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BENIGN PROSTATIC HYPERPLASIA
ORIGINAL ARTICLE

Thulium laser enucleation of the prostate (ThuLEP): Results, complications, and risk factors in 139 consecutive cases

Marco Raber [a,*], Noor N.P. Buchholz [a], Augusto Vercesi [b], Nashaat A. Hendawi [a], Vincenzo Inneo [b], Giuseppe Di Paola [b], Lorenzo Tessa [b], Ismail M. Hassan [a]

[a] *Department of Urology and Men's Health, Al Garhoud Private Hospital, Dubai, United Arab Emirates*
[b] *Department of Urology, Istituto Clinico Citta' Studi, Milan, Italy*

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Prostate enlargement;
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ABBREVIATIONS

DVT, deep vein thrombosis;
Hb, haemoglobin;
HoLEP, holmium laser enucleation of the prostate;
PVR, post-void residual urine volume;
Q_{max}, maximum

Abstract ***Objectives:*** To report our experience with the emerging technique of thulium laser enucleation of the prostate (ThuLEP) for the treatment for prostate hyperplasia.

Patients and methods: Our inclusion criteria were an International Prostate Symptom Score (IPSS) of >15 and a quality-of-life (QoL) score of >3 in patients with confirmed bladder outflow obstruction, no longer responsive to medical therapy, with a significant post-void residual urine volume (PVR; >100 mL), with or without recurrent urinary tract infection and/or acute urinary retention. Patients with neurogenic bladder, urethral strictures, bladder stones, and previously failed transurethral prostate surgery were excluded.

Results: In all, 139 men were included in the study. The mean age was 67.8 years. The IPSS and QoL score improved by 17.6 and 2.6, respectively. The flow rate increased from a mean of 9.6 mL to 31.2 mL and the PVR decreased from a mean of 131 mL to 30 mL. On univariate and multivariate analyses, operating time was a predictive factor for haemoglobin drop during the operation. Heparin prophylaxis was the only risk factor identified for postoperative bleeding. Two patients (0.01%) required blood transfusion. One patient (0.007%) required re-intervention for

* Corresponding author.
E-mail address: marcoraber1@gmail.com (M. Raber).
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urinary flow rate; QoL, quality of life; ThuLEP, thulium laser enucleation of the prostate

bleeding control, and two patients developed urethral and bladder neck strictures (0.01%).

Conclusion: ThuLEP is safe and reproducible. Whilst it significantly reduces intraoperative bleeding as compared to transurethral resection of the prostate, operating time and perioperative heparin prophylaxis may still lead to a Hb drop and constitute a risk factor for postoperative bleeding. Therefore, a potential risk of deep vein thrombosis requiring heparin prophylaxis should be carefully considered and balanced with the expected clinical benefit of the operation.

Introduction

TURP is still considered the 'gold standard' for the treatment of prostate hyperplasia. It's efficacy in alleviating BPH-related symptoms is nearly 90%. However, it is associated with an overall immediate morbidity rate of 11% [1]. To decrease this complication rate, less invasive procedures have been developed in order to reduce the complication rate, shorten the hospitalisation time, and to enhance and accelerate patient recovery.

Laser treatment of symptomatic BPH has been widely implemented during the last decade. Initial evaporation techniques were further developed to enucleation techniques, and combinations of both. The addition of morcellation techniques has allowed laser enucleation of larger prostates too.

Thulium laser enucleation of the prostate (ThuLEP) was first reported in 2009 by Imkamp et al. [2]. Since then, ThuLEP has been adopted in many centres worldwide. The latest European Association of Urology (EAU) guidelines indicate ThuLEP as a possible alternative to TURP and holmium laser enucleation of the prostate (HoLEP) in patients with moderate-to-severe LUTS, leading to immediate and mid-term objective and subjective clinical improvements [3].

In the present study, we retrospectively evaluated our initial experience of the subjective and objective results and complications in a consecutive series of patients operated with ThuLEP.

Patients and methods

Patient selection

Our inclusion criteria for this study were an IPSS of >15 and a quality-of-life (QoL) score of >3 in patients with confirmed BOO, no longer responsive to medical therapy, with a significant post-void residual urine volume (PVR; >100 mL), with or without recurrent UTI, and/or acute urinary retention. Patients with neurogenic bladder, urethral strictures, bladder stones, and previously failed transurethral prostate surgery were excluded.

