Thulium laser enucleation of the prostate (TmLEP) *vs.* transurethral resection of the prostate (TURP): evaluation of early results

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KEY WORDS

BPH ◗ thulium laser ◗ Revolix™ ◗ TmLEP ◗ TURP ◗ enucleation ◗ morcellation

ABSTRACT

Introduction. The first decade of XXI century it is a time of the thulium laser implementation to a benign prostatic hyperplasia treatment.
Objective. The objective of this paper is a comparative assessment of early results thulium laser enucleation of the prostate (TmLEP) versus transurethral resection of the prostate (TURP) in 3-months observation.
Materials and methods. Patients were randomized to BPH surgical treatment: research group (TmLEP – 54 men) or control group (TURP – 52 men). Between 02.2007-09.2009 non-consecutive patients were examined before, one month, and 3-months after surgery. Perioperative data (age, PV, time of surgery, use of laser, morcellation, catheterization, hospitalization, used energy, Hgb loss and removed tissue weight) were assessed. Before and after surgery IPSS, QoL, Qmax and PVR were controlled.
Results. Hemoglobin loss was twice lower during TmLEP than TURP [0.95 ±0.77 (0-3.2) *vs.* 1.81 ±0.97 (0.1-4.7) g/dl, p <0.0001]. Surgery time TmLEP was longer than TURP [102.2 ±38.7 (25-210) *vs.* 74.5 ±22.8 (25-140) min. p <0.0001]. Without morcellation time [28.1 ±17.9 (5-80) min.], surgery time of both procedures was comparable. Weight of resected tissue was lower in TmLEP than TURP [24.8 ±14.8 (2-65) *vs.* 34.8 ±14.1 (12-68)g]. without consideration of vaporized tissue. In both groups we noticed a distinct improvement in all parameters: IPSS, QoL, Qmax and PVR, but without any statistically significant differences between them. Complications after surgery were similar in TmLEP and TURP group.
Conclusions. The thulium laser enucleation of the prostate is safe and efficient BPH treatment method, comparable to the transurethral electroresection in 3-months observation. Lack of long-term research does not allow to form wider conclusions.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a disease that affects almost half of men over 60 years of age. A significant correlation with age causes an increased risk of morbidity in aging societies. An increasing importance of the quality of life as well as patients' self-awareness result in higher expectations concerning healthcare and a visit to a urologist in the early stage of the disease. Some of the patients decline long-term pharmacological treatment and opt for surgery with immediate effects and complete relief of lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia. One of the recent methods of BPH treatment is the removal of the prostate tissue with the use of a thulium laser through enucleation, vapoenucleation, vaporesection and others, often based on holmium laser techniques. Research on the efficiency and safety of the thulium laser has brought promising results, expanding the knowledge about the new method, competitive to the TURP "gold standard".

The objective of this article is a comparative assessment of the early results of thulium laser enucleation of the prostate (TmLEP) and transurethral resection of the prostate (TURP) during a three-month long observation period.

MATERIAL AND METHODS

In a prospective, non-consecutive randomized controlled trial, 54 patients underwent TmLEP and 52 patients were subject to TURP in a single clinical center between February 2007 and September 2009. "Non-consecutive" means that not every patient admitted to the hospital with BPH symptoms and operated on endoscopically (TmLEP or TURP) was included in the study; the reason for this is the non-consecutive work pattern of the main researcher. Randomization consisted in preparing a computer-generated list of patients that was well-balanced.

A statistical analysis was conducted with computer software, STATISTICA 8.0 of StatSoft®. The analysis of the normality of distribution revealed that only age, % of resected tissue, retrieval rate, and Hgb before and after surgery have a distribution similar to normal. Accordingly, to assess differences between groups for these variables the *t-Student test* was used for independent samples. For other parameters the U Mann-Whitney (dependent variables) and Friedmann tests (dependent variables) were used. A statistical significance of $p<0.05$ was approved and marked in red. A variability of analyzed parameters were presented as a arithmetic mean (M) and standard deviation (SD) when their distributions were similar to normal and by median (Me) and quartiles (Q_1, Q_3) for the rest of variables.

Before surgery, all required examinations, anamnesis, and physical, laboratory, and graphic studies were conducted. All patients underwent a urological examination with digital rectal examination and prostate volume evaluation by transrectal ultrasound, upper and lower urinary tract ultrasound, and prostate specific antigen (PSA) blood level. Only uroflowmetry of urodynamic pressure-flow studies was performed. Additionally IPSS, QoL, Qmax, and PVR were determined, which was also checked during the clinical control one and three months after the surgery. The inclusion criteria were: IPPS >7, Qmax <5 ml/s, and the clinically confirmed BPH. The exclusion

criteria were: previous surgical treatment for BPH, prostate cancer, and LUTS resulting from conditions other than BPH. Patients with indwelling catheter were not excluded from research.

