscopy using a 25 Fr Storz \textsuperscript{ø} cystoscope with 30 degree wide-angle optic lens and a single instrument port. Non-contact Nd-YAG laser energy was then given by the "adenoma-dependent" approach to all areas of obstructing lateral lobes through a side firing SLT\textsuperscript{ø} gold alloy tip at 40 W power set for 90 second burn times. A mean non-contact energy of 55.6 kJ (range 24.4 – 77.8 kJ) was delivered (1011 J/ml prostatic tissue). In the next step the gold alloy tip was changed to an SLT MTRL 10 contact probe. The prostatic urethra and bladder neck were tunnelled open by CLV at 40 W. At the end of the procedure a 20 Fr urethral catheter was inserted for one day. The suprapubic catheter remained until the patient was able to urinate and the PVR was less than 150 ml.
4.10. Statistical methods (I – V)

The statistical analysis was done using the SPSS for Windows program package (SPSS Inc, Chicago, USA). Differences between the study groups were tested with the Mann-Whitney U-test. The differences within the groups during the different time points was analysed using the Friedman and Wilcoxon tests. A p-value < 0.05 was considered statistically significant.
5. RESULTS

5.1. Contact laser treatment vs. transurethral resection of the prostate in the treatment of benign prostatic hyperplasia with small or moderately enlarged glands (I, IV)

5.1.1. Perioperative and short-term results (I)

There were 25 patients in the CLV treatment group and 25 in the TURP group. The mean age of the laser patients was 67 (56-76) years and that of the TURP patients 67 (56-77) years (ns). The mean preoperative prostate volume was 26 ml (10-37 ml) in CLV and 28 ml (15-38 ml) in TURP group (ns). CLV lasted longer (mean 51 min) than TURP (mean 34 min, p<0.001). TURP caused more intraoperative bleeding (mean 175 ml) compared with CLV treatment (mean 57 ml, p<0.001), but none of the patients needed a blood transfusion in either study groups. All TURP patients urinated spontaneously at discharge, whereas four CLV patients were discharged with a suprapubic catheter and consequently, mean catheterization time was longer in CLV group than in TURP group (4.3 days vs. 1.7 days, p<0.01).

At the six-month follow up all outcome parameters were improved, without significant differences between the study groups (Table 1). No re-operations were needed during the six-month follow up in either study group. Complications in the TURP group included one case of postoperative bleeding, one epididymitis and one bladder neck contracture compared with one postoperative urinary tract infection in CLV group. One prostatic carcinoma was diagnosed from the electroresected chips after TURP. At three months postoperatively, retrograde ejaculation among potent men was more common after TURP (81%) than after CLV treatment (6%) (p<0.001).
Table 1. Urodynamic and symptom score data before and at 6 months after CLV and TURP (mean, SD)

<table>
<thead>
<tr>
<th></th>
<th>CLV</th>
<th>TURP</th>
<th>p-value</th>
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<tr>
<td></td>
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<tr>
<td>Qmax (ml/s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preoperative</td>
<td>9.0 (3.8)</td>
<td>8.2 (3.2)</td>
<td>ns</td>
</tr>
<tr>
<td>at 6 months</td>
<td>17.9 (7.1)**</td>
<td>21.1 (9.7)**</td>
<td>ns</td>
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<tr>
<td>PdetQmax (cmH₂O)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>preoperative</td>
<td>69.0 (24.6)</td>
<td>77.1 (27.5)</td>
<td>ns</td>
</tr>
<tr>
<td>at 6 months</td>
<td>38.3 (9.7)**</td>
<td>31.3 (9.9)**</td>
<td>ns</td>
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<tr>
<td>PVR (ml)</td>
<td></td>
<td></td>
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<tr>
<td>preoperative</td>
<td>105 (82)</td>
<td>128 (95)</td>
<td>ns</td>
</tr>
<tr>
<td>at 6 months</td>
<td>50 (64)**</td>
<td>32 (37)**</td>
<td>ns</td>
</tr>
<tr>
<td>DanPSS</td>
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<tr>
<td>preoperative</td>
<td>20 (11)</td>
<td>21 (11)</td>
<td>ns</td>
</tr>
<tr>
<td>at 6 months</td>
<td>6 (9)**</td>
<td>5 (7)**</td>
<td>ns</td>
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</table>

p-value for the difference between the groups was not significant;
** p<0.01, *** p<0.001; significance for the difference within the groups

5.1.2. Long-term results (IV)

The final study visit was at 4 years for CLV vs. TURP patients, and 42 (81%) of the original 52 patients were evaluable.

The four-year outcomes of CLV and TURP treatments are presented in Table 2. The median DanPSS decreased 72% (p<0.001) in CLV group and 78% (P<0.001) in TURP group. The median Qmax increased 72% (P<0.001) after CLV treatment, whereas in TURP group it improved 87% (P<0.01). According to the Abrams and Griffiths nomogram all randomized patients were confirmed to have BOO preoperatively and four years later still 7/22 (32%) patients in the CLV and 2/20 (10%) in the TURP group were obstructed. According to provisional nomogram (recommended by the International Continence Society) in the present study, the number of preoperatively obstructed, equivocal and unobstructed patients in the laser group was 14/22, 5/22 and 3/22, respectively, and in the TURP group 10/20, 9/20 and 1/20. At 48 months, the respective number of patients
classified as obstructed, equivocal and unobstructed was in the laser group 2/22, 9/22 and 11/22 and in the TURP group 0/20, 1/20 and 19/20.

