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Original Article

High-energy Transurethral Microwave Thermotherapy in Patients with Benign Prostatic Hyperplasia: Comparative Study between 30-and 60-minute Single Treatments

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We retrospectively evaluated the subjective and objective treatment results of transurethral microwave thermotherapy (TUMT) for benign prostatic hyperplasia (BPH) and explored the difference in effectiveness between 30- and 60-min single treatments. From June 1997 through March 2003, 58 men with BPH underwent TUMT using the Targis device. Twenty-seven and 31 patients each received a single treatment of 60 or 30 min, respectively. Evaluations after treatment included a clinical determination of the International Prostate Symptom Score, urodynamic assessments by peak flow rate, and magnetic resonance imaging (MRI). In the 60-min treatment, the symptom score improved significantly, from 17.9 to 9.5 after 2 months. Similarly, there was a significant improvement in peak flow rate, from 6.7 to 11.2 ml/sec after 2 months. In the 30-min treatment, the symptom score also improved significantly, from 18.4 to 13.4 after 2 weeks. Similarly, there was a significant improvement in the peak flow rate, from 6.4 to 11.7 ml/sec after 1 month. MRI imaging showed necrosis of the prostate gland 2 weeks after either treatment. These results demonstrated that both the 60-min and the 30-min treatments were effective for patients with BPH. Moreover, the 30-min treatment led to quicker improvement than the 60-min treatment. Thus, a 30-min TUMT protocol is considered recommendable for this treatment.

Key words: prostate, benign prostatic hyperplasia, microwave, thermotherapy, MRI

Benign prostatic hyperplasia (BPH) is one of the most common diseases in urology, and the number of patients with BPH is likely to rise as a consequence of the worldwide aging of the population. Transurethral resection of the prostate (TURP) is still considered the standard therapy for BPH and significantly improves subjective and objective urinary symptoms. The procedure is not, however, suitable for all patients because of perioperative and postoperative complications [1].

The development of transurethral microwave thermotherapy (TUMT) has progressed well as a minimally invasive modality for patients with lower urinary tract symptoms (LUTS) due to BPH. The first-generation TUMT device (Prostatron; EDAP Technomed, Inc., Lyon, France), has been used to demonstrate that lower-energy thermotherapy (version 2.0) is a safe treatment, having low morbidity, good tolerability, few adverse effects, and effective short-term outcomes. However, in the long term, at least 40% of patients have received re-treatment [2, 3]. Recently developed high-energy TUMT (Prostatron versions 2.5 and 3.5 or Targis) devices have significantly improved symptoms, peak flow rate (Qmax), and quality of life (QOL) [4]. A long-term efficacy of at least 2 years was also reported [5]. On the

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other hand, these second-generation devices have also been associated with increased morbidity and decreased tolerability [6]. The likelihood of treatment success is related to the administration of an optimal thermal dose and a sufficiently high temperature for a sufficiently long time in order to thermoablate the target tissues [7]. Nonetheless, the optimal thermal dose that should be delivered in thermoablative microwave treatment remains uncertain. A recent modification in the treatment protocols is the reduction of treatment time. A 30-min high-energy protocol (Prostatron version 3.5) was introduced, and the initial results were promising [8].

In this study, we retrospectively explored the differences in subjective and objective treatment results between single 30- and 60-min treatments by high-energy TUMT using the Targis device, without changing the device program.

Materials and Methods

Patients. All patients met the following entry criteria: patients who suffered from aggravated LUTS caused by BPH and whose prostatic urethra length exceeded 30 mm. The severity of BPH was not restricted to a certain level of the International Prostate Symptom Score (IPSS) or uroflowmetry parameters. The exclusion criteria were: presence of vesical stone; urethral stricture; prostate or bladder cancer; active cardiac pacemaker or metal implant in the pelvis; and a prominent median lobe. Before the treatment, TRUS-guided prostate sextant biopsies were taken to confirm BPH in patients who had elevated serum PSA levels.

Between June 1997 and March 2000, 27 men with BPH underwent a 60-min TUMT treatment using the Targis device (Urologix, Inc., Minneapolis, MN, USA). Between May 2000 and March 2003, 31 patients received a 30-min single treatment. Evaluations after treatment included a clinical determination of the IPSS, urodynamic assessments by peak flow rate, and magnetic resonance imaging (MRI). All patients were treated with the Targis device, a portable system equipped with a 21 F silicon catheter containing a 28-mm-long helical dipolar antenna for monitoring the urethral temperature, and a circumferential cooling compartment.

