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Prognostic Factors for the Success of Transurethral Microwave Thermotherapy of the Prostate

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Abstract

Background: Transurethral microwave thermotherapy (TUMT) of the prostate is a minimally invasive treatment. Nevertheless, it is necessary to identify adequate candidates for a good treatment response. *Aim:* To determine and analyze prognostic factors for the success of TUMT. *Material and Methods:* A prospective study of 398 patients with benign prostatic hyperplasia (BPH) has been conducted. Initial patient related parameters were recorded before TUMT and 12 months after treatment. Statistical analysis of these parameters has been performed in order to identify prognostic factors for the success of TUMT. Prediction models of post-treatment parameters have been computed using multivariate analysis. *Results:* Based on clinical data, patients fell into three groups: 249 patients with good treatment response (62.56%), 104 patients with average response (26.13%) and 45 patients with no response or minor response (11.3%). The absence of a median prostatic lobe, a small or medium sized prostate, a moderate initial obstruction, minimal or moderate post-void residual volume and moderate initial symptoms, were significantly associated ($p<0.001$) with good treatment responses after TUMT. Positive predictive values for good or average TUMT response were high (90-98%) for the following predictors: absence of a median prostatic lobe, small or medium prostate size (<60g), light or moderate symptoms (IPSS<20), moderate obstruction (Q_{max}>5 ml), minimal or moderate PVR (<100 ml). *Conclusion:* Patients under 67 years, without median prostatic lobe, with medium-low outlet obstruction (Q_{max} above 7.8 ml), medium-low symptom scores (IPSS<21), post voiding residue under 91 ml, can be considered good candidates for TUMT.

Keywords: Prognostic factors; Transurethral microwave thermotherapy; Benign prostatic hyperplasia.

Introduction

Revolutionary changes are fast taking place in urological practice through a combination of innovative ideas and technological advances. In the treatment of benign prostatic hyperplasia (BPH), the gold standard treatment for the last decades has been by transurethral resection of the prostate (TURP). Nowadays new treatment modalities, like TransUrethral Microwave

Thermotherapy (TUMT), were introduced to serve as alternative treatment for BPH. These alternatives result from the search for cheaper, safer and less invasive treatment modalities [1, 2].

TUMT involves the insertion of a specially designed Foley-type catheter into the bladder, allowing a microwave antenna to be properly positioned within the prostatic fossa. Tissue penetration leads to electromagnetic oscillations of free charges and the polarization of small molecules, such as water, resulting in the release of kinetic energy, which increases the temperature of the tissue. Prostatic tissue undergoes coagulation necrosis, vascular injury, and apoptosis and subsequent shrinkage, when exposed to temperatures greater than 45 degrees C for 30 minutes or more [3]. An effect on adrenergic nerve endings around the bladder neck and prostatic urethral region is also postulated [4]. TUMT is a relatively simple and safe procedure that may be performed in outpatient settings, without general anesthesia [5].

The aim of this study was to determine and analyze prognostic factors for the success of TUMT, in order to optimize clinical results after thermotherapy.

Material and Methods

We conducted a prospective study on a series of 398 patients with BPH treated by TUMT using the Thermaspec machine for 60 minutes, between October 2006 and October 2009 at the Clinical Institute of Urology and Renal Transplantation and Lukmed Minimal Invasive Urologic Private Clinic.

Patient age ranged from 48 to 87 years, with a mean age of 65 years.

All patients had significant symptoms of bladder outlet obstruction.

Patients with bladder pathology (i.e. stones, bladder cancer, neurogenic bladder) and other prostate pathology (prostate cancer, prostatitis) were excluded. The general exclusion criteria are listed in Table 1.

Table 1. General exclusion criteria

Mental incapacity or inability to cooperate
Neurogenic bladder
Uncontrolled cardiac arrhythmias or pacemaker
Previous pelvic or prostate surgery
Metallic pelvic implants

Using the international prostate symptom score (IPSS), patient symptoms have been stratified in severe (IPSS > 20), moderate (IPSS 8-19) and mild (<7).

Other evaluations included uroflowmetry, residual urinary volume, and prostatic volume estimated on transabdominal or transrectal ultrasound (TRUS) [6]. In all cases, the peak urinary flow rate was under 14 ml./sec., with a mean of 8.21 ml/sec. Residual urinary volume was < 200 ml and prostate volume between 35 and 89 ml in all cases.

We used a quality of life (QoL) score regarding urological symptoms.