Preoperative evaluation

All 139 patients underwent urodynamic studies and were confirmed to have BOO resulting from BPH. The diagnostic evaluation included IPSS and QoL questionnaires, PSA level assessment, urine analysis and urine culture, serum creatinine and electrolytes, an ultrasonographic study of the urinary tract (kidneys, ureters and bladder), TRUS to assess prostate volume, and TRUS-guided prostate biopsies whenever indicated.

Patients on aspirin were asked to stop 7 days preoperatively whenever the cardiologist deemed it safe to do so. Patients with recent angioplasty were postponed to 6 months after that procedure when additional clopidogrel was safe to stop.

Patients received deep vein thrombosis (DVT) prophylaxis according to their risk, evaluated in concordance with the Guidelines of the American College of Chest Physicians [3].

We also stratified our results according to a high risk of bleeding, which included those patients that remained on heparin because of DVT risk or anticoagulant bridging therapy, and patients on aspirin because of previous coronary stenting.

Technique

All procedures were performed by one experienced urologist. In all procedures, we used the RevoLix 200 W continuous wave laser (LISA laser products OHG – Katlenburg-Lindau/Germany) with a 800-μm fibre, and a standard laserscope (Karl Storz GmbH & Co., Tuttlingen, Germany), along with a Piranha morcellator (Richard Wolf GmbH, Knittlingen, Germany) with morsoscope (Karl Storz GmbH & Co.).

A three-lobe enucleation technique was used when there was a large median lobe. A two-lobe technique was used whenever the median lobe was not significantly enlarged. The technique is described in the video 'Thulium Laser Enucleation of Prostate (ThuLEP): Step by step technique', uploaded at the following web-link: www.youtube.com/user/marcoraber. The laser incision was initiated at the 5 and 7o'clock positions, respectively. The incisions were then deepened until the capsule was reached, and extended from the bladder neck to the verumontanum. Consequently, both incisions were joined together delineating the capsule all the way along. Mechanical lifting of the lobes away from the capsule by the scope was used. Thereafter, a 12o'clock incision was made, and the lateral lobes were dissected from 12o'clock to 3o'clock, by dissecting them away from the capsule using laser energy only. Once the 5 and 3o'clock gutters were dissected, they were joined in a convex manner and the lobe was separated from the capsule. The same procedure was repeated in position 9 to 7o'clock. Laser energy was set at 70 W. Normal saline was used for irrigation. Finally, the lobes were morcellated. In prostates with insignificant median lobes, instead of the 5 and 7o'clock incisions a 6o'clock incision was used. Otherwise, the procedure remained the same. Postoperatively, a 20-F catheter was inserted and the morcellated tissue weight was recorded in grammes.

Our standard protocol planned for catheter removal on the first postoperative day. However, in cases of persisting haematuria, catheter removal could be delayed at the discretion of the treating urologist.

To assess intraoperative bleeding, we recorded the difference in haemoglobin (Hb) level between the preoperative and the first postoperative blood assessment, usually in the evening of the operation day. To assess postoperative bleeding, we recorded the difference in Hb between the first postoperative blood assessment (see above) and a Hb assessment on the day of discharge.

Postoperative evaluation and follow-up

All patients underwent a follow-up at 6 weeks, with clinical assessment and recent history after ThuLEP, completion of the IPPS questionnaire, urine culture, uroflowmetry study, and ultrasonographic PVR assessment. Further follow-ups were conducted at 6 and 12 months. At 6 months, the PSA level was also measured.

Statistical analysis

Continuous variables were compared with Student's *t*-test. Logistic regression for univariable and multivariable analyses was used for the correlation between blood loss and risk factors. A $P < 0.05$ was considered as statistically significant.

Results

In all, 139 patients with symptomatic BPH were treated with ThuLEP between January 2014 and January 2016 at our institute by a single surgeon.

Patients' characteristics

All the patients met the inclusion criteria for IPSS, QoL score and had confirmed BOO obstruction. In all, 65 patients (47%) were no longer responding to medical treatment or had side-effects from the drugs, 47 (34%) still had a significant PVR confirmed on uroflowmetry or urodynamics after failed medical treatment, and 27 (18%) were in acute urinary retention.

