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Treatment Response with Transurethral Radiofrequency Thermotherapy for Symptomatic Benign Prostatic Hyperplasia

Sung Joon Hong, Hak Ryong Choi, Tack Lee and Yoon Seog Kang

One hundred and two patients with benign prostatic hyperplasia were treated by transurethral radio-frequency thermotherapy (TURT) device (Thermex-II, Direx, Israel) with 47.5℃ in single session for 2 hours and 30 minutes from November 1992 to October 1993. Among them, 83 patients who were followed up for more than 3 months were included in this study. Twenty-seven (32.5%) patients had a history of acute retention. Pretreated values of the mean Madsen-Iversen symptom score, maximum urine flow rate, postvoiding residual urine volume, prostate volume and prostate specific antigen (PSA) were 15.4, 6.5 ml/sec., 61.3ml, 43.2ml and 0.77ng/ml respectively. Madsen-Iversen symptom score, maximum urine flow rate were measured at 2 weeks, 1 , 3 and 6 months after TURT. The residual urine volume, prostate volume and PSA level were measured at 3 and 6 months after TURT. During the follow up, the symptom score started to decrease significantly at 1 month (9.9, $p<0.01$) after TURT, and gradually decreased up to 6.9 at 3 months. The maximum flow rate showed initial significant improvement at 2 weeks (8.1 ml/sec., $p<0.01$), but no significant interval change was observed thereafter. The residual volume decreased significantly at 3 months (41.3ml, $p<0.01$) and no decrement was noted until 6 months. Neither the prostate volume nor PSA value changed significantly at 3 or 6 months after TURT. The improvement, which was defined as a change of 50% or more in at least one of subjective or objective symptoms showed in 63.9% (53/83) at 3 months and 57.1% (32/56) at 6months. Both subjective and objective improvements at 3 and 6 months after treatment showed in 24.1% and 19.6%, respectively. Upon the inquiry about the individual subjective responses in 43 patients who gave answer at 3 months after the treatment, marked improvement was noted in 55.8% and slight improvement in 25.6%. If needed, 53.4% would have a repeated TURT and only one patient would go through an operation. There was no significant differences between responders and non-responders in other clinical parameters, such as presence of median lobe enlargement, prostate volume and PSA except the history of acute retention ($p<0.05$). There was no remarkable complication except one patients with mild incontinence which improved 3 months after the treatment. In conclusion, thermal treatment cannot be seen as a substitution for surgery but as a potential alternative option with minimal complication in selected symptomatic benign prostatic hyperplasia patients who are not clear candidates for surgery or who are high-risk patients.

Key Words : Benign prostatic hyperplasia, transurethral radiofrequency thermotherapy

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Department of Urology, Yonsei University College of Medicine, C.P.O. Box 8044, Seoul, Korea
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Address reprint request to Dr. S.J. Hong, Department of Urology, Yonsei University College of Medicine, C.P.O. Box 8044, Seoul, 120-752 Korea.

Transurethral resection of the prostate (TURP) is the main surgical procedure performed by urologist in the management of most of symptomatic benign prostatic hyperplasia (BPH) and it cannot be denied that TURP is still the treatment modality of choice. The TURP is effective in improving obstructive symptoms in approximately 70 to

85% of the patients. But TURP is now critically reevaluated because of it's morbidity and certain failure rate beyond the expectation (Bruskewitz *et al.* 1986; Mebust *et al.* 1989; Roos *et al.* 1989).

Recently many alternative forms of non-surgical treatment modality were devised for the management of BPH. These alternatives include antiandrogens (Bosch *et al.* 1989), alpha adrenergic blockade (Caine *et al.* 1978; Lepor 1989), balloon dilation (Reddy *et al.* 1988) and thermal treatment (Linder *et al.* 1987). While not a few promising subjective results have been reported with the latest thermotherapy but many aspects of this new technological approach remain controversial (Astrahan *et al.* 1991; Vandenbossche *et al.* 1991; Baert *et al.* 1992; Viguier *et al.* 1993).

In this report, we evaluated the short-term safety and effectiveness in 83 BPH patients who were followed up more than 3 months after TURT, along with the comparison of the clinical parameters between responder and non-responder group to identify the prognostic factors that might predict the treatment response.