Table 2. Outcome parameters of CLV and TURP at baseline and at four years after treatment (median, range)

<table>
<thead>
<tr>
<th></th>
<th>CLV</th>
<th>TURP</th>
<th>p-value</th>
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<tr>
<td><strong>DanPSS</strong></td>
<td></td>
<td></td>
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<tr>
<td>Preoperative</td>
<td>18 (5 - 54)</td>
<td>18 (4 - 46)</td>
<td>ns</td>
</tr>
<tr>
<td>At 4 years</td>
<td>5 (0 – 34) ***</td>
<td>4 (0 –18) ***</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Qmax (ml/s)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Preoperative</td>
<td>8.3 (4.8 - 19.6)</td>
<td>8.6 (5.0 – 15.9)</td>
<td>ns</td>
</tr>
<tr>
<td>At 4 years</td>
<td>14.3 (10.1 - 33.6) ***</td>
<td>16.1 (7.7 – 39.6) **</td>
<td>ns</td>
</tr>
<tr>
<td><strong>PdetQmax (cmH2O)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>64 (32 - 112)</td>
<td>57 (40 - 137)</td>
<td>ns</td>
</tr>
<tr>
<td>At 4 years</td>
<td>38 (18 - 65) ***</td>
<td>28 (9 - 44) ***</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Prostate volume (ml)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>30 (15 – 37)</td>
<td>28 (15 – 38)</td>
<td>ns</td>
</tr>
<tr>
<td>At 4 years</td>
<td>29 (18- 43)</td>
<td>20 (12 – 36) *</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td><strong>PVR (ml)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>87 (0 – 331)</td>
<td>83 (8 – 350)</td>
<td>ns</td>
</tr>
<tr>
<td>At 4 years</td>
<td>60 (0 – 380)</td>
<td>10 (0 – 90) **</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

p-value is for the difference between the groups;
* p<0.05, ** p<0.01, *** p<0.001; significance for the difference within the groups

5.2. Hybrid laser vs. transurethral resection of the prostate in the treatment of benign prostatic hyperplasia with big glands

5.2.1. Perioperative and short-term results (II)

Twenty one patients underwent HL treatment and 24 patients were treated by TURP. Forty (19 laser and 21 TURP) patients completed the six-month follow up.

HL treatment took longer (mean 75 min) than TURP (mean 44 min, p<0.001) but bled less (mean 68 ml vs. 332 ml, p<0.001). Bladder drainage time after HL treatment was longer
(mean 10.6 days) compared with TURP (mean 2.2 days, p<0.001). All TURP patients urinated at discharge, but eight HL patients were discharged with suprapubic catheter (p<0.01).

Both treatments improved DanPSS, Qmax and PdetQmax and decreased prostate volume during the six-month follow up (Table 3). In the pressure-flow study 7/19 (37%) patients were still obstructed in the laser arm after six months, compared with 2/21 (10%) in the TURP group (p<0.05). The urologist’s subjective estimation in the urethrocytostoscopic examination revealed that the prostatic urethra was wider after TURP than after laser treatment.

Table 3. Efficacy variables of HL and TURP patients during the six month follow up (mean, range).

<table>
<thead>
<tr>
<th></th>
<th>HL</th>
<th>TURP</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DanPSS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preoperative</td>
<td>18.6 (5-40)</td>
<td>23.3 (5-69)</td>
<td>ns</td>
</tr>
<tr>
<td>at 6 months</td>
<td>5.5 (0-21) **</td>
<td>4.7 (0-22) ***</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Qmax (ml/s)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preoperative</td>
<td>8.5 (2.3-17.2)</td>
<td>7.2 (3.7-14.8)</td>
<td>ns</td>
</tr>
<tr>
<td>at 6 months</td>
<td>14.4 (7.9-20.7) ***</td>
<td>19.6 (4.1-43.2) ***</td>
<td>ns</td>
</tr>
<tr>
<td><strong>PdetQmax (cmH2O)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preoperative</td>
<td>79 (47-131) **</td>
<td>83 (47-137)</td>
<td>ns</td>
</tr>
<tr>
<td>at 6 months</td>
<td>53 (26-109) **</td>
<td>36 (7-63) ***</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>PVR (ml)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preoperative</td>
<td>125 (0-350)</td>
<td>144 (0-450)</td>
<td>ns</td>
</tr>
<tr>
<td>at 6 months</td>
<td>69 (0-160)</td>
<td>45 (0-177) **</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Prostate volume (ml)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preoperative</td>
<td>55 (42-83)</td>
<td>55 (40-95)</td>
<td>ns</td>
</tr>
<tr>
<td>at 6 months</td>
<td>49 (32-77) *</td>
<td>29 (19-42) ***</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

p-value is for the difference between the groups;
* p<0.05, ** p<0.01, *** p<0.001; significance for the difference within the groups
5.2.2. Two-year results (III)

Of the 46 randomized patients (21 HL and 25 TURP), 37 (80%) were available at the 24-month follow up.

The long-term results are shown in Table 4. The decrease in DanPSS from baseline at 24 months was 51.0% in the HL (p<0.01) and 80.0% in the TURP group (p<0.001), with no statistically significant differences between the groups. The early improvement in objective urinary parameters of Qmax and PVR at six months (II) showed deterioration in the HL group during longer follow up, whereas in the TURP group the improvement was sustained.

Table 4. Symptoms and urinary indices before and two years after HL treatment and TURP (mean, range).

<table>
<thead>
<tr>
<th></th>
<th>HL</th>
<th>TURP</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DanPSS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preoperative</td>
<td>18.6 (5-40)</td>
<td>22.8 (5-69)</td>
<td>ns</td>
</tr>
<tr>
<td>at 2 years</td>
<td>7.2 (0-25)**</td>
<td>3.4 (0-21)***</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Qmax (ml/s)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preoperative</td>
<td>8.5 (2.3-17.2)</td>
<td>7.2 (3.7-14.8)</td>
<td>ns</td>
</tr>
<tr>
<td>at 2 years</td>
<td>10.3 (5.8-15.0)</td>
<td>20.6 (9.5-38.9)***</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>PVR (ml)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preoperative</td>
<td>125 (0-350)</td>
<td>138 (0-450)</td>
<td>ns</td>
</tr>
<tr>
<td>at 2 years</td>
<td>114 (28-202)</td>
<td>58 (0-166)*</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

p-value is for the difference between the groups;
* p<0.05, ** p<0.01, *** p<0.001; significance for the difference within the groups
5.3. Impact of Nd:YAG laser treatment and TURP on sexual function (V)

The prevalence of sexual function in LUTS patients was estimated by DanPSS Sex questionnaires. Evaluation was based on 83 of 98 (85%) patients who completed the questionnaire also one year postoperatively, of those patients 41 were in laser (CLV + HL) and 42 in TURP group. The median age (±SD) of patients was 67±7 (range 46 – 82) years. Sexual dysfunction in men suffering from LUTS was common and increased with age, as presented in Table 5. There was no correlation between three different categories of the severity of DanPSS urinary symptoms and ED. Erectile dysfunction, subjectively reported reduced ejaculatory volume and pain/discomfort on ejaculation was considered problematic by 79%, 63% and 100% of the patients, respectively.