In the pre-treatment assessment, urine culture was performed in all cases to exclude a urinary tract infection (UTI). Creatinine/Urea and abdominal ultrasound were also performed to rule out obstructive uropathy. The Prostatic Specific Antigen (PSA) level has been investigated before digital rectal examination (DRE) for all cases and, in case of a positive result; biopsy has been performed in order to detect prostate cancer. A cystoscopy was done routinely to measure the length of the prostate urethra, to visualize the presence of a median lobe and to exclude any bladder pathology. TUMT treatment was done on an ambulatory basis in a single 60 minutes session. All patients were given prophylactic antibiotics and mild sedation. The prostate was then heated to between 45 degrees Celsius and 65 degrees Celsius for 60 minutes. Following the TUMT session, a catheter was reinserted for 5 to 7 days. Patients were evaluated at 2 weeks, 3 months, 6 months and 12 months after TUMT.

Good treatment responders satisfied clinical response criteria presented in Table 2.

Minor responders (or failures) were defined as patients who required another definitive treatment (i.e. a TURP or a repeated TUMT), due to a poor response, as defined in Table 2.

Average responders (or partial responders) were defined as patients whose response did not satisfy neither good nor minor responders criteria.

Table 2. Clinical response criteria

Good responders
Peak flow rate post-treatment >15 ml/sec and increase >+50%
IPSS score < 7 and decrease > -50%
Post-void residual volume < 100 ml and decrease > - 50%
Minor responders
Peak flow rate post-treatment < 10 ml/sec and increase < +20%
IPSS post-treatment >20 and decrease < - 50%
Post-void residual volume > 200 ml. and decrease < - 50%

Statistical Methods

Descriptive statistics and statistical analyses were performed using SPSS version 13.

Mean values and their 95% CI, standard deviations, standard errors and extreme values have been computed for quantitative variables before TUMT (age, prostate size, IPSS, Q max, PVR).

Mean values have then been compared between the 3 investigated groups (good, average and minor TUMT responders), using analysis of variance (ANOVA) and appropriate post-hoc tests (Bonferroni – for variables exhibiting variance homogeneity; Tamhane – for variables not exhibiting variance homogeneity).

Categorical predictor variables have been derived from the above mentioned quantitative predictors based on internationally recognized boundary levels (Table 3).

Table 3. Categorical predictor variables derived from quantitative predictors

Initial prostate size: **large**: >60 g; **medium**: 45-60 g; **small**: <45 g
Initial symptoms (IPSS): **severe**: >20; **moderate**: 7-20; **light**: <7
Initial obstruction (Q_{max}): **severe**: <5 ml; **moderate**: 5-15 ml
Post-void residual volume (PVR): **severe**: >100 ml; **moderate**: 50-100 ml; **minimal**: <50 ml

Further comparison regarding frequencies of these categorical predictor variables has been performed between the 3 investigated groups (good, average and minor TUMT responders) using Pearson Chi-square tests in cases when no expected count was less than 5 and Fisher's exact tests in cases where at least one expected count was less than 5.

Positive and negative predictive values of certain pre-TUMT parameters have been computed.

Multivariate analyses of covariance (MANCOVA) have been performed in order to predict three post-treatment parameters ($IPSS_{postTUMT}$, $Qmax_{postTUMT}$ and $PVR_{postTUMT}$), based on measurable pre-treatment parameters (prostate size, $IPSS_{preTUMT}$, $Qmax_{preTUMT}$ and $PVR_{preTUMT}$).

Results

General treatment results were assessed in terms of improvement in mean IPSS score, mean Qmax, mean PVR and mean QoL as shown in Tables 4 to 7.

Table 4. Mean improvement of international prostate symptom score (IPSS)

Mean IPSS	Mean	Range	% change
Preoperative	18.21	3-34	- 25.86%
Postoperative	11.73	0-35	

Table 5. Mean improvement of peak urinary flow rate (Q_{max})

Mean Q_{max}	Mean	Range	% change
Preoperative	9.94	3-14	+26.37%
Postoperative	13.5	3-21	

Table 6. Mean improvement of post void residual (PVR)

Mean PVR	Mean	Range	% change
Preoperative	73.95	15-200	- 27.89%
Postoperative	53.32	0-200	

Table 7. Mean improvement of quality of life (QoL)

Mean QoL	Mean	Range	% change
Preoperative	3.16	0-6	- 49.05%
Postoperative	1.61	0-6	

All parameters showed improvements at all stages of follow-up except for TRUS prostatic volume at one-month which, at 56.65 ml, represented an increase of 1.2% over the pre-treatment volume. However there was a 10% observer variation in measuring prostate volume and changes less than 10 % were not considered significant.