MATERIALS AND METHODS

From November 1992 to October 1993, 102 patients suffering from moderate to severe obstructive symptoms due to BPH were treated with transurethral thermotherapy. Among them, the number of patients followed up for more than 3 months and 6 months were 83 and 56, respectively. The Thermex-II (Direx) equipment is a radiofrequency heating system. After intraurethral lidocaine jelly instillation, a 16Fr. thermal electrode catheter was indwelled. The catheter was lightly tractioned and fixed to the inner thigh. Two steering electrodes were attached to the inner thigh or sacral area. The maintenance temperature was 47.5℃ and total duration was 2 hours and 30 minutes. After thermotherapy, a 18Fr. or 20Fr. urethral Foley catheter was indwelled for 3 days in all cases. The inclusion criteria were : symptoms of infravesical obstruction; benign aspect of prostate on evaluation; maximal flow rate lower than 10ml/sec.; no other associated problems that may cause the aggrevation of voiding symptoms. No selection of patients by age or prostatic volume was done in this series. The prostate was evaluated with digital rectal examination, transrectal ultrasonography, and serum level of prostatic specific antigen (PSA) by enzyme immunoassay. Patients with urethral stricture, prostatic abscess, previous prostatic surgery, and evidence of blood coagulation disorders and elevated PSA were excluded. High surgical risk patients were not excluded. If the urine culture was positive, the infection was treated before thermotherapy. The initial subjective symptoms were evaluated according to Madsen-Iversen symptom score (Madsen and Iversen, 1983). The objective findings were assessed with maximum flow rate, residual urine volume and prostate volume. The prostate volume (PV) was calculated by determination of the height (h), width (w) and length (l) by transrectal ultrasound, according to the formula: $PV = h \times w \times l \times 0.523$. Madsen-Iversen symptom score, maximum urine flow rate were measured at 2 weeks, 1, 3 and 6 months after TURT. The residual urine volume, prostate volume and PSA level were measured at 3 and 6 months after TURT. The clinical improvement was estimated both subjectively and objectively. The subjective improvement was defined as more than 50% decrement in Madsen-Iversen symptom score. More than 50 % increment in maximal flow rate and more than 50% decrement in residual volume was defined as objective improvement. Residual urine volume was measured either by insertion of 14 Fr. nelaton catheter or by transabdominal ultrasonography. Clinical parameters (e.g. Madsen-Iversen score, maximum flow rate and residual urine volume) for pretreatment, and 3 months and 6 months after the treatment were compared using the repeated ANOVA. And those for 3 months and 6 months after the treatment were compared with the pretreatment value using the Bonferoni method with the significance level of $\alpha/2$. In this study, we set the significant level (α) at 0.05. Interval changes of symptom score and maximum flow rate after the thermotherapy were compared with paired t test.

Other clinical parameters such as median lobe enlargement and history of acute retention were compared by chi-squared (χ^2) test and prostate volume and PSA level were compared by unpaired t test between responder and non-responder group. We also investigated on 43 patients on the individual subjective responses and the treatment modality they prefer if symptom recurs.

RESULTS

The mean age of the patients was 68.3 years and mean duration of symptoms was 23.4 months. Among the 83 patients, 27 (32.5%) patients had a history of acute urinary retention, 36 (43.4%) patients showed enlarged median lobe on transrectal ultrasonography and 10 (12.0%) patients had urinary tract infection. There were 53 cases of associated medical disease in 39 (47.0%) BPH patients (Table 1). Pretreated values of the mean Madsen-Iversen symptom score, maximum urine flow rate, postvoiding residual urine volume, prostate volume and PSA were 15.4, 6.5ml/sec., 61.3ml, 43.2ml and 0.77ng/ml respectively. Following 3 months after thermotherapy, clinical parameters such as Madsen-Iversen symptom score (6.9), maximum flow rate (8.1ml/sec) and residual urine volume (41.3ml) improved significantly compared with the initial pretreated values (each $p<0.01$). There also were significant differences between pretreated and at 6 months' values. But no significant differences were noted between values at 3 and 6 months. Neither the prostate volume nor PSA value changed significantly at 3 or 6 months follow up periods compared with pretreated values (Table 2). The average symptom score started to decrease significantly from 15.4 to 9.9 at 1