Table 5. Presence of sexual dysfunction in men with lower urinary tract symptoms according to age.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>&lt;60</th>
<th>60 - 69</th>
<th>&gt;69</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erectile dysfunction</td>
<td>6/10 (60)</td>
<td>41/48 (85)</td>
<td>24/25 (96)</td>
<td>71/83 (86)</td>
</tr>
<tr>
<td>Ejaculatory dysfunction</td>
<td>6/10 (60)</td>
<td>41/48 (85)</td>
<td>23/25 (92)</td>
<td>70/83 (84)</td>
</tr>
<tr>
<td>Pain/discomfort on ejaculation</td>
<td>2/10 (20)</td>
<td>12/48 (25)</td>
<td>7/25 (28)</td>
<td>21/83 (25)</td>
</tr>
</tbody>
</table>

The prevalence of sexual dysfunction before and one year after Nd:YAG laser treatment or TURP is presented in Table 6. The increase in total impotence rate in TURP patients was significant. Total absence of ejaculate was not significantly associated with laser treatment. Both treatments reduced the number of men reporting pain or discomfort on ejaculation without differences between the groups.
Table 6. Sexual dysfunction before and after treatment. Figures are numbers (percentages) of patients.

<table>
<thead>
<tr>
<th></th>
<th>Laser (41)</th>
<th>TURP (42)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>1 year</td>
</tr>
<tr>
<td>Erectile dysfunction</td>
<td>34 (83)</td>
<td>35 (85)</td>
</tr>
<tr>
<td>No erection</td>
<td>2 (5)</td>
<td>5 (12)</td>
</tr>
<tr>
<td>Reduced or absent ejaculate</td>
<td>34 (83)</td>
<td>33 (81)</td>
</tr>
<tr>
<td>No ejaculate</td>
<td>11 (27)</td>
<td>10 (24)</td>
</tr>
<tr>
<td>Pain/discomfort on ejaculation</td>
<td>9 (22)</td>
<td>3 (7)*</td>
</tr>
</tbody>
</table>

p-value is for the difference in the change of sexual dysfunction between groups; *p<0.05, **p<0.01, ***p<0.001; significance for the difference in the change of sexual dysfunction within groups
6. DISCUSSION

6.1. Review of study sample and design

6.1.1. Study sample

The sample size in our study is considered small at the present time. When this study was started ten years ago, however, preliminary studies were common, and critical aspects of clinical studies on the treatment of BPH were still becoming established. At the moment, we know that to detect a difference of five points in symptom scores evaluated by DanPSS at 5% significance and 80% power level, 126 patients would have been required into the study. Furthermore, we should have taken into consideration that in studies with a long-term follow up a high rate of patients are lost from follow up (Keoghane et al 2000, Gilling et al 2000, Tubaro et al 2000, McAllister et al 2000). On the other hand, it is reality, that in small urological centre it is not possible to recruit sufficient number of patients in a reasonable time. Consequently, the number of the patients in this study was small, and the power to detect differences between the study groups was limited. When we started this study in 1994, devices suitable for Nd:YAG treatment of the prostate were rare in Finnish hospitals, and it was not possible to conduct a multicenter study.

6.1.2. Study design

TURP is the gold standard of operative treatment of BPH against which all other invasive treatments should be compared. When we started the study there were only few preliminary reports of CLV (Daughtry and Rodan 1992, Daughtry and Rodan 1993, Watson 1992, Shumaker 1994), and no publications on HL treatment. In our study (I–IV) patients were randomized according to prostate volume due to technical reasons. CLV involves some critical problems that affect the success of the operation. First, extensive training and experience is required, and second, large glands are very difficult to treat technically. The procedure also requires patience due to prolonged operation time. These problems associated with CLV have been later reported also by other investigators (Watson 1995, Keoghane et al 1996a, Floratos et al 2000). The results of V-LAP were far from optimal, and it was proposed that combining CLV and V-LAP in the treatment of big prostates would improve the outcome. Consequently, taking into account
all these things, we decided to randomize patients with prostate volume less than 40 ml to CLV and larger than 40 ml to HL treatment and compare the results with traditional TURP in both volume categories. To optimize the learning curve effect all the operations were performed by the same experienced urologist. In this way possible bias due to different techniques in performing TURP or Nd:YAG treatments is also avoided. We first performed non-contact coagulation of the prostate and then opened the prostatic urethra by contact tip. Doing the procedure the other way around might have resulted in more pronounced removal of prostatic tissue and a better outcome. There are no studies to support this speculation, because all trials reporting results of HL treatment have used different methods.

Although the decrease in symptoms and improvement in QoL are considered the main goals of BPH treatment, invasive treatment should also remove infravesical obstruction to make sure that severe and irreversible changes in the detrusor muscle will not develop (Elbadawi et al 1993). Pressure-flow studies are essential in the evaluation of the efficacy of any new therapeutic modality that interventionally removes prostatic tissue (Floratos and de la Rosette 2000, Horniger et al 1997). In our trial all patients underwent pressure-flow studies preoperatively, and only urodynamically obstructed patients were included. The relief of obstruction in the pressure-flow study after treatments was assessed in both the short (I, II) and long term (IV).

