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Original Article

Safety and feasibility of thulium laser transurethral resection of prostate for the treatment of benign prostatic enlargement in overweight patients

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Abstract *Objective:* We aimed to determine safety and feasibility of thulium laser transurethral vapoenucleation of prostate (ThuVEP) for treatment of obese patients affected by benign prostatic hyperplasia (BPH).

Methods: We retrospectively analysed data of 452 patients with BPH who underwent ThuVEP from February 2012 to March 2016 in a single center. Patients were divided into three groups according to body mass index (BMI, kg/m²): Normal weight ($18.5 \leq \text{BMI} < 25$; Group A), overweight ($25 \leq \text{BMI} < 30$; Group B) and obese ($\text{BMI} \geq 30$; Group C), for a total of 412 patients evaluable for this study. Preoperative total serum prostate-specific antigen (PSA), digital rectal examination of the prostate, transrectal ultrasound (TRUS), renal ultrasound, urine culture, uroflowmetry, International Prostate Symptoms Score (IPSS), and Quality of Life (QoL) score were analyzed. Post-operative complications, hospital stay and days of catheterization, questionnaires and uroflowmetry at 1 and 3 months after surgery were evaluated. Preoperative data, surgical outcomes, complication rate and clinical outcomes were compared between groups.

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Results: The median age of patients was 69 years (Interquartile Range [IQR 10]). The preoperative median IPSS among groups was 19 (IQR 8.75), 20 (IQR 10), and 18 (IQR 10) respectively. At 1 and 3 months of follow-up, this value was 8 (IQR 7), 8 (IQR 4), 7 (IQR 5) and 5 (IQR 6.25), 5 (IQR 6), 6 (IQR 5), respectively (all p between groups > 0.05). There was no statistically significant difference among three groups as for hospital stay and days of catheterization ($p > 0.05$).

Conclusion: Our results showed that ThuVEP was safe and feasible even in overweight patients with substantially enlarged prostate.

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1. Introduction

Since the last decades of the 20th century the increase of bodyweight has progressively become a worldwide epidemic disorder, leading to higher incidence of morbidity and mortality [1].

More recently in the United States, 20% of adults were clinically obese (defined by a body mass index [BMI] of 30 kg/m^2 or higher), while 30% were defined as overweight (BMI between 25 and 30 kg/m^2) [2].

Benign prostatic hyperplasia (BPH) is one of the most common diseases in men, with an incidence that increases with aging, observed in about 20% of men in the fourth decade of life with a rising trend that reaches almost the 80% after 80 years of age [3,4].

Even though there are many standards to define an excess of bodyweight, several studies reported the association between obesity and BPH, showing the central obesity among the top risk factors for development of prostate enlargement. Lee et al. [5] described how an increase of waist circumference was significantly and positively associated with serum prostate-specific antigen (PSA), prostate volume, and International Prostate Symptom Score (IPSS), with a consequent worsening in voiding function.

The most established operative methods in the treatment of prostate enlargement are the transvesical prostatectomy and the transurethral resection of prostate (TURP).

According to EAU-Guidelines-Management-of-non-neurogenic-male-LUTS-2016, TURP is the current surgical standard procedure for men with prostate size of 30–80 mL, meanwhile open prostatectomy (OP) and laser endoscopic enucleation are the gold standard in men with enlarged prostate >80 mL.

However, it is widely described that OP is associated with a high morbidity rate, noteworthy blood loss and prolonged hospitalization [6].

Furthermore, some studies demonstrated an association between obesity and metabolic syndrome with worse urinary symptoms recovery after TURP or OP [7,8].

Among the minimally invasive alternatives that have been proposed in the clinical practice field, one is the thulium laser, a technology that uses wavelengths ranging from $1.75 \text{ }\mu\text{m}$ to $2.22 \text{ }\mu\text{m}$ to vaporize or enucleate the prostate tissue.

It has been demonstrated that thulium vapoenucleation of the prostate (ThuVEP) is effective, reliable, and safe when employed for the treatment of prostate enlargement [9].

However, currently published reports on thulium laser treatment of large prostates are still rare.

The aim of our study is to assess the safety and feasibility of the thulium laser treatment for prostate enlargement, assessing the perioperative and functional outcomes stratifying the population for BMI and comparing normal weight patients to overweighted.

2. Patients and methods

We studied 452 consecutive patients who underwent ThuVEP in a single Center.

