TREATMENT OF BENIGN PROSTATIC HYPERPLASIA BY TRANSURETHRAL ULTRASOUND-GUIDED LASER-INDUCED PROSTATECTOMY (TULIP): EFFECTS ON URODYNAMIC PARAMETERS AND SYMPTOMS

J.L.H. RUUD BOSCH, M.D.
JAN GROEN, M.D.
FRITZ H. SCHRÖDER, M.D., PH.D.

From the Department of Urology, Erasmus University and Academic Hospital, Rotterdam, The Netherlands

ABSTRACT—**Objectives.** This prospective study was undertaken to evaluate the effects of transurethral ultrasound-guided laser-induced prostatectomy (TULIP) on urodynamic, symptomatic, and prostate volume parameters as well as serum prostate-specific antigen.

Methods. The TULIP procedure was performed in 33 patients with benign prostatic hyperplasia with a mean age of 66 years. Patients were evaluated by pressure–flow studies, prostate volume measurement by transrectal ultrasound, and the American Urological Association (AUA) symptom score.

Results. At 3-month follow-up, laser prostatectomy has resulted in an increased maximum flow rate from 6.6 ± 0.5 to 11.2 ± 0.6 mL/s and in an objectively proven relief of the urodynamic obstruction, as is evident by a decrease of the average value of the urethral resistance parameter URA and the detrusor pressure at maximum flow rate from 38.3 ± 2.7 to 21.3 ± 1.3 cm water and from 62.7 ± 4 to 38.9 ± 2.1 cm water, respectively. Symptomatic improvement is evident from a decrease in the AUA symptom score from 20.4 at baseline to 8.8 at 6-month follow-up. Although the total symptom score did not change significantly between 6 months and 1 year follow-up, the score of the symptom "weak stream" was significantly higher again at 12 months follow-up.

Conclusions. The TULIP procedure is a urodynamically and symptomatically effective treatment. Conclusions about the durability of this treatment modality should be made with reservations.

Transurethral neodymium:yttrium-aluminum-garnet (Nd:YAG) laser treatment is one of the alternatives to transurethral resection of the prostate that is currently being investigated for the treatment of benign prostatic hyperplasia. Several methods of laser energy delivery to prostatic tissue are available.[1] Noncontact side-firing laser fibers operate by the creation of deep coagulation necrosis of the prostatic tissue without direct tissue contact. Contact fibers can vaporize tissue at a sufficiently high power when in direct contact with the tissue. Although most side-firing fibers are operated under direct vision, transurethral ultrasound-guided laser-induced prostatectomy (TULIP) is a technology that utilizes the side-firing principle under ultrasound guidance. Via the transurethral route, the prostate is irradiated in a systematic way by a Nd:YAG laser source.

This study was initiated to determine objectively the effects of this treatment modality on urodynamic (urethral resistance) parameters, symptom score, prostate volume, and serum prostate-specific antigen (PSA).

Data on symptomatic changes and changes in uroflowmetry values have been reported previously

Submitted: April 26, 1994, accepted (with revisions): June 2, 1994

for the TULIP procedure[2] and for visual laser ablation of the prostate (VLAP).[3,4] This study addresses changes in urethral resistance parameters after laser treatment for benign prostatic hyperplasia.

MATERIAL AND METHODS

Procedure

The TULIP system consists of an ultrasound imager and a 20 F transurethral probe that incorporates a side-firing laser window positioned between two halves of a split ultrasound transducer. The TULIP probe is enclosed in a sleeve that incorporates a balloon at its distal end. The balloon, which is filled and pressurized with sterile water, creates a constant standoff from the tissue, stabilizes the system in the prostatic urethra, and decreases blood flow in the tissue. The 2 atmospheres of balloon pressurization are not associated with a dilation effect.[5] The part of the probe that contains the laser window and the ultrasound transducer can be moved in a longitudinal and rotational fashion in the working window, which is created by the pressurized balloon. The TULIP system was coupled to a 60 W Nd:YAG laser set at 40 W. The procedure has been described in detail by McCullough *et al.*[2] In the present series 48 F balloons were used in all but 2 patients. Laser passes were initiated with a 5-second dwelling time at the bladder neck followed by a pull rate of 1 mm/s. Laser passes were terminated when the thickness of the prostatic tissue became 1 cm on the ultrasound imager. An average of 8 to 10 passes in different positions were made per patient. After the procedure, cystoscopy was performed to check for blanching of the prostatic urethra, and a suprapubic catheter was inserted.