A histological specimen is not available after CLV and HL treatments. It is therefore possible that prostate carcinoma may remain undetected. We found that in spite of all available preoperative investigations three (6%) prostate carcinomas were diagnosed in the TURP groups from the electroreseected chips (I, II). On average in patients not screened for prostate carcinoma, carcinoma is expected to be found in approximately in 12% of patients undergoing TURP (Mebust et al 1989, Doll et al 1992). To minimize the risk of undiagnosed prostate cancer in laser treatment patients it is possible to take multiple prostate biopsies routinely in the beginning of the procedure. It is well known that carcinoma typically begins in the peripheral zone of the prostate. Because usually only the enlarged transitional zone is removed by TURP, we can not truly rely on the negative histopathological analysis of the TURP specimens.
The exclusion of patients in the TURP groups based on carcinoma in the prostate specimen in the primary operation may cause bias patients with occult carcinoma might be included in laser arms. Undiagnosed prostate cancer patients probably change the outcome of trial results. Patients in both groups were followed in the same way, and in case of cancer suspicion, TRUS guided biopsies were taken. Two prostatic carcinomas were further diagnosed during follow up, one in the TURP group from prostatic biopsies two years after the primary operation, and one in the HL group from electroresected ships in TURP 17 months after initial treatment. These patients were managed by hormonal treatment and excluded from the study, since hormonal treatment obviously interferes with the results of the treatment.

In study V the impact of Nd:YAG laser treatment and TURP on sexual function was evaluated by combining two different Nd-YAG laser (contact and hybrid) treated patients into same group, which may be criticized. We hypothesized that because both laser treatment methods use same Nd:YAG laser energy, the destroying effect on prostatic tissue is probably similar and will likely have the same impact on sexual function.

6.1.3. Problems associated with long-term clinical trial

In this study the patients accepted the follow-up investigations including invasive pressure-flow studies exceptionally well. In studies after one (V), two (III) and four years (IV) the percentages of evaluable patients were 85, 80 and 81, respectively. Only two patients refused further assessment during the long term follow up, probably because of good symptomatic treatment outcome. The questions related to intimate sexual aspects were left unanswered by two patients. Other drop-outs were only due to adverse events or deaths, which decreases bias and improves the value of this study (I – V). The study was conducted in a small city with population of 100 000 and surrounded by a rural area. Low population mobility may be contributed to the low number of patients of lost to follow up. Other long-term studies comparing laser treatments and TURP report five years results based on 38% to 46% of originally treated patients (Keoghane et al 2000, McAllister et al 2000). Based on preliminary analyses of HL vs. TURP the recruitment was stopped after two years and nine months (II) due to the superiority of TURP to HL in efficacy, because it was unethical to continue the recruitment.
6.2. Short-term results of contact laser vaporization vs. transurethral resection of the prostate (I)

VLAP was the first minimally invasive procedure to gain wide popularity in the treatment for BPH, with promising preliminary efficacy and safety (Costello et al 1992). VLAP is, however, associated with many difficulties postoperatively, including prolonged catheterization time (Schatzl et al 2000, Te Slaa et al 1996, Anson et al 1995). Daughtry and Rodan (1992) introduced first the CLV for the treatment of BPH into clinical practice. At the time we started this study in September 1994, the literature provided only a few other reports of CLV as a choice of treatment for BPH (Watson 1992, Daughtry and Rodan 1992, Daughtry and Rodan 1993, Shumaker 1994). At that time it was proposed that CLV would offer some advantages over VLAP, especially with regard to early postoperative voiding.

We observed that in the short term both CLV and TURP equally improve urinary symptoms, Qmax and PVR, which is in accordance with other prospective, randomized, controlled trials (Keoghane et al 1996a, Van Melick et al 2002) and other non-randomized studies, (Horniger et al 1997, Floratos et al 2000, Gomella et al 1995, Watson 1995). As far as the authors are aware, the current study is the first to compare the efficacy of CLV and TURP by including pressure-flow studies in a prospective, randomized trial. In the present study both treatments caused equal and significant decrease in PdetQmax reflecting the equal efficacy in relieving the infravesical obstruction, and postoperatively 90% of the CLV and 100% of the TURP patients were unobstructed. Van Melick and co-workers (2002) report similar findings in their randomized, controlled trial comparing urodynamic effects of TURP, CLV and TUEP. The efficacy of TURP in relieving obstruction is well known (Abrams et al 1979, Horniger et al 1997), and CLV has also been shown to decrease PdetQmax (Horniger et al 1997, Bryan et al 2000).

The most common perioperative complication of TURP is associated with bleeding (Mebust et al 1989). In our study the intraoperative bleeding was estimated from the hemoglobin concentration in the irrigant effluent using a Haemocue photometer, which is a well accepted method. The blood loss was less during CLV compared with TURP, which is in line with other studies reporting minimal intraoperative bleeding during CLV (Keoghane et al 1996a, Horniger et al 1997, Daughtry and Rodan 1992). The clinical
relevance of less intraoperative bleeding during CLV is not clear as no blood transfusion was needed in either group, and only one TURP patient had postoperative clot retention. Only patients with small prostates were included and an experienced operator performed all the procedures. This may explain why we were able to avoid technical problems and crossover to TURP during CLV reported in some cases by Keoghane and co-workers (1996a).

It was expected that immediate removal of prostatic tissue by CLV would enable early postoperative voiding. However, in the preset study we found that 16% of CLV patients needed prolonged catheterization after discharge, and consequently, the mean postoperative drainage time was longer after CLV compared with TURP. Keoghane and co-workers (1996a) did not find any difference in catheterization times, but recatheterization rate was higher after CLV than after TURP.

At six months estimation by cystoscopy revealed that prostatic urethra was wider and measurement of prostate volume by TRUS confirmed that prostate size was smaller in TURP group compared with CLV group. Consequently, TURP removes prostatic adenoma more radically than CLV.