Data were prospectively collected and retrospectively analyzed. All patients referring to the Urology Department of our centre were routinely requested to sign an informed consent form to retrieve clinical data to be used for research purposes. The possibility of receiving phone calls and undergoing follow-up visits and diagnostic procedures was included in the consent form. Men who denied their consensus were excluded. Based on EAU guidelines, patients who suffered from symptomatic BPH and had surgical indications were enrolled from February 2012 to March 2016. Patients with less than 3 months follow-up and less than 18.5 kg/m^2 of BMI were excluded. Patients were divided into two groups according to BMI (kg/m^2): Group A normal weight ($18.5 \leq \text{BMI} < 25$); Group B overweight ($\text{BMI} \geq 25$), for a total of 412 patients evaluable for this study. We then selected a subgroup of obese patients ($\text{BMI} \geq 30$, Group C) from Group B and compared these patients to Group A.

Before surgery, patients underwent digital rectal examination of the prostate, transrectal ultrasound (TRUS) to measure prostate and adenoma volume, renal ultrasound, urine culture, and uroflowmetry. In addition, total PSA, IPSS score, Quality of Life (QoL) score were evaluated. Patients with PSA level $>4 \text{ ng/mL}$ underwent TRUS biopsy to exclude prostate carcinoma.

Patients were evaluated with questionnaires and uroflowmetry preoperatively and at one and three months after surgery. Urinary outcomes (IPSS score, QoL, and Q_{max}) were compared among the three groups of patients.

2.1. Surgical technique

All surgical procedures were performed by the same surgical team (three surgeons) who was fully trained in ThuVEP. Surgeries were performed by using the Cyber TM 150 or 200 (Quanta System Cyber TM, Samarate, Italy). With the patient in the lithotomy position, a laser resectoscope with an $800 \text{ }\mu\text{m}$ end firing fiber was introduced into the urethra using saline solution as an irrigant. Ureteral orifices and urinary sphincter were identified and marked using a very low-power setting

(40 W). An inverted “U” mark was performed proximal to the verumontanum, which was used for orientation (power setting, 40 W). Subsequently, an incision was made down to the capsule fibers at the 05:00 and 07:00 positions from the bladder neck to the inverted “U” mark. Then, complete vaporessection of the middle lobe up to the abovementioned mark was performed (power setting, 150 W), followed by vapoenucleation of the lateral lobes down to the capsule and on the ventral side to the level of the verumontanum (power setting, 150 W). Then, prior to retrograde vapoenucleation of the lobes (power setting, 150 W), circular vapoenucleation of the internal bladder neck was performed by means of apical vapoenucleation (power setting, 150 W), employing the verumontanum as a distal border. After introduction of a nephroscope and maintaining bladder distension, prostate lobes were morcellated using the Piranha (Wolf), followed by a final check to confirm absence of obstruction or hemorrhage. Finally, a temporary indwelling catheter was placed (Dufour 20 Ch) with temporary bladder irrigation.

2.2. Statistical analysis

Non normally distributed data were reported as median and interquartile range (IQR), while categorical data were reported as absolute values or percentages. Continuous data were analyzed by using the Mann–Whitney U test. Categorical data were analyzed by using the Chi-square test. SPSS software (IBM® SPSS Statistics®v.21, IBM Corp, Armonk, NY, USA) was used for all statistical analyses, with p values of <0.05 considered as statistically significant.

3. Results

The study took place from February 2012 to March 2016, and 412 consecutive patients who underwent ThuVEP were analyzed. Results are reported in Table 1.

Comparison between the Group A and the Group B + C showed no statistically significant differences in anamnographical characteristics (age, $p = 0.853$). The American Society of Anesthesiologist (ASA) score, the presence of diabetes and the use of anticoagulant or antiplatelet therapy were analyzed to evaluate comorbidities. No statistically significant difference was found between Group A and Group C (all $p > 0.05$).

Preoperative data reviewed regarding prostate characteristics were PSA level, prostate volume, presence of α blocker therapy and indwelling catheter. None of these showed significant difference in the two groups except for the prostate volume, which resulted higher in the overweight patients (median 75 mL vs. 60 mL, $p < 0.001$).

Similar considerations resulted from comparison between the normal weight and the obese group. The only significantly different parameter was the prostate volume, resulting higher in the obese patients (78.5 mL vs. 60.0 mL, $p < 0.003$).

Perioperative characteristics analyzed were operative time, haemoglobin drop, bladder irrigation time, catheterization time, and length of hospital stay. No difference was found between Group A and Group B + C with regards to all these parameters (Table 1).

Comparison of normal weight patients with obese patients leads to similar results, except for the haemoglobin

decrease in the obese group, which was significantly lower (median 0.8 vs. 1.0 mg/mL, $p = 0.031$).