TmLEP enucleation procedures were performed using the "mushroom" technique with the thulium laser Tm:YAG RevoLix® of LisaLaser at 70 W maximum power and continuous wave of 2.013 µm. The laser fiber was a multiple use optical fiber RigiFib® of LisaLaser. Each time the fiber was used, the tip used previously was cut off until the unchanged spot and the fiber sheath that was removed was ~1-2 mm length from the tip. Morcellation was performed with a Wolf morcellator in the oscillating mode cutting knife rotation of 750/min. All TmLEP procedures were performed with a 26F resectoscope using continuous flow of irrigation fluid (normal saline solution). Monopolar TURP was performed in a classical way with the use of a Wolf 26F resectoscope and Gyrus diathermia. TmLEP and TURP procedures were performed by three experienced surgeons (1 – TURP, 1 – TmLEP, 1 – TURP and TmLEP). After the surgery, indwelling catheterization with the 22F catheter was applied, which was sustained until hematuria receded and clear urine appeared. Irrigation was not a standard procedure after the surgery except in the case of intensive postoperative bleeding in which permanent irrigation was applied and, in addition, a transfusion of two blood units. All peri- and postoperative complications were recorded.

RESULTS

Perioperative data

One hundred and six patients were included in the research: 54 underwent TmLEP (based group) and 52 underwent TURP (control group). Indwelling catheter was present in: 17 – TmLEP and 19 – TURP. All perioperative data are presented in Table 1.

During the control check-up before the surgery and one and three months after the surgery the following parameters were examined: IPSS, QoL, Qmax, and PVR. Results of these characteristics are shown in Table 2. Statistically significant correlations between groups of IPPS and Quality of Life are presented on Fig. 1.

During the research all complications were recorded in both groups. Perioperative complications were noticed during hospitalization; postoperative complications were noticed during the control check-up one and three months after the surgery (Table 3).

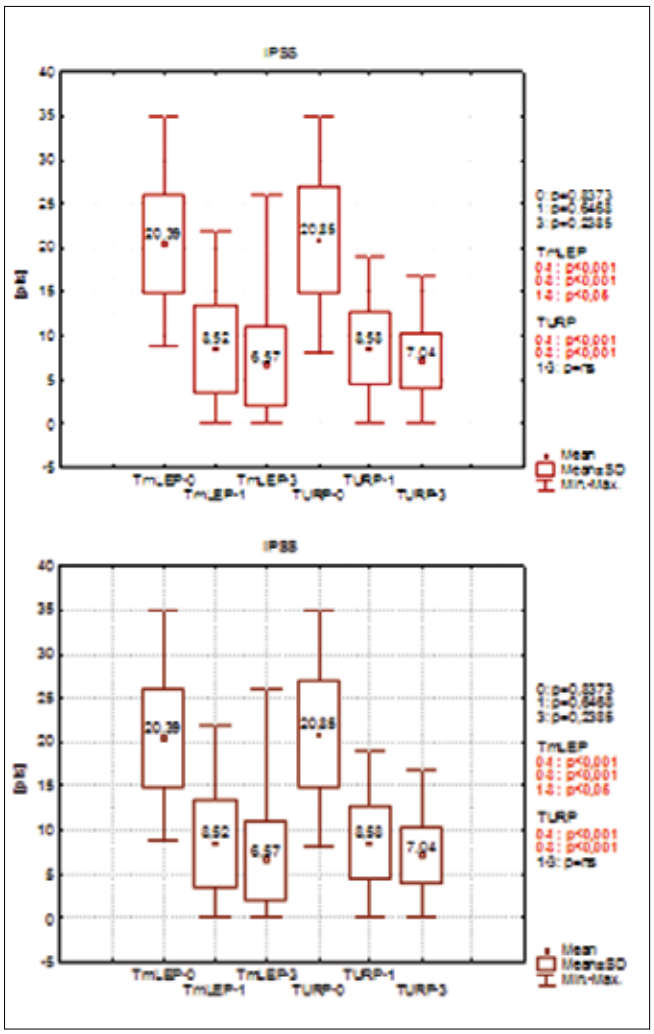

Fig. 1. Correlations between groups of IPSS and QoL.
Legend: 0 – before surgery; 1 – 1 month after surgery; 3 – 3 months after surgery