45 patients (11.3%) were considered failures after TUMT, having minor treatment response.

The observed morbidity rate was low. Temporary retention requiring prolonged catheterization was the most common complication following TUMT, occurring in 42 patients (10.55%). Gross haematuria was observed in 7.03% of patients and 35 patients (8.79%) developed urinary tract infections. There was no mortality directly related to TUMT.

Descriptive statistics for age, prostate size, IPSS, Qmax, and PVR before TUMT are presented in Table 8, for good, average and minor TUMT response groups.

Table 8. Descriptive statistics for age, prostate size, IPSS, Q_{max}, and PVR in good, average and minor TUMT response groups

Variable (before TUMT)	TUMT response	Mean	Std. Dev.	Std. Error	95% CI for Mean		Minimum	Maximum
					Lower bound	Upper bound		
Age (years)	minor	70.33	9.06	1.35	67.61	73.05	50	85
	average	65.18	10.29	1.01	63.18	67.18	48	87
	good	63.89	9.75	.62	62.68	65.11	48	84
Prostate size (g)	minor	69.82	10.06	1.5	66.80	72.84	43	89
	average	61.38	14.20	1.39	58.62	64.15	35	89
	good	51.23	11.11	.70	49.84	52.62	35	89
IPSS	minor	28.44	6.16	.92	26.59	30.30	5	34
	average	19.30	8.41	.83	17.66	20.93	3	34
	good	15.91	6.08	.39	15.15	16.67	3	33
Q_{max} (ml)	minor	4.69	1.33	.20	4.29	5.09	3	8
	average	8.29	2.49	.24	7.80	8.77	3	14
	good	11.59	1.99	.13	11.34	11.84	5	14
PVR (ml)	minor	148.11	43.62	6.50	135.01	161.22	20	200
	average	83.89	37.82	3.71	76.54	91.25	15	175
	good	56.41	25.72	1.63	53.20	59.62	15	120

Highly significant mean differences (p<0.001) have been found by analysis of variance (ANOVA) and corresponding post hoc tests between age, prostate size, IPSS, Qmax and PVR for most compared patient groups (exhibiting good, average respectively minor treatment responses).

The main analysis results, including the 95% CI for the observed mean differences between compared groups are presented in Table 9.

Table 9. Mean differences in age, prostate size, IPSS, Qmax, and PVR between good, average and minor TUMT response groups. Results of post hoc tests after analysis of variance (ANOVA)

Post hoc test	Compared variable (before TUMT)	Compared groups (TUMT response)		Mean Difference	Std. error	p-value	95% CI for Mean Difference	
							Lower bound	Upper bound
Bonferroni	Age (years)	good	minor	-6.44	1.59	<0.001	-10.27	-2.62
			average	-1.29	1.15	0.782	-4.05	1.46
		average	minor	-5.15	1.76	<0.001	-9.36	-.94
Tamhane	Prostate size (g)	good	minor	-18.59	1.66	<0.001	-22.65	-14.53
			average	-10.16	1.56	<0.001	-13.92	-6.39
		average	minor	-8.44	2.05	<0.001	-13.40	-3.48
	IPSS	good	minor	-12.54	0.99	<0.001	-14.98	-10.09
			average	-3.39	0.91	0.001	-5.59	-1.19
		average	minor	-9.15	1.23	<0.001	-12.14	-6.15
	Qmax (ml)	good	minor	6.90	0.24	<0.001	6.33	7.47
			average	3.30	0.28	<0.001	2.64	3.96
		average	minor	3.60	0.31	<0.001	2.84	4.36
	PVR (ml)	good	minor	-91.71	6.70	<0.001	-108.27	-75.14
			average	-27.49	4.05	<0.001	-37.27	-17.70
		average	minor	-64.22	7.49	<0.001	-82.50	-45.93

The absence of a median prostatic lobe was significantly associated with an increase in life quality after TUMT (p<0.001, $\chi 2=90.59$, Chi square test with 1 degree of freedom), as illustrated in Figure 1.