Functional data were assessed preoperatively, at 1 and 3 months postoperative, with the IPSS, QoL score and uroflowmetry (Table 1). A statistically significant difference was found at 1 month after surgery for PVR with lower values (Group A vs. Group B + C, $p = 0.03$). Another statistically significant difference was reported in terms of QoL: Group A had a better improvement compared to Group C ($p = 0.028$). However these differences were no more observed at 3 months follow-up. None of our patients reported temporary urge incontinence.

Complications are reported in Table 1 with no differences between all groups (all $p > 0.05$).

4. Discussion

To our knowledge this is the first study in literature reporting the use of thulium laser for BPH surgery in overweight patients. Furthermore, there is a lack of papers also regarding the outcomes of obese patients treated with other surgical approaches for BPH.

Thulium laser technique has been introduced as a size-independent, minimally invasive treatment of benign prostatic obstruction [10, 11].

In EAU guidelines, thulium laser transurethral vapoenucleation or vaporization of the prostate is an alternative to transurethral resection of the prostate (TURP) for small- and medium-sized prostates (LE 1b GR A), and ThuLEP can be offered as an alternative to TURP, to holmium laser enucleation of the prostate, and open simple prostatectomy for large prostates (LE 1b, 2b GR B).

Our results confirm ThuVEP as effective, reliable, and safe both in normal and overweight patients. Therefore, no significant differences were found in terms of operative time.

As described in literature [5], our results confirmed a positive correlation between an increased BMI and prostate volume, a slight arise of serum PSA and a major use of alpha-blockers, meanwhile no differences have been reported in IPSS, QoL and need of catheterization due to acute urinary retention.

Moreover, comparing the groups no discrepancies have been reported in preoperative uroflowmetry parameters confirming that the BPH urinary symptoms are correlated not only with prostate volume growth, but it could be described as multifactor pathology.

Haemoglobin decreased surprisingly lesser in Group C than Group A, even considering the slight higher, but clinically significant, rate of acetylsalicylic acid assumption in overweight and obese patients. Comparing postoperative results between Group A and B + C, and Group A and C alone, no differences have been reported in catheterization days and hospitalization length. Furthermore, complication rate and grade were similar between Group A and B + C and between Group A and Group C alone.

As mentioned before, it has been reported that there was a correlation between obesity and metabolic syndrome, and worse urinary symptoms recovery after prostatic surgery [12]. Sener et al. [8] demonstrated a worse LUTS relief after TURP in patients with metabolic syndrome. A study conducted by Gacci et al. [7] reported incomplete recovery of total IPSS and

Table 1 Patients characteristics, preoperative functional characteristics, perioperative data, 1 and 3 months follow-up functional data, and postoperative complications.