DISCUSSION

The first paper about the clinical results of the use of the thulium laser was written by Xia et al. [1] , but he reports the use of a 50W power laser. In recent years there were a few research projects assessing the safety and effectiveness of the use of the thulium laser in BPH treatment. On the basis of these publications the first international consensus paper summarizing the initial experience with the thulium laser has been published [2]. The thulium laser can be used in various procedures of removing prostatic tissue: from "pure" vaporization through vaporesection and vapoenucleation to enucleation. In this paper the enucleation technique was investigated, but the authors are aware that the procedure is always vapoenucleation with a varied proportion of vaporization and enucleation intensity. What can be observed is the lack of standardization in research on the thulium laser, and all of them are characteristically specific of basic principle, as well as inclusion and exclusion criteria. Until now the effectiveness of the thulium laser was compared with TURP [3, 4] or HoLEP [5], but mostly it was assessed without confrontation analysis or by conducting the analysis inside the checked group by dividing patients into subgroups depending on prostate volume [6] or indwelling catheter presence [7, 8]. The most comprehensive research projects in laboratory conditions were conducted by N. Fried et al. [9, 10], and in clinical conditions by T. Bach et al. [11-14].

The size of this study's control groups allowed for statistical analysis (TmLEP – 54, TURP – 52). Patients with indwelling catheters before surgery were not excluded, as was the case in other research projects with thulium laser. This allows for preservation of the research structure and a control group that is similar to a natural one. Unfortunately it makes it impossible to perform on all patients the test to assess free urine flow (Q_{max} and PVR), which may in some way disturb the statistical evaluation.

Analyzing the differences in the time of surgery performance between particular studies is quite significant. The time of surgery elongated by the time of morcellation and the resulting higher risk of complications caused by morcellation (e.g. bladder mucosa injury, technical troubles with morcellator tightness) suggests improvement in the thulium laser techniques of removing prostatic tissue to vapoenucleation and even vaporesection. These techniques seem to be easier to learn, and because of that their learning curve could be shorter. Comparing the amount of energy used to perform the surgery to the few researches that noticed this parameter [7, 12], we could assume that the energy needed to remove an enlarged prostate does not depend on the time of the surgery, but rather on the prostate volume. Commenting on the longer time of surgery in TmLEP, two issues have to be pointed out. First of all, Tm-

Table 1. Perioperative data

	TmLEP	TURP	*p* – value (TmLEP *vs.* TURP)
Observation period	Before, 1 and 3 months after surgery	Before, 1 and 3 months after surgery	
Age (years)	68.3 ±6.8 (55-84)	69.3 ±7.2 (54-87)	0.4589
No. of patients	54	52	
No. of patients with indwelling catheter	37	33	
No. of patients without indwelling catheter	17	19	
Prostate volume (cm^3)	62.03 ±23.7 (28-126.4)	66.5 ±22 (27.6-117.9)	0.3336
Resected tissue weight (g)	24.8 ±14.8 (2-65)	34.8 ±14.1 (12-68)	0.0005
% of resected tissue (%)	37.8 ±14.2 (2.7-75)	51.9 ±11.2 (28.4-75)	<0.0001
Retrieval rate (g/min)	0.326 ±0.136 (0.04-0.65)	0.467 ±0.122 (0.13-0.68)	<0.0001
Surgery time (min)	102.2 ±38.7 (25-210)	74.5 ±22.8 (25-140)	<0.0001
Laser use time (min)	74.2 ±28.4 (20-135)	–	
Morcellation time (min)	28.1 ±17.9 (5-80)	–	
Used energy (kJ)	119.4 ±16.4 (13.2-268)	–	
Catheterization time (days)	2.1 ±0.8 (1-6)	2.0 ±0.9 (1-5)	0.6154
Hospitalization time (days)	3.6 ±0.9 (2-7)	3.5 ±0.8 (2-6)	0.9446
Hgb level before surgery (g/dl)	14.2 ±1.4 (10.8-16.90)	14.4 ±1.6 (10.4-17.9)	0.3692
Hgb level after surgery (g/dl)	13.2 ±1.4 (10.4-16.9)	12.6 ±1.7 (8.3-16.4)	0.0527
Hgb loss (g/dl)	0.95 ±0.77 (0-3.2)	1.81 ±0.97 (0.1-4.7)	<0.0001
PSA (ng/ml)	3.37 +/-2.02 (0.46-7.9)	3.73 +/-2.79 (0.25-19.72)	0.4370
Nocturia (micturition quantity/night)	3.02	2.73	0.1317
Indications for surgery:			
- LUTS	64% (35)	59.6% (31)	
- urinary retention	31.5% (17)	36.5% (19)	
- hematuria	3.7% (2)	3.8% (2)	