Study Parameters

Prostate volume was measured by transrectal ultrasound with a 7 MHz Bruel and Kjaer multiplane sector scanning probe. The planimetric technique of volume measurement was used at baseline and 3 months post-treatment.[6] Serum PSA levels (Hybritech-Tandem) were measured at baseline and 24 and 48 hours, 1 week, and 3 months postoperatively. Prostate biopsies were performed in all men with PSA more than 10 ng/mL and in all men who had hypoechogenic lesions on transrectal ultrasound. No prostate cancers were detected in the men included in this study.

The American Urological Association (AUA) symptom index was determined at baseline and 3, 6, and 12 months post-treatment.[7]

The postvoid residual urine volume (in milliliters) was measured by transabdominal ultrasound using an Aloka machine with a 3.5 MHz handheld probe using the formula: $\pi/6 \times (\text{width}) \times (\text{height}) \times (\text{depth})$.[8] Measurements were done at baseline and 3, 6, and 12 months post-treatment.

Flow rates at 6 and 12 months are not reported because most patients did not produce voided volumes in excess of 100 mL, whereas voided volumes varied widely on different occasions, which would make comparisons not very relevant. Only the flow rates obtained during the controlled situation of the urodynamic tests at baseline and at 3 months follow-up are considered.

At baseline and 3 months post-treatment, urodynamic studies, including pressure–flow studies, were done: the parameters URA (a group-specific urethral resistance factor),[9] $P_{det.Qmax}$, Q_{max}, and W_{max}[10] (a bladder contractility parameter) were determined. The values for $P_{det.Qmax}$ were plotted in the Abrams-Griffiths nomogram.[11]

The protocol allows for repeat urodynamic studies after the 3-month period if during further follow-up the symptom index showed a significant deterioration (increase of 7 or more points, ie, an average increase of at least 1 point per symptom) together with an increase or stabilization of the residual urine volume above 50 mL.

Patients

The 33 patients had an average age of 66 years (range, 50 to 79 years). The average prostate volume was 56 cm^3 (range, 20 to 118 cm^3). The average preoperative symptom score as measured by the AUA-7 index was 21.3 (range, 5 to 35). Two patients were in retention before the treatment. All patients had a 5-day course of prophylactic antibiotics. A minimum follow-up of 3 months is available in all patients. Twenty-six and 17 patients were followed for 6 and 12 months, respectively.

Statistical Analysis

Wilcoxon's matched pairs signed rank test was used to determine the significance of differences between two series of measurements of a particular parameter at two different times. The level of significance was set at $p < 0.05$.

RESULTS

The average amount of energy (± SE) delivered to the prostate was 13,272 ± 936 J.

Patients were discharged after an average of 3.4 days (range, 2 to 10). The first micturition per urethra occurred after an average of 2.7 days (range, 1 to 29). The suprapubic catheter was removed after an average of 19 days (range, 1 to 139) when the residual urine was less than one third of the initial

TABLE I. *Changes in serum prostate-specific antigen values in relation to the transurethral ultrasound-guided laser-induced prostatectomy procedure**

	Prostate-Specific Antigen (ng/mL)	
Preoperative	4.5 ± 0.9	(0.8–27.3)
24 h postoperative	61.9 ± 18.7	(1.6–354)
48 h postoperative	28.9 ± 6.8	(1.4–136)
1 week postoperative	10.2 ± 1.9	(1.0–33.8)
3 months postoperative	2.9 ± 0.5	(0.4–10.3)

*Values are means ± standard error with ranges in parentheses.

bladder volume on at least two consecutive occasions.

PROSTATE-SPECIFIC ANTIGEN

The effect of laser treatment of the prostate on the serum PSA value is shown in Table I. There is on average a 14-fold increase in serum PSA after 24 hours. By the 3-month follow-up, the serum PSA has on average dropped below the baseline value.

PROSTATE VOLUME

The effects of laser treatment on prostate volume are summarized in Table II. The average prostate volume as measured by transrectal ultrasound did not change significantly after the procedure. A clear conical defect in the prostatic urethra was seen in only 8 men after the procedure.