6.3. **Long-term results of contact laser vaporization and transurethral resection of the prostate (IV)**

A simple objective and important measurement for assessing the long-term success of the treatments of BPH is to compare the rates of secondary interventions associated with each therapy. In our trial during the four-year follow up only one patient (4%) in the TURP and one patient (4%) in the CLV group needed secondary intervention, which correlates with previous reports of the outcome of TURP (Borboroglu et al 1999, Roos et al 1989). Secondary intervention rates for CLV ranging from 4.8% to 23.3% during 2 – 5 year follow ups have been reported in literature, which means that our results are slightly better than earlier results (Tubaro et al 2000, Keoghane et al 2000a, Floratos et al 2000, Bryan et al 2000).
In the present study, the improvement in DanPSS was equal and sustained during the four-year follow-up after CLV treatment (72%) and TURP (78%). Similar to our results, Keoghane and co-workers (2000) reported in their five-year follow-up study of CLV and TURP treatments that the AUA symptom score decreased from 19.5 to 9.7 and from 20.2 to 7.0, respectively. In a non-randomized study comparing different laser treatments IPSS decreased 64% after CLV during a four-year follow-up (Floratos et al. 2000). Average improvement of symptom score after TURP is 68% (Gajewski 2000).

The 72% and 87% improvement of Qmax four years after CLV and TURP was more pronounced in our trial compared with the respective changes in Qmax from 12.0 ml/s to 14 ml/s (14%) and from 9.0 ml/s to 14.0 ml/s (56%) in another randomized controlled study with a five-year follow-up (Keoghane et al. 2000). Floratos and co-workers (2000) reported the initial improvement in Qmax after CLV (from 8.3 ml/s to 18.5 ml/s) to worsen to near the baseline value (11.1 ml/s) during a four-year follow-up, which was not seen in our study. In a study comparing CLV and VLAP the increase in Qmax in CLV arm at two years was quite similar, rising from 10.0 ml/s to 15.5 ml/s and in VLAP arm from 10.0 ml/s to 15.9 ml/s (Bryan et al. 2000).

At four years both treatments effectively lowered PdetQmax, but there were fewer urodynamically obstructed patients and mean PdetQmax was lower in TURP group compared with CVL group. Despite avid research in the field of urodynamics in the treatment of BPH, the long-term effect of CLV and TURP on BOO has not been previously reported in the literature. More prostatic tissue is removed by TURP than by CLV (I). A small residual prostatic weight ratio after TURP in BPH has been proved to correlate to good clinical outcome (Chen et al. 2000). In our study the better long term results of PdetQmax after TURP compared with CLV may be explained with the completeness of removal of the obstructing adenoma.

The explanation for a favorable secondary intervention rate and good long-term outcome of both treatment modalities might be due to strict inclusion criteria in our trial, as only LUTS patients with urodynamically confirmed BOO and with small or moderately enlarged prostates were included. This concept is supported by the observation that clearly
obstructed groups of BPH patients subjected to laser prostatectomy had the most impressive results, emphasizing the value of urodynamics in the initial evaluation of BPH (Floratos and de la Rosette 2000). Obstructed BPH patients have also shown to get better symptomatic relief after TURP compared with unobstructed ones (Floratos and de la Rosette 2000). In clinical practise, to what extent the urodynamic studies should be done before the operative treatment of BPH is a controversial issue. Preoperative pressure-flow studies improve the diagnosis of real obstruction and thereby that improve the results of operative treatment of BPH and reduce the number of unnecessary operations (Jensen et al 1996). On the other hand, we have to balance these benefits with the costs and invasiveness of the pressure-flow studies.

6.4. Short-term results of hybrid laser treatment and transurethral resection of the prostate (II)

In the beginning of the 1990s there were promising reports of Nd-YAG laser energy for the treatment of BPE either by CLV or the non-contact VLAP method (Costello et al 1992, Watson 1992, Daughtry and Rodan 1992, Daughtry and Rodan 1993, Shumaker 1994). CLV is better applicable for the treatment of small and moderately enlarged prostates because treatment of large ones is technically difficult and time consuming (Watson 1995, Keoghane et al 1996a, Floratos et al 2000). VLAP is an attractive alternative to TURP because blood loss is minimal and technique is easy to learn (Costello et al 1992). Outflow obstruction caused by a large prostate cannot be ablated satisfactorily by VLAP (Jung et al 1996), and furthermore, it is associated with prolonged catheterization time and severe irritative voiding symptoms for many weeks after the operation (Schatzl et al 2000, Te Slaa et al 1996, Anson et al 1995). The main objectives of the present study were to assess whether combining VLAP and CLV could solve the problems associated with these treatment modalities alone in the treatment of BPH with large prostates and compare these results with conventional TURP.

In our study HL treatment could not totally eliminate the need for prolonged catheterization as 30% of HL treated patients were discharged with a suprapubic catheter, whereas all TURP patients were able to urinate at discharge. Consequently bladder drainage time was longer after HL treatment compared with TURP, which contradicts the only other published randomized controlled trial comparing HL and TURP (Carter et al
1999a). However, they used different method, performing initial KTP vaporizing bladder neck incisions and prostatectomies followed by a “free-paint” application of Nd:YAG coagulation, and furthermore prostates were smaller in their study. Another study comparing HL and VLAP concluded KTP laser bladder neck incisions to enhance the outcome, with early catheter removal, improved flow rates and symptom scores (Langley et al 1997).

In the present study the improvement in symptoms, Qmax and PVR were significant and equal in both treatments during the short-term follow up, which is similar to the findings by Carter and co-workers (1999a). In spite of that, in our study HL treatment did not remove infravesical obstruction caused by a large prostate as effectively as TURP. The effects of HL treatment on BOO have not been previously published. It is known that TURP can eliminate infravesical obstruction caused by BPE in almost all patients (Abrams and Griffiths 1979, Horniger et al 1997). One possible explanation for the difference in desobstructive ability of these two treatment modalities is the observation that less prostatic tissue is removed by HL treatment than by TURP, which was confirmed by bigger prostate volume and narrower prostatic urethra in cystoscopy as at six months in HL group. In comparing different treatment modalities in patients with BPH, the role of pressure-flow studies is emphasized to select patients who are truly obstructed and will therefore benefit from the desobstructive procedure (Floratos and de la Rosette 2000).