LEP is a newly launched operation procedure, which surgeons have just learned and may still be on the learning curve, but certainly not on the initial part of it. Many years of experience and a large number of TURPs has allowed for a certain standardization of this procedure. Hence, the two procedures have to be treated differently as far as experience is concerned. On the other hand, individual predispositions and preferences of the operating surgeon determine the speed and manner of performing the operation. To make a detailed analysis we should compare the time of TmLEP and TURP as performed by a particular surgeon, after finishing the learning curve and reaching a stable level of results without statistically significant changes in the long-term observation. The vaporization process in the TmLEP technique could explain differences concerning the weight of the resected tissue. Accordingly, it seems justified to remark that the name of the procedure describes the technique rather than the presence or lack of vaporization.

What deserves attention is the statistically significant hemoglobin loss, which was approximately twice as low in TmLEP than TURP [(0.95 ±0.77 g/dl (0-3.2) *vs.* 1.81 ±0.97 g/dl (0.1-4.7)]. The same observation was made by Xia et al. [3] and Shao et al. [5] Good hemostasis and little hemoglobin loss could give hope that BPH patients with blood coagulation disorders or those taking anticoagulants could be operated on with the use of thulium laser. This issue needs further detailed investigations. Catheterization time in the research and control groups respectively was 2.1 ±0.8 (1-6) *vs.* 2.0 ±0.9 (1-5) days, and hospitalization time was 3.6 ±0.9 (2-7) *vs.* 3.5 ±0.8 (2-6) days. The catheter inside the urinary bladder depends on postoperative bleeding intensity. In the case of insignificant or lack of bleeding it is possible to avoid catheterization, but usually it is used at least until the effect of anesthesia wears off. Catheterization and hospitalization time to a large extent depends on the individual attitude of the surgeon (active or conservative), whether the surgeon looks after the patient carefully during the postoperative time or only during common rounds at a ward.

Parameters of the operation efficacy measured on the IPPS scale, Q_{max} flow, and PVR volume reveal improvement one month after the operation and it was sustained or progressed during the three month-long observation. LUTS receded after removing the bladder obstruction to the level satisfactory for patients, and the quality of life (QoL) improved from "mostly dissatisfied - unhappy" [4.7 +/-1.0 (3-6) TmLEP *vs.* 4.9 +/-1.0 (2-6) TURP] to "satisfied – mixed" [1.5 +/-1.1 (0-4)] TmLEP *vs.* 1.3+/-0.9 (0-4) TURP] three months after operation. In Xia et al. [3], Shao et al. [5], and Mattioli et al. [6] research, where PVR and Q_{max} (objective data) with IPSS and QoL (subjective data) were assessed just after operation or before discharge from hospital it could be noticed that no statistically significant improvement or deterioration was observed in further controls several months after the surgery. It could suggest that the improvement that patients feel after BPH surgical treatment will remain at a satisfactory level for at least one year. There is lack of evidence that would allow for the assessment of the efficacy of BPH thulium laser treatment longer than 16.5 months [13].

If Q_{max} assessment is done by electronic device and depends more on patient's temporary disposition then the PVR volume is assessed subjectively by an urologist. This might be the factor re-