URODYNAMIC DATA

Comparative urodynamic data including pressure–flow studies are available for 30 patients (Table II). For the other 3 patients, baseline and follow-up residual urine volumes are available: both patients who were in retention and the one patient who refused invasive testing at 3 months had an excellent symptomatic result and voided

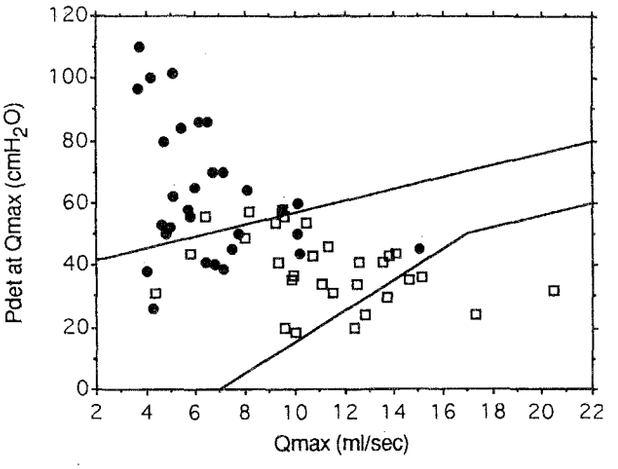

FIGURE 1. *Effect of transurethral ultrasound-guided laser-induced prostatectomy procedure on pressure–flow parameters. Values for detrusor pressure at maximum flow rate are plotted in Abrams-Griffiths nomogram. Closed circles indicate pretreatment measurements and open squares indicate post-treatment measurements.*

well with residual urine volumes of 0, 60, and 74 mL, respectively. The obstruction parameters $P_{det.Qmax}$ and URA decreased significantly. On average the URA value was in the nonobstructed range at the 3-month urodynamic follow-up. The bladder contraction strength parameter W_{max} showed a small but significant decrease. The flow rate increased significantly. However, the residual urine volume did not change significantly. If, however, the residual urine volumes of the 2 patients who were in retention preoperatively and the 1 patient who did not undergo invasive urodynamic testing at 3 months are included, there is a significant ($p = 0.02$) decrease of the average (± SE) residual urine volume from 163 ± 71 to 57 ± 18 mL.

When $P_{det.Qmax}$ is plotted in the Abrams-Griffiths nomogram (Fig. 1), it becomes clear that 12 and 4

TABLE II. *Effects of transurethral ultrasound-guided laser-induced prostatectomy procedure on urodynamic (n = 30), symptomatic (n = 32), and prostate volume parameters (n = 33) at 3 months follow-up**

Parameter	Baseline	3 Month Follow-up	p Value
AUA-7 index	21.3 (5–35)	10.7 (2–23)	0.0001
Prostate volume (cm^3)	56 (20–118)	51 (15–125)	NS
$P_{det.Qmax}$ (cm H_2O)	63 (26–110)	39 (18–58)	0.0001
Maximal flow (mL/s)	6.6 (3.7–15)	11.2 (4.4–20.4)	0.0001
Residual urine (mL)	87 (0–330)	58 (0–400)	NS
URA (cm H_2O)	38 (17–78)	21 (11–35)	0.0001
W_{max} (W/m^2)	9.8 (3.4–16.6)	8.6 (4.3–14.6)	0.04

KEY: NS = not significant.
*Values are means with ranges in parentheses.

TABLE III. *Effects of transurethral ultrasound-guided laser-induced prostatectomy procedure on individual symptoms and total AUA symptom score at 3 and 6 months follow-up**

Symptoms	Baseline	Follow-up	
		3 Months (n = 26)	6 Months (n = 26)
Emptying	3.1 (0–5)	1.4 (0–5)	1.2 (0–5)
Frequency	3.4 (0–5)	2.3 (0–5)	1.7 (0–5)
Intermittency	2.8 (0–5)	0.8 (0–4)	1.0 (0–5)
Urgency	2.6 (0–5)	2.2 (0–5)*	1.5 (0–5)
Weak stream	4.2 (2–5)	1.3 (0–5)	1.3 (0–5)
Hesitancy	1.5 (0–5)	0.3 (0–2)	0.4 (0–4)
Nocturia	2.7 (1–5)	2.0 (0–5)	1.8 (0–4)
AUA-7 index	20.4 (5–35)	10.3 (2–23)	8.8 (1–26)

**Values are means with ranges in parentheses. All changes in scores are statistically significant ($p < 0.05$) when compared with baseline, except that marked with an asterisk.*

patients, respectively, move from the obstructed area to the equivocal area and from the obstructed to the nonobstructive area. Three patients move from the equivocal to the nonobstructed area. Four and 7 patients, respectively, remain in the obstructed and in the equivocal areas. Preoperatively, 20 patients were in the obstructive and 10 in the equivocal range, whereas at the 3-month urodynamic follow-up, 4 men remained in the obstructive area and 19 and 7 were in the equivocal and nonobstructive areas, respectively.