The main perioperative complication of TURP is bleeding, and 6 - 31% of patients need blood transfusions (Mebust et al 1989, Melchior et al 1974a). In our study blood transfusion was necessary in 8% of TURP patients. Furthermore, two of the patients required bladder irrigation with a syringe to relieve clot retention during the immediate postoperative period. Complications associated with bleeding could not be totally avoided in HL treatment as one patient needed a blood transfusion and two had clot retentions. Besides the current study there are no other reports comparing intraoperative blood loss between HL treatment and TURP. In our study HL treatment caused less intraoperative bleeding compared with TURP, which is consistent with other studies reporting low incidence of perioperative complications associated with bleeding after HL (Carter et al 1999a, Langley et al 1997, Chahal et al 2000). Operation time of HL treatment in our study was longer than that of TURP, reflecting the difficulties in technique. Intraoperative
data of HL treatment is difficult to compare with other studies because of the differences in treatment methods.

6.5. Long term results of hybrid laser treatment and transurethral resection of the prostate (III)

The literature concerning long term effects of HL treatment is scarce. In addition to the present trial there is only one non-randomized study with a two-year follow up (Chahal et al 2000), and two papers reporting results from a randomized controlled study of HL vs. TURP with a one-year follow up (Carter et al 1999a, Carter et al 1999b). In previous studies HL treatment has been conducted using a variety of equipment and power settings, making comparison between studies difficult or impossible.

In our study, the total re-operation rate was 8.0% after TURP and 14.3% after HL treatment during 24 months. Carter and co-workers (1999a) reported a very low (2.1%) re-operation rate at one year after HL treatment, but they included only those patients requiring re-treatment because of inadequate initial prostate tissue removal. In a series of 137 patients treated by HL and followed for two years the re-treatment rate was 3.6% (Chahal et al 2000).

The symptomatic improvement was good in both treatment arms, lasting at least 24 months. These findings are similar to other papers reporting one to two-year follow up results after HL treatment (Chahal et al 2000, Carter et al 1999a, Langley et al 1997). Carter and associates (1999b) also observed equal QoL one year after HL treatment and TURP.

The mean peak urinary flow increased by 186% after TURP and by 21% after HL treatment at 24 months compared with baseline values. Carter and co-workers (1999a) reported comparable results of TURP and HL treatment in maximal flow rates after one year. Shorter follow-up time and smaller prostates in their study may be explanations to this difference. In our trial there was no difference in Qmax between the study arms at six months. Longer follow up showed a fall-off in the improvement of flow rate in the HL treatment arm, however, whereas the improvement in Qmax after TURP was sustained
during the two-year follow up. This phenomenon of a fall-off in the improvement in flow rates despite sustained improvement in symptom scores has also been reported after long-term follow up of VLAP (Beerlage et al 1998). This might be due to inadequate prostatic adenoma removal after these minimally invasive treatments compared with TURP.

6.6. Sexual function of patients with lower urinary tract symptoms (V)

LUTS and ED are common problems among aging men (Garraway et al 1991, Feldman et al 1994, Sagnier et al 1996, Frankel et al 1998). There is evidence that sexual dysfunction and urinary symptoms are associated with each other (Rosen et al 2002, Frankel et al 1998, Macfarlane et al 1996) and they both have been identified as important components of QoL in men (Calais Da Silva et al 1997). In our material the prevalence of ED 86%, ejaculatory dysfunction 84% and discomfort or pain on ejaculation 25% in LUTS patients was high compared with previous reports, in which the respective numbers are 60% - 71%, 62% - 70% and 17% - 18% (Brookes et al 2002, Frankel et al 1998). The median age of our patients was 67 years. The occurrence of sexual dysfunction increases with advancing age (Macfarlane et al 1996). A wide variation in the prevalence of sexual dysfunction in different countries has been reported (Frankel et al 1998). In a Finnish community based survey the prevalence of ED was 76% at the age of 60 years and 83% at the age of 70 years (Koskimäki et al 1998). Our data in LUTS patients supports a high prevalence of sexual dysfunction among aging Finnish men. We did not observe the association between the severity of LUTS and ED reported by Vallancien ad associates (2003), which may be due to small sample size in the present study. Most men in our study perceived sexual dysfunction as bothersome, in line with other studies (Brookes et al 2002, Frankel et al 1998).

6.7. The impact of Nd:YAG laser treatment and transurethral resection of the prostate on sexual function (I, II,V)

The impact of TURP on erectile function is controversial. There is a wide variation in the literature, ranging from 40% impotence rate to improvement of erectile function (Finkle and Priam 1966, Wasson et al 1995, Kunelius et al 1997, Brookes et al 2002). We found no significant effect of either Nd:YAG laser or TURP treatments on erectile function. Some patients with severe ED preoperatively reported total impotence one year after TURP and
CLV. This change was marginally significant after TURP. Because there was no control group, we do not know whether the increase of totally impotent men was due to treatment or natural course of erectile function deterioration with age. Many earlier studies reporting a high rate of ED after TURP have been criticized because of their retrospective nature and the possibility of biased data. A review article of various standard surgical and alternative instrumental techniques used for BPH reported an increase in impotence of 0% to 15% (Zlotta and Schulman 1999). Brookes et al (2002) reported in their randomized study an improvement of erectile function after TURP, with only a few new cases of impotence, but no effect on erectile function after non-contact laser treatment. In a randomized controlled trial Keoghane et al (1996b) found that 4% and 3% of previously potent men were impotent three months after contact laser vaporization and TURP, respectively. One study reported high interference of sexual function following KTP/YAG HL prostatectomy as 33% of the patients had a significant change in the strength of erections (Chahal et al 2000). However, they could not explain the reason for such a high incidence of sexual dysfunction. In any case, based on our study and literature we think that there is not a big difference in the risk of ED between Nd:YAG laser treatment and TURP.