Table 2. Parameters evaluated before and after surgery

	Before surgery	(1) 1 month after surgery	(3) 3 months after surgery	0–1 p-value	0–3 p-value	1–3 p-value
IPSS TmLEP [score]	20.38 +/-2.59 (9-35)	8.52 +/-4.99 (0-22)	6.57 +/-4.46 (0-26)	p <0.001	p <0.001	p <0.05
IPSS TURP [score]	20.8 5 +/-6.03 (8-35)	8.58 +/-4.06 (0-19)	7.04 +/-3.19 (0-17)	p <0.001	p <0.001	non significant
IPSS p-value (TmLEP *vs.* TURP)	0,8373	0.6468	0,2385			
QoL TmLEP [score]	4.7 +/-1.0 (3-6)	1.9 +/-1.3 (0-5)	1.5 +/-1.1 (0-4)	p <0.001	p <0.001	non significant
QoL TURP [score]	4.9 +/-1.0 (2-6)	1.6 +/-0.9 (0-4)	1.3 +/-0.9 (0-4)	p <0.001	p <0.001	non significant
QoL p-value (TmLEP *vs.* TURP)	0.3165	0.2855	0.2488			
Qmax TmLEP [ml/s]	7.73 +/-3.52 (1.6-14.5)*	21.88 +/-9.62 (5.3-45.4)	23.0 +/-8.30(4-43.4)			
Qmax TURP [ml/s]	8.57 +/-3.61 (2.5-14.7) *	23.93 +/-7.78 (13.3-43.2)	26.04 +/-8.52(13.7-51.9)			
Qmax p-value (TmLEP *vs.* TURP)	0.3650*	0.5315	0.6491			
PVR TmLEP [ml]	166.2 +/-110.5 20-450) *	33.3 +/-35.1(0-150)	26.5 +/-28.8 (0-150)			
PVR TURP [ml]	152.0 +/-112.2 (20-470) *	36.2 +/-28.2 (0-120)	28.6 +/-24.3 (0-100)			
PVR p-value (TmLEP *vs.* TURP)	0.5603*	0.2488	0.0555			

* group concerned without indwelling catheter

sponsible for differences in research results However, if we assume that PVR measurement before and after surgery is performed by the same person, in the same way, with the same ultrasonography device, then possible measurement mistakes are repeatable and the obtained results have a clinical value. So that relative alterations of PVR before and after surgery are more important than specific absolute values.

Complications recorded during and after the operation are typical for endoscopic BPH treatment. In the TURP group, blood transfusion was required twice, but postoperative bleeding in both groups was at a similar level. Complications typical for the TmLEP include injury of the bladder mucosa, which is usually caused during morcellation of enucleated tissue by incidental aspiration of the bladder wall. The significant percentage of retrograde ejaculation is an important and relevant factor when it comes to reducing patients' quality of life after endoscopic interventions. It concerns such an important domain of life as sexual life, therefore informing patients about the possibility of retrograde ejaculation is compulsory for each surgeon. Comparing thulium laser to other operative laser techniques reveals fairly promising results as regards the quantity and quality of peri- and postoperative complications [15]. The irritative symptoms that we recorded are typical for LUTS: frequency, urgency, dysuria, nocturia, and odynuria. Stress urinary incontinence noticed after the surgery (four in TURP group *vs.* one in TmLEP group) is one of the possible complications after BPH. The cause of this is mostly associated with bladder overactivity (which existed prior to the operation), the healing process of the operation wound in prostate gland, or with the infection that occurred in some cases.

The three-month observation was undertaken because that period is the shortest time to evaluate the long-term effects of the operation. After reviewing papers assessing outcomes of endoscopic BPH treatment, results achieved after three months are mostly preserved. Authors know that the time of the observation is relatively short, but this is a preliminary paper of a long observation schedule, so focusing on long-term observation is our main objective.

CONCLUSIONS

In short-term observation, TmLEP is a safe and efficient method for the treatment of BPH. The efficiency and durability of clinical improvement felt by patients is very good. Compared to TURP, it has twice as low Hgb loss, which could make it a promising treatment of choice for patients with low Hgb level before the surgery. The time of surgery is, however, longer in TmLEP than TURP. At this time, the lack of long-term studies does not allow for wider conclusions. More multicenter RCT assessing the thulium laser in BPH treatment during a long-time observation period are desirable.

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Table 3. Perioperative and postoperative complications

Perioperative complications	TmLEP		TURP	
	n	%	n	%
Capsule perforation	0	0.00	2	3.85
Bladder perforation	0	0.00	0	0.00
Injury of bladder mucosa / bladder neck / urethra	3	5.56	0	0.00
Bleeding requiring transfusion	0	0.00	2	3.85
Bleeding requiring irrigation	4	7.41	3	5.77
Pain	6	11.11	6	11.54
Urinary tract infection	2	3.70	4	7.69
Acute urinary retention and re-catheterization	0	0.00	3	5.77
Acute transient urinary incontinence	2	3.70	2	3.85
TURP Syndrome	0	0.00	0	0.00
others	0	0.00	0	0.00
Postoperative complications	**TmLEP**		**TURP**	
	n	%	n	%
Retrograde ejaculation	19	35.19	17	32.69
Stress urinary incontinence	1	1.85	4	7.69
Urethral stricture	3	5.56	0	0.00
Bladder neck contracture	0	0.00	0	0.00
Recurrent infections	3	5.56	2	3.85
Irrative symptoms	10	18.52	6	11.54
Reoperation of recurrent tissue	2	3.70	0	0.00

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