The average (± SE) residual urine volumes at 6 and 12 months were 34 ± 12 and 35 ± 12 mL, respectively; these values were not significantly different from the values at the 3-month follow-up.

Symptoms

Baseline and 3-month symptom score data were available for 32 patients (Table II; 1 patient did not complete a symptom score preoperatively). There was no correlation between the percentage change in urethral resistance (URA) and the percentage change in the total symptom score ($r = 0.13$; $p = 0.537$) at the 3-month follow-up.

The baseline, 3- and 6-month follow-up symptom data of the 26 patients who have completed a minimum follow-up of 6 months are summarized in Table III. Laser treatment of the prostate results in a significant improvement of the individual symptoms and the total score on the AUA-7 index. It takes between 3 and 6 months for the symptom "urgency" to improve significantly. This reflects the severe irritative symptoms that are sometimes encountered in the first weeks after the procedure.

In 17 patients the 12-month follow-up has been reached. The total score and the scores for the individual symptoms were not significantly different from the 6-months data, except for the symptom "weak stream" which showed an increase from 0.9 to 1.6 ($p = 0.03$).

Repeat Urodynamics After 3 Months and Retreatment

At 6 months, the symptom index had increased again significantly in 1 patient, but the residual urine volume in this patient was 0 mL as opposed to 80 mL preoperatively. At 12 months, a repeat urodynamic study was done in 1 patient because of a deteriorating symptom score and an increasing residual urine volume. The urodynamic study showed an increased urethral resistance and a transurethral resection of the prostate (TURP) was subsequently performed in this patient. A TURP was performed in 1 additional patient at the 12-month follow-up. This patient developed macroscopic hematuria due to his benign prostatic hyperplasia and underwent a TURP in spite of the fact that the AUA symptom score remained low.

Complications

Few complications were seen. The procedure had to be abandoned in 1 patient, who is not included in this series, because of a false passage of the TULIP probe. Water intoxication did not occur in any of the patients. No blood transfusions were necessary. In 1 patient a transurethral catheter had to be inserted for bladder irrigation because of bleeding blocking the thin suprapubic catheter. This catheter was removed again 3 hours later. One patient needed intravenous antibiotics because of septicemia. In another patient drug fever developed due to the routinely administered antibiotics. No urethral strictures have been found during follow-up. No patient has complained of incontinence.

COMMENT

There is still a paucity of articles dealing with results of laser treatment of the prostate. Kabalin[1] has compared the results of TURP and VLAP in 12 and 13 patients, respectively, and found comparable improvements in symptom score and maximum flow rate at 3 and 6 months follow-up. A 10-fold increase in serum PSA was noted after laser treatment. In the present series a 14-fold increase was found on average. Norris *et al.*[4] reported an average increase in flow rate from 7.6 to 12 mL/s after visual laser ablation of the prostate. McCullough *et al.*[2] have reported on the results at 6 months follow-up in 63 patients treated with the TULIP procedure. In these men the modified

Boyarsky symptom score[12] decreased from 18.8 ± 5 to 6.1 ± 4.4 and the maximum flow rate increased from 6.7 ± 3.2 to 11.9 ± 4.7 mL/s. These results are comparable to the results of the present series.

No objective data on changes in urethral resistance and pressure–flow parameters in relation to laser prostatectomy are available in the literature. In the present study, the average (± SE) value of the parameter URA showed a decrease from 38.3 ± 2.7 to 21.3 ± 1.3 cm water, which represents an average change from the clearly obstructed range to the unobstructed range. These improvements are also apparent when the preoperative and postoperative values for $P_{det.Qmax}$ are plotted in the Abrams-Griffiths nomogram (Fig. 1). These results indicate that laser treatment of the prostate is clearly effective from a urodynamic point of view. The magnitude of the average change in the value of the urethral resistance parameter is comparable to the improvement seen in a group of 29 TURP patients as reported by Rollema and van Mastrigt,[13] who found an average change from 41 to 16 cm water for the parameter URA.