Comparison of the prevalence of ejaculatory problems at baseline and at one year was based on DanPSS sex questionnaire. The number of men with total loss of ejaculate did not change after Nd:YAG treatment, but increased after TURP, and there was a significant difference between the groups. Ejaculatory volume decrease or absence is a well-known and common consequence of TURP, as observed also in our study. In a meta-analysis of TURP patients the incidence of retrograde ejaculation was 70.4% (Roehrborn 1996). In a small group of 24 patients treated by CLV Watson (1995) reported a 35% rate of significantly reduced or absent ejaculate postoperatively. An exceptionally high rate of decreased ejaculate in 79% of patients after HL treatment was reported by Chahal and associates (2000), but they could not explain the reason for that. Differences in ejaculatory problems after BPH treatments between studies may be confusing partly due to differences in methods used to collect data.
In our study both TURP and laser treatments decreased the number of patients with discomfort or pain on ejaculation. Brookes et al (2002) demonstrated this favourable effect after TURP, but not after non-contact laser treatment. There are no other reports concerning effects of Nd:YAG treatment on discomfort/pain during ejaculation. Pain/discomfort during ejaculation is usually associated with CPPS. Whether patients in our study reporting pain or discomfort could be diagnosed as having CPPS is unclear. This syndrome involves various other symptoms, and the etiology is unknown. Invasive treatment of CPPS has been disappointing (Leskinen et al 2002). Consequently, our observation that TURP and Nd:YAG laser treatment relieve pain/discomfort during ejaculation is interesting. BPH patients with pain or discomfort on ejaculation may be informed about this possible advantage of invasive treatment.

6.8. Future perspectives

Minimally invasive treatments cover broad spectrum of different operations. There are procedures that can be done under local anesthesia in an office setting and moderately improve urinary symptoms and objective urinary parameters (VLAP, ILC, TUMT, TUNA). These procedures should perhaps be considered preferably as an alternative to medical treatment rather than TURP (Djavan and Marberger 2001). On the other hand, there are more aggressive operations based on immediate removal of prostatic tissue (Nd:YAG CLV and HL, KTP high power laser, TUEP and HoLEP), which improve symptoms and objective urinary parameters comparable with TURP in the short term. For the time being long-term results of minimally invasive treatments are sparse. TURP is considered as the gold standard of operative treatment of BPH against which new treatment modalities are compared. In the rapidly evolving field of minimally invasive treatments for BPH it remains to be seen which procedures will stand the test of time and remain real options or even replace TURP. Based on our results CLV could be considered an alternative to TURP in the treatment of BPH with a small or moderately enlarged obstructing gland. However, few urologists are familiar with this technique, and most hospitals do not have laser equipment suitable for CLV treatment. The initial enthusiasm concerning Nd:YAG laser treatments (VLAP, CLV and HL) in their present form is decreasing. It seems clear that they are steps in the development of more sophisticated laser treatment modalities. Recently promising short-term results with excellent efficacy
and low complication rates have been reported for the KTP high power laser and HoLEP (Tan et al 2003, Hai and Malek 2003).
7. SUMMARY AND CONCLUSIONS

Based on the present study the following conclusions can be drawn:

1. In the treatment of BPH with small or moderately enlarged prostates CLV proved to be a safe procedure that improved subjective symptoms and objective urinary parameters as effectively as TURP in short term (6 months). CLV did not offer any substantial advantages over TURP concerning perioperative morbidity. Due to less intraoperative bleeding CLV can be offered as an option for patients with bleeding disorders.

2. The HL treatment proved to be a safe method and improved symptoms and urinary flow equally compared with TURP in the treatment of BPH with glands between 40 and 100 ml in short term (6 months). HL was inferior to TURP with respect to operation time, catheterization time, removal of BOO and decreasing prostate volume, which favors TURP in these cases.

3. Both HL treatment and TURP give good and equal symptomatic relief lasting at least two years, but HL treatment is associated with inferior outcome in objective urinary parameters and a higher re-operation rate. Consequently, HL treatment should not be a routine procedure in the management of LUTS associated with big prostates and BOO necessitating invasive treatment.

4. Long-term data of CLV and TURP treatments showed equal and sustained subjective relief and a low re-operation rate. However, extended follow up revealed a slight advantage of TURP over CLV in most objective outcome parameters. CLV can be considered as an alternative to TURP in the treatment of BPH with small or moderately enlarged obstructing gland.

5. The prevalence of sexual dysfunction in patients with LUTS is high and perceived mostly as bothersome. TURP or Nd-YAG laser treatment did not increase erectile dysfunction, but did decrease pain or discomfort during ejaculation. The only significant difference between these treatments in respect to sexual function was a higher incidence of decreased or absent ejaculate after TURP. For a LUTS patient with small or moderately enlarged prostate who consider normal ejaculation important, CLV could be a better alternative than TURP.
8. REFERENCES


Finkle AL, Prian DV. Sexual potency in elderly men before and after prostatectomy. JAMA 1966;196:139-43.


McConnel JD. Why pressure-flow studies should be optional and not mandatory studies for evaluating men with benign prostatic hyperplasia. Urology 1994;44:158.