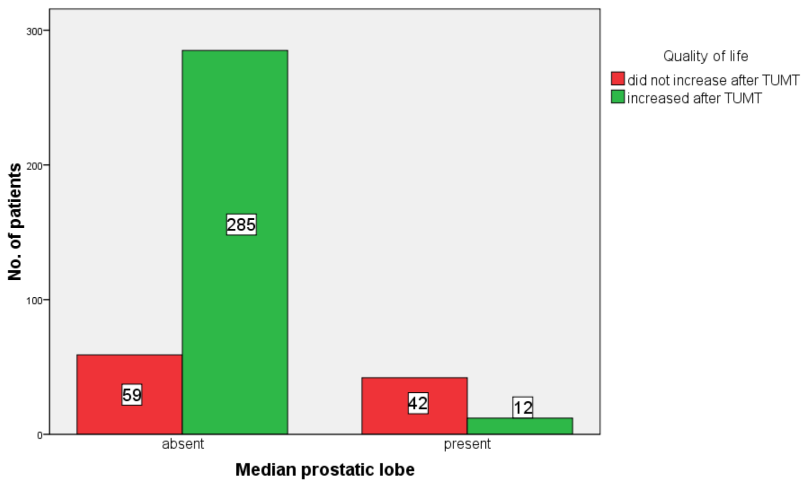

Figure 1. Influence of the median prostatic lobe on life quality increase after TUMT

The absence of a median prostatic lobe was significantly associated with good treatment responses, while the presence of a median prostatic lobe was significantly associated with minor treatment responses after TUMT ($p<0.001$, $\chi^2 = 183.3$, Chi square test with 2 degrees of freedom), as illustrated in Figure 2.

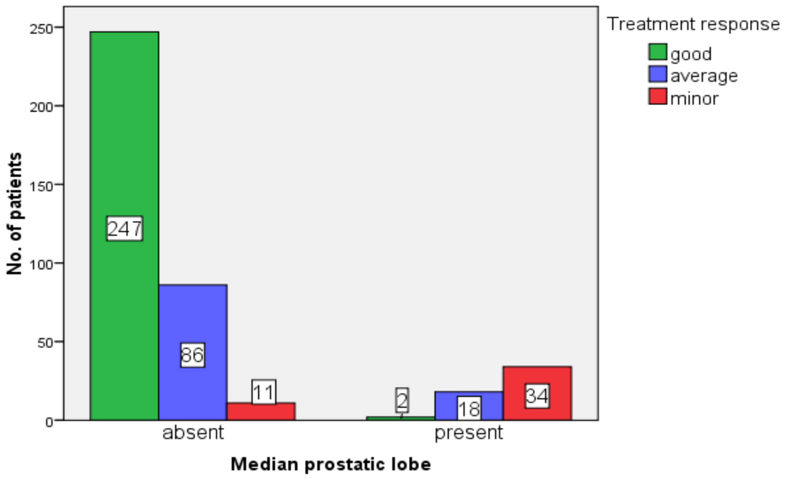

Figure 2. Influence of the median prostatic lobe on TUMT response

A small or medium sized prostate was significantly associated with good treatment responses after TUMT, as opposed to a large sized prostate, which was significantly associated with average or minor treatment responses after TUMT ($p<0.001$, $\chi^2 = 136.4$, Chi square test with 4 degrees of freedom), as illustrated in Figure 3.

Moderate initial symptoms (IPSS between 7 and 20) were significantly associated with good treatment responses after TUMT ($p<0.001$, test statistic=88.68, Fisher's exact test with 4 degrees of freedom), as illustrated in Figure 4.