The mean (SD, range) age was 67.8 (8.2, 51–82) years; mean (SD, range) prostate volume was 66.9 (24.6, 33–133) mL; mean (SD, range) adenoma volume was 43.3 (21.7, 14–112) mL; and mean (SD, range) detrusor pressure was 97.7 (31.6, 43–159) cmH_2O. The mean (SD, range) Charlson Co-Morbidity Index score was 0.29 (0.55, 0–2). A sub-group of 87 patients (62%) was at medium- or high-risk of DVT and received heparin prophylaxis.

Operative results

The mean (SD, range) operative time was 63.7 (20.5, 32–120) min and the mean (SD, range) weight of enucleated tissue was 23.8 (13.8, 3–74) g.

Postoperative results

At the 1-month postoperative evaluation, 137 patients (99%) had spontaneous voiding and had significantly improved IPSS, QoL score, maximum urinary flow rate (Q_{max}), and PVR. The postoperative changes in the IPSS and QoL score, Q_{max}, PVR, PSA level, and Hb are listed in Table 1. All these variables significantly changed after ThuLEP. IPSS and QoL score improved, Q_{max} increased, and PVR decreased. The mean (SD,

Table 1 Preoperative and postoperative patient characteristics, their variation, and results at 1-year follow-up.

Variable, mean (SD; range)	Preoperative	Postoperative*	1-year follow-up
PSA level, ng/mL	4.5 (4.5;1–18)	1.2 (2.8; 0.10–5.4)	1.3 (1.4; 0.15–5.6)
IPSS	21.2 (3.9; 15–31)	3.6 (2.1; 0–10)	3.2 (2.0; 0–10)
QoL score	4.4 (0.7; 3–5)	1.8 (0.8; 0–3)	1.6 (0.9; 0–3)
Q_{max}, mL/s	9.6 (2.9; 5–16)	31.2 (11.5; 21–50)	33.1 (12; 22–48)
PVR, mL	131 (87; 0–350)	30 (5; 0–70)	35 (6; 0–65)
Hb level, g/dL	14.6 (1.6; 11.6–18.8)	12.7 (1.9; 9.1–17)	–

* All variables significantly improved postoperatively ($P < 0.001$).

range) catheterisation time was 38.4 (7, 12–72) h. In all, 11 patients (8%) were discharged after re-catheterisation and started spontaneous voiding 2 weeks later after a trial without catheter, with two (1%) using clean intermittent self-catheterisation.

There was a significant Hb drop when comparing the preoperative and pre-discharge Hb values (Table 1), and we could differentiate between the intraoperative and postoperative Hb drop. Table 2 shows changes in Hb levels on postoperative day 1 and the values at discharge. Both, the Hb drop immediately after the procedure and postoperatively were significant.

Results of statistical analyses

At univariate and multivariate analyses, operating time was predictive of a Hb drop during ThuLEP. Heparin prophylaxis was the only risk factor for postoperative bleeding with both tests. Results of the logistic regression are shown in Table 3.

Complications

The overall complication rate was 3.6% (Clavien–Dindo Grade II and IIIa). Two patients (0.014%) required blood transfusion. One patient (0.007%) required immediate endoscopic bleeding control. Late urethral and bladder neck strictures occurred in two patients (0.014%) after 6 months.

Follow-up

At 12 months, the PSA level, IPSS, QoL score, Q_{max} and PVR were still comparable with the immediate postoperative data (Table 1).

Discussion

Our present study analysed 139 consecutive patients undergoing ThuLEP for BPH. Although evaluated retrospectively, we attempted to assess the effect of the learning curve, and the clinical outcomes in terms of complications and results.

Table 2 Baseline Hb compared with immediately postoperative and at the time of patient discharge.

	Hb level, g/dL		P	Hb level, g/dL	P
	Preoperative	Postoperative day 1		At discharge	
Mean (SD)	14.3 (1.3)	13.8 (1.3)	0.01	12.6 (1.5)	< 0.001
Range	11.2–18.8	11–18		9.1–17	

Table 3 The difference between basal Hb level and its value at the patient's discharge (ΔHb), as well as the Hb difference related to the operation (ΔHb1) and the postoperative period (ΔHb2) were evaluated as independent variables.