Symptomatically, there is a clear effect as well. The average (± SE) AUA symptom score had decreased from 21.3 ± 1.4 to 10.7 ± 1.0 at 3 months follow-up. This change is comparable to the change found by Barry *et al.*[7] in a group of 27 TURP patients who showed a decrease from 17.6 to 7.1 at 4 weeks post-TURP. A further decrease to 8.8 at 6 months follow-up, which is found in the present series, is mainly due to an improvement of frequency and urgency, which reflects the late improvement of the sometimes severe irritative symptoms in the early postoperative period. Seventeen patients have been followed for 12 months or longer and the scores for the individual symptoms did not change significantly between 6 and 12 months except for the score of the symptom "weak stream," which increased from 0.9 to 1.6 on average ($p = 0.03$).

The results of this series show that a significant decrease in prostate volume as measured by transrectal ultrasound is not necessary to achieve a clear urodynamic and symptomatic improvement. The minimal changes in prostate volume may not accurately reflect the effect on the prostate because there is a 14-fold increase in serum PSA 24 hours after the treatment, which indicates that considerable tissue damage has taken place. Furthermore, the average serum PSA at the 3-month follow-up has fallen below the baseline value, which may indicate that tissue loss has taken place. The TULIP procedure is an effective treatment for benign prostatic hyperplasia. The long-term results have to be awaited. The fact that the score of at least one symptom, that is, "weak stream" shows deterioration at the 12-month follow-up indicates that further studies of the durability of the effect of laser treatment of the prostate are certainly necessary.

J.L.H. Ruud Bosch, M.D.
Department of Urology
AZR-Dijkzigt, H 1073
Dr. Molewaterplein 40
3015 GD Rotterdam, The Netherlands

REFERENCES

1. Milam DF, and Smith JA Jr: Lasers in urologic surgery—current status (part 2). AUA Update Series 13: 126–131, 1994.

2. McCullough DL, Roth RA, Babayan RK, Gordon JO, Reese JH, Crawford ED, Fuselier HA, Smith JA, Murchison RJ, and Kaye KW: Transurethral ultrasound-guided laser-induced prostatectomy: National Human Cooperative Study results. J Urol 150: 1607–1611, 1993.

3. Kabalin JN: Laser prostatectomy performed with a right angle firing neodymium:YAG laser fiber at 40 watts power setting. J Urol 150: 95–99, 1993.

4. Norris JP, Norris DM, Lee RD, and Rubenstein MA: Visual laser ablation of the prostate: clinical experience in 108 patients. J Urol 150: 1612–1614, 1993.

5. Roth RA, and Aretz HT: Transurethral ultrasound-guided laser-induced prostatectomy (TULIP procedure): a canine prostate feasibility study. J Urol 146: 1128–1135, 1991.

6. Torp-Pedersen S, Juul N, and Jakobsen H: Transrectal prostatic ultrasonography. Equipment, normal findings, benign hyperplasia and cancer. Scand J Urol Nephrol (Suppl) 107: 19–25, 1988.

7. Barry MJ, Fowler FJ Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, and Cockett ATK: The American Urological Association symptom index for benign prostatic hyperplasia. The measurement committee of the American Urological Association. J Urol 148: 1549–1557, 1992.

8. Roehrborn CG, and Peters PC: Can transabdominal ultrasound estimation of postvoiding residual (PVR) replace catheterization? Urology 31: 445–449, 1988.

9. Griffiths D, van Mastrigt R, and Bosch R: Quantification of urethral resistance and bladder function during voiding, with special reference to the effects of prostate size reduction on urethral obstruction due to benign prostatic hyperplasia. Neurourol Urodyn 8: 17–27, 1989.

10. Griffiths DJ, Constantinou CE, and van Mastrigt R: Urinary bladder function and its control in healthy females. Am J Physiol 251: R225–R230, 1986.

11. Abrams PH, and Griffiths DJ: The assessment of prostatic obstruction from urodynamic measurements and from residual urine. Br J Urol 51: 129–134, 1979.

12. Boyarsky S, Jones G, Paulson DF, and Prout GR Jr: A new look at bladder neck obstruction by the Food and Drug Administration regulators: guide lines for the investigation of benign prostatic hypertrophy. Trans Am Assoc Genitourin Surg 68: 29–32, 1976.

13. Rollema HJ, and van Mastrigt R: Improved indication and followup in transurethral resection of the prostate using the computer program CLIM: a prospective study. J Urol 148: 111–116, 1992.