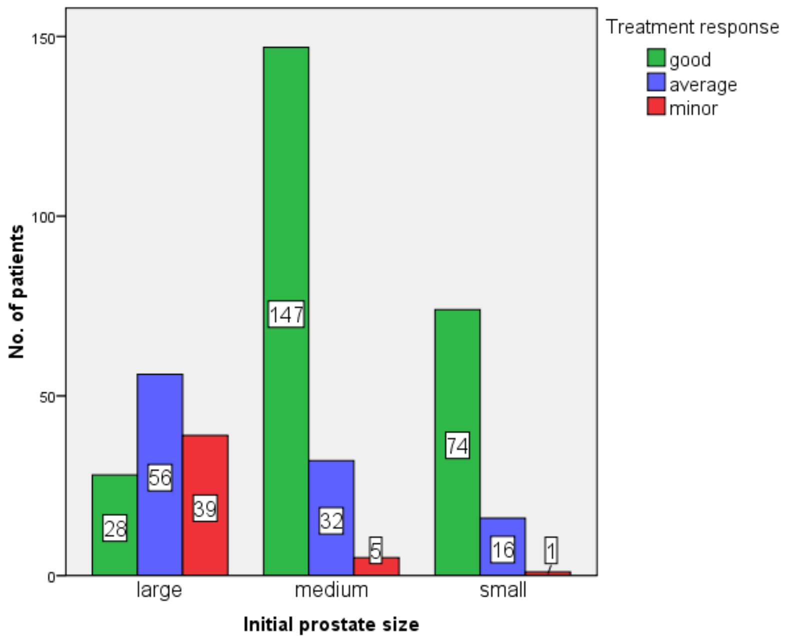

Figure 3. Influence of initial prostate size on TUMT response (large: >60g; medium: 45-60g; small: <45g)

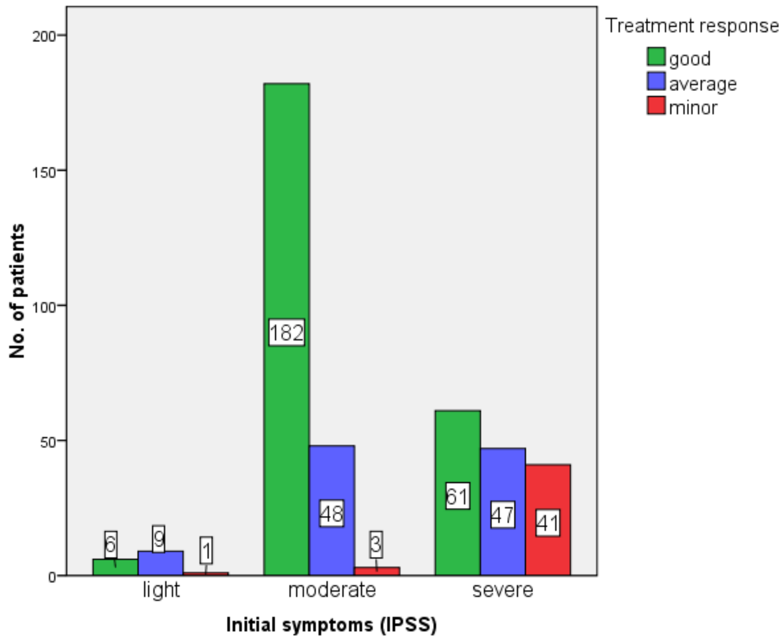

Figure 4. Influence of initial symptoms (IPSS) on TUMT response (severe: >20; moderate: 7-20; light: <7)

A moderate initial obstruction (Q_{max} between 5 and 15 ml) was significantly associated with a good treatment response, while patients exhibiting severe initial obstruction (Q_{max} < 5 ml) were more likely to have only a minor treatment response after TUMT ($p<0.001$, test statistic=77.51, Fisher's exact test with 2 degrees of freedom), as illustrated in Figure 5.

Figure 5. Influence of initial obstruction (Qmax) on TUMT response (severe: <5 ml; moderate: 5-15 ml)

A minimal or moderate post-mictional residue (PVR) was significantly associated with a good treatment response, while patients with severe post-mictional residue were significantly associated with a minor treatment response after TUMT ($p<0.001$, $\chi^2 = 195$, Chi square test with 4 degrees of freedom), as illustrated in Figure 6.

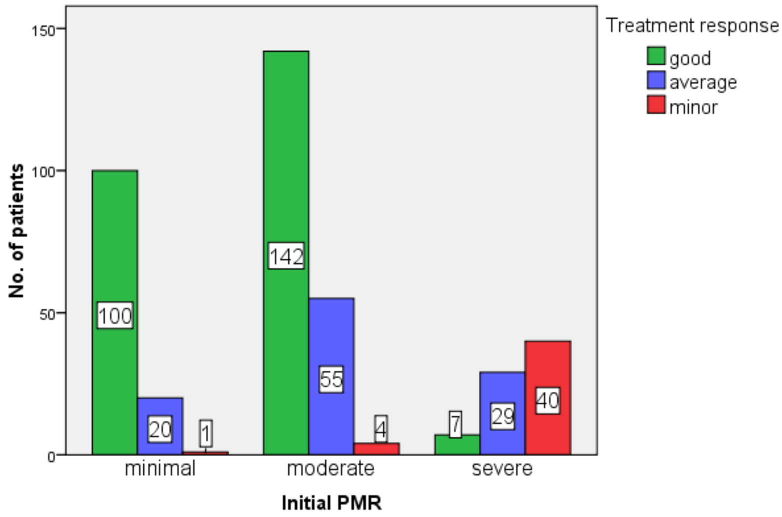

Figure 6. Influence of post-mictional residue (PMR) on TUMT response (severe: >100 ml; moderate: 50-100 ml; minimal: <50 ml)

Positive and negative predictive values for pre-treatment prognostic parameters of a good or average treatment response have been computed and are presented in Table 10.