	Prostate volume		Operative time				Enucleated weight		High-risk bleeding group			
	Univariable		Univariable		Multivariable		Univariable		Univariable		Multivariable	
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI	P
ΔHb	1.01 (0.9–1.0)	0.27	1.01 (0.9–1.0)	0.14	–	–	1.02 (0.9–1.0)	0.11	3.13 (1.1–8.2)	0.02	3.07 (1.0–8.9)	0.03
ΔHb1	1.02 (0.9–1.0)	0.31	1.04 (1.0–1.0)	0.03	1.04 (0.9–1.0)	0.05	1.02 (0.9–1.0)	0.49	1.04 (1.5–2.4)	0.56	–	–
ΔHb2	1.01 (0.9–1.0)	0.19	1.00 (0.9–1.0)	0.72	–	–	1.03 (0.9–1.0)	0.14	10.42 (3.9–27.7)	< 0.001	11.2 (3.9–31.5)	< 0.001

As to the learning curve, the single operator in our present study had already performed a number of HoLEPs and thus was familiar with laser enucleation of prostate [4]. This may explain to a certain extent why there were no significant differences in operating time, enucleated tissue weight and blood loss between the first and the last 20 cases in our present series. Nevertheless, prostate volume increased with the number of operations performed, indicating a gain in confidence and skills to tackle larger and more complex prostates with ThuLEP over time. Notably, TURP is no longer performed in our institute and ThuLEP has been adopted as the first-line therapy for BOO. Whether this is advantageous in terms of health economy remains to be seen and a cost analysis needs to be conducted.

As to the results, our present study is consistent with other published reports [5–8]. As our initial series, previous experience with laser enucleation probably made ThuLEP easier to master and accelerated the learning curve. Compared to HoLEP our impression is that ThuLEP vaporises more tissue, makes a wider incision, and the plane between adenoma and prostate capsule is always clearly visible and can be better and more easily developed. Moreover, the wide incision allows the hydrostatic pressure to help in developing the aforementioned plane.

There was a discrepancy between the mean prostate volumes as measured on preoperative TRUS (43 g) and the enucleated weight (24 g). This contrasts to the normally quite reliable correlation between TRUS measurement and resected tissue [9] and might be explained by the high power of the thulium laser, which leads to vaporisation of some of the resected tissue. Admittedly, inter-investigator variability cannot be entirely excluded, too.

In our present series, we noticed a significant decrease in Hb from baseline to those values measured at the time of patient discharge. The same significant decrease was shown in the intraoperative period and in the postoperative time from operation to discharge. In the logistic regression, we showed that the only risk factor for intraoperative bleeding detected with univariate analysis, and confirmed with multivariate analysis, was operative time. The longer the operation the more pronounced the Hb drop was. Interestingly, according to our statistical analyses, patients when stratified into a high-risk bleeding group were not at a higher risk of an intraoperative Hb drop. In contrast, these patients were at a higher risk of postoperative bleeding in the days between ThuLEP and discharge from hospital. Patients were usually kept on postoperative i.v. fluids only on the day of the operation. Therefore, a dilution effect by over hydration seems unlikely. Despite these significant Hb drops, the transfusion rate remained very low and only one case required re-intervention for bleeding control.

If there was intraoperative bleeding it did not affect the procedure or surgical outcome overall. Gross bleeding was only sporadic when for any reason the bladder pressure decreased during the procedure (low fluid flow, resectoscope leakage etc.). Surgeons should ensure that they always have a full bladder pressure during both, enucleation and morcellation, in order to proceed. In fact, it can be said that morcellation is the more delicate part of the procedure insofar as an impaired view by bleeding may increase the risk of bladder injury. Other complications in the present study were comparable with those reported in the literature [10,11].

Conclusion

ThuLEP provides good results in terms of obstruction and symptom relief. The technique appears to be safe, easy to learn and to apply. Although prostate laser procedures are claimed to be 'bloodless', there may be a significant drop in Hb, which is directly related to operating time during the operation. In the days following the procedure, a further Hb drop can be expected, particularly in patients having DVT prophylaxis with heparin or aspirin. This risk needs to be balanced carefully against the clinical gain of the procedure itself.

Conflict of interest

None.

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