After adequately lubricating the urethra, the treatment catheter was inserted and the balloon was filled with 10 cc water. The catheter was then pulled back into the bladder neck. It was kept in the normal anteroposterior orientation by a special catheter-holding device. A rectal thermal unit, containing 5 thermosensors to monitor the rectal temperature during therapy, was then inserted. Continuous recording of the rectal temperature by a rectal thermal unit prevented rectal overheating through a programmed automatic shutdown at temperatures exceeding 42.5 °C. In our patients, this rectal temperature limit was never achieved.

Microwave power was applied to reach a urethral temperature generally of 39 ± 1 °C. The treatment was continued for 30 or 60 min after the temperature exceeded 37 °C. After the therapy, the urethra was cooled for another 5 min.

A urethral catheter was placed in each patient for 5 days, and the patients were evaluated at 2 weeks and again at 1, 2, 3, 6, and 12 months after TUMT. Clinically, the patients were evaluated using the IPSS questionnaire. Urodynamically, the patients were assessed by free uroflowmetry. Three patients in the 30-min treatment group were not assessed at 12 months. Radiologically, 25 of the 27 patients in the 60-min treatment, as well as 6 of the 31 patients in the 30-min treatment, were assessed by MRI of the prostate 2 to 3 weeks after TUMT. In this study, MRI (Siemens Inc., 1.5 Tesla) was performed with gadolinium enhancement. This fast T1-weighted sequence was obtained roughly every 30 sec and was repeated before and after gadolinium enhancement (0.2 ml/kg; 2 ml/sec) with dynamic series of images at 1, 2, 3, and 4 min.

Statistical Analysis. All results are expressed as mean $\pm$ SD. The Wilcoxon signed rank test was used to evaluate intra-group differences. Differences of $P < 0.05$ were considered statistically significant.

Results

The therapy was well tolerated by all patients, with no complications during TUMT. The patients' baseline data are shown in Table 1.

Sixty-minute treatment protocol. The mean prostate volume was 38.2 (15–71.2) mL, and the mean administered treatment energy was 199.6 (150.9–270.2) KJ. The mean IPSS improved significantly, from 17.9 to 9.5 after 2 months; it stabilized at 10.3 after 12 months (Fig. 1). There was a statistically significant improvement from the baseline to 12 months, and the QOL parameters also improved significantly (Fig. 2).

The mean Qmax at the baseline was 6.7 ml/s, and

Table I The patients' baseline data

	30-min (n = 31)	60-min (n = 27)	Statistical analysis
Age	64 – 86 (69.4 ± 7.6)	58 – 83 (75.3 ± 5.7)	$P = 0.005$
IPSS	6 – 34 (18.4 ± 8.5)	4 – 33 (17.9 ± 8.2)	$P = 0.8619$
QOL index	3 – 6 (4.6 ± 0.9)	2 – 6 (4.7 ± 1.1)	$P = 0.6669$
Qmax (ml/s)	1 – 19.5 (6.5 ± 4.5)	0 – 14.8 (6.7 ± 3.7)	$P = 0.6012$
Post-void residual (ml)	0 –160 (58.8 ± 101.5)	0 –440 (81.7 ± 133.5)	$P = 0.6919$
prostate volume (ml)	19.7–107.0 (39.4 ± 21.3)	15.0– 71.2 (38.2 ± 16.0)	$P = 0.6081$

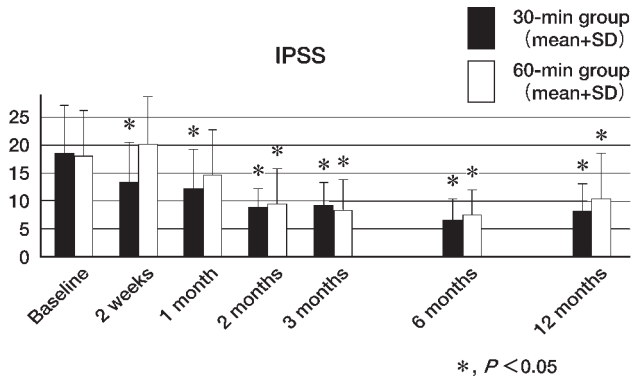

Fig. 1 Pretreatment and post-treatment parameter change in IPSS.