Parameters	Group A	Group B + C	Group C	p-Value	
	18.5 kg/m ² ≤ BMI < 25 kg/m ² n = 177	BMI ≥ 25 kg/m ² n = 235	BMI ≥ 30 kg/m ² n = 54	A vs. B	A vs. C
Age, year; mean (SD)/median (IQR)	70 (11)	69 (10)	68 (8.5)	0.853	0.804
PSA, ng/mL; mean (SD)/median (IQR)	2.50 (2.96)	2.91 (3.7)	3.34 (3)	0.241	0.163
Prostate volume, mL; mean (SD)/median (IQR)	60 (47.65)	75 (52)	78.5 (45)	<0.001	0.003
Indwelling catheter, n (%)					
Yes	47 (25.4)	51 (21.7)	8 (14.8)		
No	130 (74.6)	184 (78.3)	46 (85.2)	0.232	0.077
Diabetes, n (%)					
Yes	17 (9.6)	33 (14.0)	10 (19)		
No	125 (70.6)	148 (63)	34 (62)		
Unknown	35 (19.8)	54 (23)	10 (19)	0.157	0.078
Alpha blocker, n (%)					
Yes	116 (65.5)	167 (71)	39 (72.2)		
No	61 (34.5)	68 (29)	15 (27.8)	0.253	0.361
Antiplatelet or anticoagulant medications, n (%)					
Acetylsalicylic acid	37 (21)	60 (25.5)	15 (27.8)	0.310	0.290
Other antiplatelet drugs	9 (5.0)	8 (3.4)	1 (1.8)	0.537	0.307
Anticoagulant drugs	13 (7.4)	14 (6)	4 (7.4)	0.905	0.988
No	118 (66.6)	153 (65.1)	34 (63.0)	0.163	0.051
ASA score, n (%)					
1	31 (17.5)	38 (16.1)	6 (11.1)	0.837	0.261
2	110 (62.7)	154 (65.6)	35 (64.8)	0.495	0.597
3	36 (19.8)	43 (18.3)	13 (24.1)	0.280	0.495
4	0	0	0	0	1
IPSS preop, median (IQR)	19 (8.75)	20 (10)	18 (10)	0.236	0.603
QoL score preop, median (IQR)	4 (2)	4 (2)	4 (2)	0.206	0.681
Q _{max} , mL/s preop; median (IQR)	8.4 (4.6)	8.0 (3.9)	8.5 (3.6)	0.702	0.913
PVR, mL preop; median (IQR)	122 (145)	120 (152.5)	109 (160)	0.743	0.968
Operative time (min); median (IQR)	70 (40)	75 (40)	85 (50)	0.096	0.066
Hb decrease (g/dL); median (IQR)	1 (1.28)	1 (1.2)	0.8 (1.15)	0.600	0.031
Bladder irrigation time (h); median (IQR)	20 (6)	20 (6)	20 (6)	0.684	0.758
Catheterization time (h); median (IQR)	34 (20)	28 (22)	28 (19.5)	0.710	0.951
Hospital stay (day); median (IQR)	2 (1)	2 (1)	2 (1)	0.902	0.732
1 month IPSS, median (IQR)	8 (7)	8 (4)	7 (5)	0.356	0.161
1 month QoL score, median (IQR)	2 (2)	2 (2)	1 (2)	0.170	0.028
1 month Q _{max} , mL/s; median (IQR)	16.6 (9.35)	16.1 (10.3)	18 (11.78)	0.880	0.262
1 month PVR (mL); median (IQR)	30 (39)	40 (86)	25 (83.5)	0.030	0.570
3 month IPSS, median (IQR)	5 (6.25)	5 (6)	6 (5)	0.765	0.475
3 month QoL score, median (IQR)	1 (2)	1 (2)	1 (2)	0.839	0.830
3 month Q _{max} , mL/s; median (IQR)	21 (9.48)	20 (9.78)	21.35 (10.8)	0.727	0.380
3 month PVR, mL; median (IQR)	15 (28.5)	0 (51)	15 (76)	0.869	0.380
AUR with recatheterization (Clavien II), n	18	29	7	0.709	0.650
Delayed morcellation (Clavien IIIa), n	1	1	0	0.840	0.580
Transfusion rate, n	4	1	0	0.169	0.575
UTI (Clavien II), n	0	2	1	0.131	0.070
MI/stroke (Clavien IV), n	1	1	0	0.840	0.580
Bladder injury (Clavien I), n	1	0	0	0.249	0.580

ASA, American Society of Anesthesiologists; IPSS, International Prostatic Symptoms Score; IQR, interquartile range; QoL, quality of life; Q_{max}, maximum flow; PVR, post-void residual volume; AUR, acute urinary retention; UTI, urinary tract infection; MI, myocardial infarction.

storage IPSS in patients with waist circumference > 102 cm after OP and TURP. Also Cui et al. [13]. have recently shown a not-negligible rate of transitory urge incontinence (19% vs. 23%) and dysuria (28% vs. 16%) after holmium laser enucleation of the prostate (HoLEP) and OP, respectively. These

results were not observed in our study: Post operative IPSS and Q_{max} at 1 and 3 months were significantly improved both in normal and overweight patients suggesting that thulium approach can offer better functional post-operative results irrespectively of patients' weight than TURP, HoLEP or OP.

The present study is subject to limitations. Firstly, it is a single center, nonrandomized study, with a limited number of patients forming Group C. However, the prospective collection of data, the standardization of the ThuVEP technique along with the detailed statistical analysis may compensate its main limits. Secondly, the study lacks of a long-term follow-up, however a statistically significant improvement in the analysed functional parameters was already observed. Finally, the majority of patients have not undergone a urodynamic examination, because, as shown in the literature, impaired detrusor contractility is not a contraindication to surgery [14].

In our opinion a longer-term follow-up is needed to evaluate the durability and possible morbidity for ThuVEP in overweight patients.

5. Conclusion

Compared with normal weight population, overweight and obese patients did not show a statistically significant difference about complication rate and clinical outcomes. Our results described ThuVEP as a safe and feasible treatment option even in obese and overweight patients and substantially enlarged prostate.

Author contributions

Study design: Luca Carmignani, Damiano Vizziello, Alessandro Mistretta Francesco.

Data acquisition: Sebastiano Nazzani, Damiano Vizziello, Michele Clementi, Claudia Signorini, Gloria Motta.

Data analysis: Luca Carmignani, Damiano Vizziello, Alessandro Mistretta Francesco, Sebastiano Nazzani, Elisa De Lorenzis.

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Critical revision of the manuscript: Luca Carmignani.

Conflicts of interest

The authors declare no conflict of interest.

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