9. **APPENDIX**

**Appendix 1**: Danish Prostate Symptoms Score questionnaire (Hald et al 1991).

<table>
<thead>
<tr>
<th>1 A</th>
<th>Do you have to wait for urination to start?</th>
<th>1 B</th>
<th>If you have to wait to start urination, is this a problem for you?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Answers: 0 – No; 1 – Rarely; 2 – Daily; 3 – Every time</td>
<td></td>
<td>Answers: 0 – No problem; 1 – Small problem; 2 – Moderate problem; 3- Major problem</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2 A</th>
<th>I your urinary stream weak or dribbling?</th>
<th>2 B</th>
<th>If your urinary stream is weak or dribbling, is this a problem for you?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Answers: 0 – Normal; 1 – Weak; 2 – Very weak; 3 - Dribbling</td>
<td></td>
<td>Answers: 0 – No problem; 1 – Small problem; 2 – Moderate problem; 3- Major problem</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3 A</th>
<th>Do you feel that you empty your bladder completely?</th>
<th>3 B</th>
<th>If you feel that you do not empty your bladder completely, is this a problem for you?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Answers: 0 – Always; 1 - Occasionally; 2 – Rarely; 3 - Never</td>
<td></td>
<td>Answers: 0 – No problem; 1 – Small problem; 2 – Moderate problem; 3- Major problem</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4 A</th>
<th>Do you have to train to start and/or maintain urination?</th>
<th>4 B</th>
<th>If you have to strain, is this a problem for you?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Answers: 0 - No; 1 – Rarely; 2 – Daily; 3 - Always</td>
<td></td>
<td>Answers: 0 – No problem; 1 – Small problem; 2 – Moderate problem; 3- Major problem</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5 A</th>
<th>What is the longest interval between each urination, from you wake up until you go to bed?</th>
<th>5 B</th>
<th>Do you consider your frequency of urination a problem?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Answer: 0 – More than three hour; 1 – Two to three hours; 2 – One to two hours; 3 – Less than one hour</td>
<td></td>
<td>Answers: 0 – No problem; 1 – Small problem; 2 – Moderate problem; 3- Major problem</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6 A</th>
<th>How many times do you have to urinate during the night?</th>
<th>6 B</th>
<th>If you have to urinate during the night, is this a problem for you?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Answers: 0 – None; 1 – One to two times; 2 – Three to four times; 3 – Five times or more</td>
<td></td>
<td>Answers: 0 – No problem; 1 – Small problem; 2 – Moderate problem; 3- Major problem</td>
</tr>
<tr>
<td></td>
<td>Question</td>
<td></td>
<td>Question</td>
</tr>
<tr>
<td>---</td>
<td>-------------------------------------------------------------------------</td>
<td>---</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>7 A</td>
<td>Do you experience an imperative urge to urinate?</td>
<td>7 B</td>
<td>If you have an imperative urge to urinate, is this a problem for you?</td>
</tr>
<tr>
<td></td>
<td>Answers: 0 – Never; 1 – Rarely; 2 – Daily; 3 - Always</td>
<td></td>
<td>Answers: 0 – No problem; 1 – Small problem; 2 – Moderate problem; 3- Major problem</td>
</tr>
<tr>
<td>8 A</td>
<td>Is the urge to urinate so strong that urine starts to flow before you reach the toilet?</td>
<td>8 B</td>
<td>If the urge to urinate is so strong that urine starts to flow before you reach the toilet, is this a problem for you?</td>
</tr>
<tr>
<td></td>
<td>Answers: 0 – Never; 1 – Rarely; 2 – Daily; 3 – Every time</td>
<td></td>
<td>Answers: 0 – No problem; 1 – Small problem; 2 – Moderate problem; 3- Major problem</td>
</tr>
<tr>
<td>9 A</td>
<td>Does it hurt or burn when you urinate?</td>
<td>9 B</td>
<td>If it hurts or burns when you urinate, is this a problem for you?</td>
</tr>
<tr>
<td></td>
<td>Answers: 0 – Never; 1 – Rarely; 2 – Daily; 3 - Always</td>
<td></td>
<td>Answers: 0 – No problem; 1 – Small problem; 2 – Moderate problem; 3- Major problem</td>
</tr>
<tr>
<td>10 A</td>
<td>Do you experience dribbling after voiding, when you have finished voiding?</td>
<td>10 B</td>
<td>If you experience dribbling after voiding, is this a problem for you?</td>
</tr>
<tr>
<td></td>
<td>Answers: 0 – Never; 1 – In the toilet; 2 – Small amounts in the trousers; 3 – Large amounts in the trousers</td>
<td></td>
<td>Answers: 0 – No problem; 1 – Small problem; 2 – Moderate problem; 3- Major problem</td>
</tr>
<tr>
<td>11 A</td>
<td>Do you experience leakage of urin when physically active (e.g. lifting, sneezing, coughing)?</td>
<td>11 B</td>
<td>If you experience leakage of urine when physically active, is this a problem for you?</td>
</tr>
<tr>
<td></td>
<td>Answers: 0 – Never; 1 – Rarely; 2 – Often; 3 - Always</td>
<td></td>
<td>Answers: 0 – No problem; 1 – Small problem; 2 – Moderate problem; 3- Major problem</td>
</tr>
<tr>
<td>12 A</td>
<td>Do you experience urinary leakage without urge or physical activity?</td>
<td>12 B</td>
<td>If you experience urinary leakage without urge or physical activity, do you consider this a problem</td>
</tr>
<tr>
<td></td>
<td>Answers: 0 – Never; 1 – Rarely; 2 – Often; 3 - Always</td>
<td></td>
<td>Answers: 0 – No problem; 1 – Small problem; 2 – Moderate problem; 3- Major problem</td>
</tr>
</tbody>
</table>
Appendix 2: Danish Prostate Symptom Score Sex questionnaire (Hald et al 1991).

1 A Are you able to get an erection? 1 B If you are troubled getting an erection, is this a problem for you?

Answers: 
0 – Yes, with normal rigidity
1 – Yes, with slightly reduced rigidity
2 – Yes, with severely reduced rigidity
3 – No, erection not possible

Answers: 
0 – No problem
1 – Small problem
2 – Moderate problem
3 – Major problem

2 A Do you have ejaculation of semen? 2 B If your ejaculation of semen is reduced or absent, is this a problem for you?

Answers: 
0 – Yes, in normal quantity
1 – Yes, in slightly reduced quantity
2 – Yes, in significantly reduced quantity
3 – No

Answers: 
0 – No problem, 
1 – Small problem
2 – Moderate problem
3 – Major problem

3 A Do you have pain/discomfort during ejaculation? 3 B If you have pain/discomfort during ejaculation, is this a problem for you?

Answers: 
0 – No
1 – Yes, slight pain/discomfort
2 – Yes, moderate pain/discomfort
3 – Yes, severe pain/discomfort

Answers: 
0 – No problem
1 – Small problem
2 – Moderate problem
3 – Major problem
10. ORIGINAL PUBLICATIONS I TO V