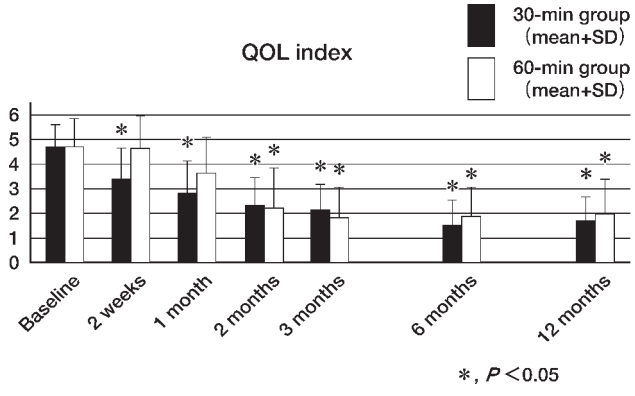

Fig. 2 Pretreatment and post-treatment parameter change in QOL index.

Qmax improved significantly, to 11.2 ml/s after 2 months. The efficacy stabilized at 11.9 ml/s after 12 months (Fig. 3). MRI performed 3 weeks after TUMT showed a necrotic change in the central zone of the prostate on enhanced T1-weighted images (Fig. 4). The mean necrotic volume of the prostatic gland was 9.9 (2.3–29.3) ml. There was no correlation between the necrotic area and total energy.

Prolonged post-treatment catheterization (2 weeks) was needed in 5 patients because of acute urinary retention. Two patients required TURP or retropubic simple prostatectomy because the treatment had not improved their urination. Another 2 patients required internal urethrotomy due to urethral stenosis after treatment. Four patients developed epididymitis, for which they received antibiotic treatment.

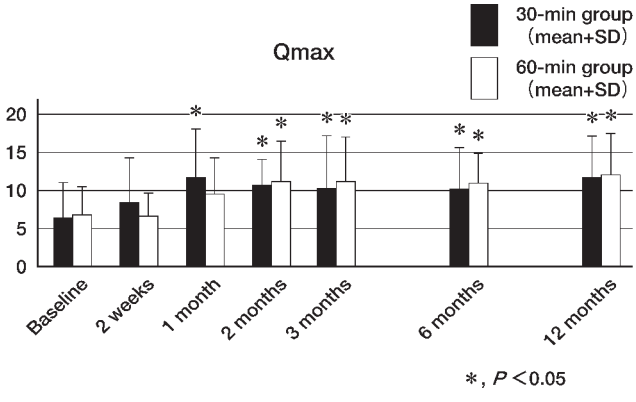

Fig. 3 Pretreatment and post-treatment parameter change in Qmax.

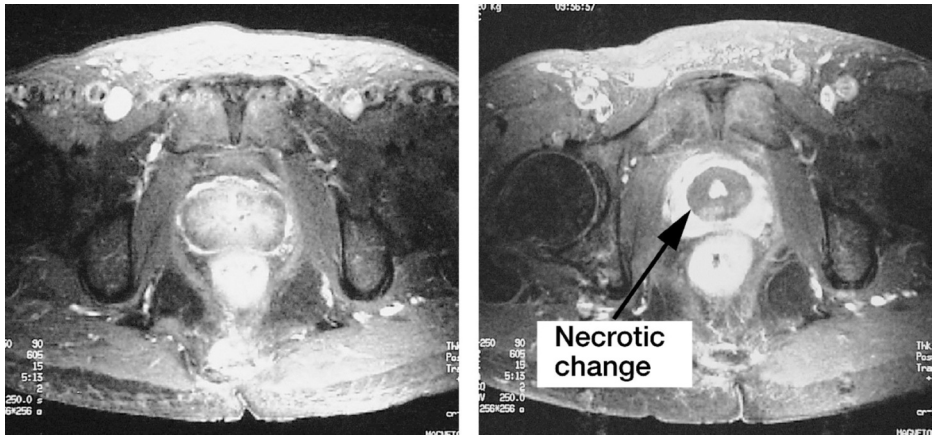

Fig. 4 Enhanced T1-weight MRI in a, pretreatment and b, the central zone perfusion defect 3 weeks after TUMT.

Thirty-minute treatment protocol. The mean prostate volume was 39.4 (19.7–107) mL, and the mean administered treatment energy was 73.6 (49.8–120.9) KJ. The mean IPSS improved significantly, from 18.4 to 13.4 after 2 weeks; it stabilized at 8.0 after 12 months (Fig. 1). There was a statistically significant improvement from the baseline to 12 months, and the QOL parameters also improved significantly (Fig. 2).