Table 1. characteristics of 83 benign prostatic hyperplasia patients

Demographics of patients		Associated diseases	
Mean Age	68.3±9.7	Cardiovascular disease	21(25.3%)
Symptom duration	23.4±18.4	Pulmonary disease	10(12.0%)
History of acute retention	27(32.5%)	Diabetes mellitus	12(14.5%)
History of urinary infection	10(12.0%)	Malignant tumor	3(3.6%)
Median lobe enlargement	36(43.4%)	gastric ulcer	3(3.6%)
		Others	7(8.4%)
		Total 53 cases in 39 (47.%)patients	

Table 2. Changes of clinical values after thermotherapy

Clinical paramenters	Pretreatment	Posttreatment	
		3month	6month
	N=83	N=83	N=56
Madsen-Iversen score	15.4±3.2	6.9±3.7*	7.1±3.9*
Maximum flow rate(ml/sec.)	6.5±3.1	8.1±3.6*	7.9±3.4*
Residual urine volume(ml)	61.3±34.5	41.3±33.9*	36.0±28.9*
Prostate volume(ml)	43.2±14.8	38.9±15.1	45.6±21.9
PSA**(ng/ml)	0.77±0.32	0.85±0.53	0.76±0.38

*$p<0.05$, compared to pretreatment parameters

** PSA; prostate specific antigen

month after TURT ($p<0.01$), and gradually decreased up to 6.9 at 3 months. The peak flow rate improved from 6.5ml/sec. to 8.1ml/sec. at 2 weeks after TURT ($p<0.01$), but showed no significant interval change thereafter (Fig. 1). The subjective improvement were in 56.6% and 51.7% patients and the objective improvement were in 31.3% and 25.0% patients at 3 and 6 months follow up respectively. Only 24.1% and 19.6% of patients showed more than 50% of both subjective and objective improvement at 3 and 6 months follow up. So the overall improvement rates, defined as a change of 50% or more in at least one of either subjective or objective symptom at 3 and 6 months, were in 63.9% (53/83) and 57.1% (32/56) of the patients respectively. But 36.1% and 42.9% of the patients showed no responses (Table 3). There was no significant differences between reponders and non-responders in the parameters such as prostate volume, PSA, and median lobe enlargement except the history of acute retention ($p<0.05$) (Table 4).

Upon the inquiry about the individual sub-

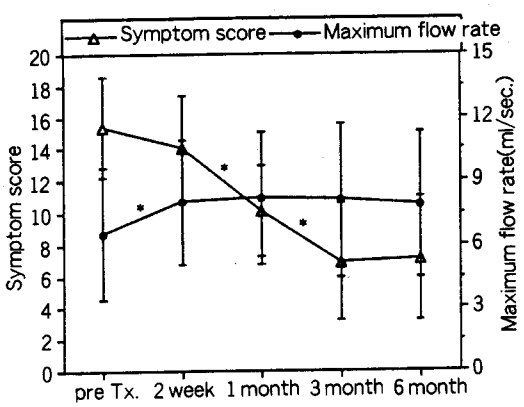

Fig. 1. *Interval changes of symptom score and maximum flow rate after thermotherapy.*
**$p<0.01$, paired test, compared with preceding value*

Table 3. Improvement rates after thermotherapy

Improvement		postreatment period (No. of patients) 3 months(83)	6 months(59)
Yes	Overall*	63.9%(53)	57.1%(32)
	Subjective	56.6%(47)	51.7%(30)
	Objective	31.3%(26)	25.0%(15)
	Both	24.1%(20)	19.6%(12)
No		36.1%(30)	42.9%(27)

* defined as a change of 50% or more in at least one of either subjective or objective symptom

Table 4. Comparison of clinical outcome according to the history of acute retention 3 months after thermotherapy

	History of acute retention	
	positive	negative
Responder	22(81.5%)	31(55.4%)
Non-responder	5(18.5%)	25(44.6%)
total: 83	27	56

*chi-squared(X^2)test, $p<0.05$

Table 5. Outcome of questionaire on the individual subjective responses after thermotherapy

Degree of improvement	No. of patients	If recur, wants		
		Thermotherapy	Operation	No answer
Marked	24(55.8%)	19	0	5
Slight	11(25.6%)	4	0	7
No	7(16.3%)	0	0	7
Worse	1(2.3%)	0	1	0
Total	43	23(53.5%)	1(2.3%)	19(44.2%)

Table 6. Immediate complications within 1 month after themotherapy among 83 patients

Complications	No. patients	%
Urinary retention	8	9.6
Hematuria	4	4.8
Urinary tract infection	3	3.6
Incontinence	1	1.2
Hemospermia	1	1.2
Heat intolerance*	1	1.2