Table 10. Positive and negative predictive values (PPV and NPV) for pre-treatment prognostic factors of a good or average TUMT response

Prognostic factor	PPV (%)	NPV (%)
absence of median prostatic lobe	96.80	62.96
small or medium prostate size (<60 g)	97.82	31.71
light or moderate symptoms (IPSS <20)	98.39	27.52
moderate obstruction (Q_{max}>5 ml)	92.95	65.52
minimal or moderate PMR (<100 ml)	98.45	52.63

Multivariate analysis of covariance (MANCOVA) for pre-treatment parameters rendered the following highly significant ($p<0.001$) prediction models of post-treatment IPSS, Q_{max} and PVR (statistical power for all modeled parameter estimates equaled or closely approached 1):

$$\mathbf{IPSS_{postTUMT} = 0.099P_{size} - 0.277Qmax_{preTUMT} + 0.029PMR_{preTUMT} + 0.889IPSS_{preTUMT} - 9.374}$$

$$\mathbf{Qmax_{postTUMT} = -0.024P_{size} + 1.116Qmax_{preTUMT} - 0.017PMR_{preTUMT} + 5.307}$$

$$\mathbf{PVR_{postTUMT} = 0.392P_{size} - 1.981Qmax_{preTUMT} + 0.88PMR_{preTUMT} + 0.317IPSS_{preTUMT} - 19.761}$$

Discussion

Morbidity and mortality related to TURP, especially in patients with poor medical status, limit general use of this treatment [7]. Alternatives to TURP include TUMT. Being an ambulatory procedure; patients need no hospitalization for TUMT, thus resulting in minimal disruption to work and lifestyle [8]. In the long run, this translates into health costs savings [1].

We assessed clinical results after TUMT treatment in 398 BPH patients and found good subjective and objective responses to TUMT. Nevertheless, it became highly useful to determine the profile of the "ideal patient" for TUMT, in order to optimize treatment outcome.

Positive predictive values for a good or average TUMT response were excellent (ranging between 90 -98%) for the following predictors: absence of median prostatic lobe, small or medium prostate size (<60 g), light or moderate symptoms (IPSS<20), moderate obstruction (Qmax >5 ml), minimal or moderate PVR (<100 ml).

The absence of a median prostatic lobe a small or medium sized prostate, a moderate initial obstruction, minimal or moderate post-mictional residue and moderate initial symptoms, were significantly associated ($p<0.001$) with good treatment responses after TUMT.

Based on these highly significant differences found between compared groups and on their corresponding descriptive parameters and their 95% CI highlighted in Table 8, we inferred that patients aged under 67 years, with a prostate size < 64 g, without a median prostatic lobe, with medium-low outlet obstruction (Q_{max}>7.8 ml), medium-low symptom scores (IPSS <21), and moderate or low post-void residual volume (PVR < 91 ml), can be considered "ideal candidates" for TUMT, resulting in a good or at least average TUMT response.

These findings were close to those found by other authors [9- 12].

Thus, careful selection of patients undergoing TUMT is absolutely necessary to acquire the maximum expected treatment effect. However, for patients exhibiting severe obstruction or a median prostatic lobe resulting in high PVR and back pressure changes, TURP remains the gold standard in the surgical management of BPH [12- 14].

In order to assist with this patient selection, highly significant ($p<0.001$) prediction models have been computed and may be used in order to predict post-TUMT parameters based on pre-treatment measurements of prostate size, Q_{max}, PVR and IPSS. The large sample size from which these models have been inferred also ensured excellent statistical power for all parameter estimates included in these models.

Conclusion

In conclusion, we found TUMT to be a viable alternative to TURP as a treatment for BPH in certain patients.

Patients aged under 67 years, with a prostate size < 64 g, without a median prostatic lobe, with medium-low outlet obstruction (Q_{max}>7.8 ml), medium-low symptom scores (IPSS<21), and moderate or low post void residual volume (PVR<91 ml), can be considered "ideal candidates" for TUMT.

Conflict of Interest

The authors declare that they have no conflict of interest.

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