The mean Qmax improved significantly, from a baseline of 6.5 ml/s to 11.7 ml/s after 1 month; the efficacy stabilized at 11.6 ml/s after 12 months (Fig. 3). MRI 2–3 weeks after TUMT showed a necrotic change in the central zone of the prostate on enhanced T1-weighted images in all patients who received MRI. The mean necrotic volume of the prostatic gland was 6.0 (0.5–20.3) ml.

Two patients should have received clean intermittent catheterization due to acute urinary retention. However, they no longer needed it within one month after the treatment. Two patients developed epididymitis or prostatitis, for which they received antibiotic treatment. No patient required a second treatment during this follow-up period.

Discussion

Among the alternatives to TURP, TUMT is the only one that can be applied during local anesthesia, a feature that renders this modality very attractive to both the patient and the treating physician. The reduction in therapy time is based on the need of both physicians and patients for a more comfortable treatment that has the same efficacy as TURP. De la Rosette *et al.* reported that high-energy TUMT by the Prostatron device showed significantly less morbidity and maintained its efficacy for at least 1 year [8–10]. Moreover, those authors concluded that a 30-min Prostasoft 3.5 treatment reduced pain and discomfort and did not impair the clinical outcome relative to that by the conventional 60-min Prostasoft 2.5 [11–13]. In this study, we operated a Targis system equipped with a transurethral catheter containing a helical dipolar antenna, at 902–928 MH. The Prostatron device operates at 1296 MHz. De Wild *et al.* reported that radiation at 1296 MHz has special properties that make it superior to other commonly used frequencies [14]. However, Bolmsjö *et al.* reported that the design of the microwave antenna is a very important factor, and that it makes no difference whether a healing device operates at 900 or 1300 MHz [15]. To our knowledge, the present study is the first to examine 30-min TUMT treatment data using the Targis system. Our findings were similar to the results obtained for the Prostatron device. The objective and subjective results showed a significant improvement, and although the follow-up was relatively short, the results were similar to those of the 60-min treatment. Moreover, patients who received the 30-min treatment improved sooner than those who received the 60-min treatment.

D'Ancona *et al.* reported that the total amount of energy is important in treatment outcome [16]. How-

ever, our findings did not show a significant correlation between the total energy and a favorable result. Furthermore, MRI findings showed the same effect on the prostate gland for each therapeutic period. In the Targis device, a continuous high temperature of 45 ℃ or more may be more important than the total therapeutic energy in causing uniform thermoablation of the prostate tissue [17]. Nordenstam *et al.* showed that low-energy TUMT induced an increase in the T2-weighted signal only, with no evidence of necrosis [18]. In this study, MRI of the prostate after TUMT confirmed that high-energy TUMT induced considerable necrosis of the prostate. However, Osman *et al.* reported that a high percentage of patients (77%) with a well-defined cavity at 1 year were not reproducible (17.5%) [19]. Longer follow-up would be necessary to evaluate this therapy.

The re-treatment rate for high-energy TUMT was reported to be only 7.3% [20]. In the present study, 2 patients (7.4%) received re-treatment (TURP or retropubic prostatectomy) in the 60-min group, and none of the patients received re-treatment in the 30-min group during this follow-up period.

To date, the complication rate of the 30-min treatment has been relatively low compared with that of the 60-min treatment. In the 60-min group, 5 patients (18.5%) required an indwelling catheter again, due to urinary retention after the first catheter was removed 5 days after TUMT. On the other hand, only 2 patients (6.4%) suffered from temporary urinary retention after treatment in the 30-min protocol. Considering the high efficacy and low rate of adverse effects, we believe it is fair to recommend this 30-min treatment protocol for all patients treated with the Targis device.

Although the results of TUMT were generally satisfactory for most patients, it is still difficult to predict a specific individual's response to therapy. Djavan *et al.* reported that higher PSA levels were significantly predictive of more favorable outcomes [21]. D'Ancona *et al.* reported that older patients have less favorable outcomes after TUMT as compared to younger patients [22]. In this study, however, we did not demonstrate a correlation between PSA level, patient age, and favorable outcome in either group. To further improve the treatment efficacy, the treatment protocol may have to be adjusted for each patient. A particular energy level applied for a given period may be enough to induce sufficient tissue ablation to reduce obstruction and relieve the symptoms.

In conclusion, high-energy TUMT using the Targis device is a safe and effective treatment for patients with LUTS caused by BPH. The 30-min TUMT does not impair the clinical outcome. The subjective and objective improvements were almost the same, and appeared sooner than they did in the 60-min TUMT. We consider the 30-min TUMT a recommendable therapeutic time in this treatment. A longer follow-up is needed to assess the durability of this new treatment protocol.

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