* couldn't sustain the procedure

jective responses at 3 month follow up, 43 patients answered the question. Among them, marked improvement was noted in 55.8% (24/43) and slight improvement in 25.6% (11/43). And 53.5% (23/43) would have a repeated TURT if necessary and only one patient (2.3%) would choose an operation. Others gave no answer (Table 5). There were various treatment-associated complications but most of them were transient. All 11 cases of immediate acute urinary retention resolved spontaneously within 2 weeks with the temporary indwelling of urethral catheter. One patient who showed mild incontinence after the removal of urethral catheter, had the symptom resolved after 3 months without special management. Treatments were well tolerated by all the patients except one (0.98%) whose treatment had to be stopped due to the heating sense and bladder spasm (Table 6).

DISCUSSION

The TURP is the primary mode of treatment for symptomatic BPH patients. Although the mortalities of TURP are low (1-3%), the morbidities such as incontinence, retrograde ejaculation, urethral stricture, impotence and urinary tract infection are relatively high (Bruskewitz *et al.* 1986). Recently Mebust *et al.* (1989) reported a immediate postoperative morbidity rate of 18% among 3,885 cases who underwent TURP. Furthermore, because of aged and many other combined medical disease, it is not always easy to perform a proper anesthesia needed for operation for BPH patients. In our cases, about 47% (39/83) of the patients had preexisting medical diseases and unsuitable for the conventional TURP under anesthesia.

Recently, hyperthermia or thermotherapy has been proposed as an alternative form of treatment for the symptomatic BPH. Intraprostatic temperature in excess of 45℃ can produce coagulation necrosis and fibrosis (Leib *et al.* 1986). Because benign cells are destroyed at 44℃, the treatment using the temperature below 45℃ is defined as hyperthermia and the temperature above 45℃ as thermotherapy (Harzmann and Weckermann, 1991). The main sources of energy are either microwave or radiofrequency type. Thermex-II is a transurethral radiofrequency heating device and temperatures up to 48℃ can be reached in the prostatic urethra without a cooling system (Vandenbossche *et al.* 1993).

Until now whatever device had been used, the overall subjective improvement was in 50~70% and the objective improvement was less prominent (Vandenbossche and Schulman, 1992; Zerbib *et al.* 1992). In this study, the overall improvement rate after 3 months was 63.9%. Most of the improvement occured within the first 3 months. But only 24.1% of patients showed both subjective and objective improvement. We can not exclude the possibility of some placebo effect in the early symptomatic improvement. Zerbib *et al.* (1992) reported the result of a prospective randomized study. They observed a statistically significant subjective improvement in sham group (33%) that was not accompanied by any significant objective improvement. But in the treated group the subjective improvement was significant regarding number of patients (66%) and response rate, and was substantiated by a significant improvement in all symptoms (53% of patients). Lepor *et al.* (1992) also reported a 10~30% of well-known placebo effect in medical treatment. To define the real effect of thermotherapy, longer follow up terms, and a double blind placebo-controlled study will be essential.

However with 55.8% of patients of marked subjective improvement and 53.4% of patients who would have another session if necessary,

shows that TURT is an acceptable treatment option in more than half of symptomatic BPH patients.

There was no significant difference in clinical parameters between responder and non-responder except the history of acute retention. We can not explain exactly why the patients with history of acute retention showed better reponse. However increment of sympathetic activity is considered to be one of the major causes in acute urinary retention (Caine 1983), we assumed that the thermotherapy at this temperature is more effective on dynamic factors than static factors as proposed before by Corica *et al.* (1993). No changes in prostate size after thermotherapy in our study could support this hypothesis, but the real mechanism of thermotherapy remains to be defined.

There were few complications, and most of them were transient. Only one patient could not sustained the heat. So there is no absolute contraindications for thermotherapy except the urethral problem such as stricture and so on. In one case, mild incontinence ceased spontaneously 3 months after the thermotherapy, which was attributed to improper position of thermal electrode catheter which probably slipped by blowing up of the balloon.

Thermotherapy in BPH has it's value in safety and no operative risks but the effect is not high enough to replace the conventional transurethral resection especially in the relief of obstructive symptoms. However we think that the thermotherapy could play a role in the management of selected symptomatic BPH patients with the technical development in the near future. In addition, combination of other non-surgical modalities can provide much more chances to increase the success rate and avoid the burden of operative risks.

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