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Original Article

Feasibility of *en bloc* thulium laser enucleation of the prostate in a large case series. Are results enhanced by experience?

Giovanni Saredi [a], Giacomo Maria Pirola [b,*], Francesca Ambrosini [a], Simone Barbieri [c], Lorenzo Berti [a], Andrea Pacchetti [d], Domenico Iovino [e], Giuseppe Ietto [e], Letizia Libassi [e], Giulio Carcano [e]

[a] *Department of Urology, Ospedale di Circolo e Fondazione Macchi, Varese, Italy*
[b] *Department of Urology, Usl Toscana Sud Est, San Donato Hospital, Arezzo, Italy*
[c] *Centro Cardiologico Monzino, IRCCS, Milan, Italy*
[d] *Department of Urology, University of Genova, Genova, Italy*
[e] *Department of Surgery, University of Insubria, Varese, Italy*

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Abstract *Objective:* To provide the first large single-operator case series of patients who undergo "*en bloc*" thulium laser enucleation of the prostate (ThuLEP) and to demonstrate an improvement in enucleation efficacy with experience.
Methods: We prospectively evaluated a cohort of patients with symptomatic benign prostatic hyperplasia (BPH) who underwent "*en bloc*" ThuLEP between May 2015 and November 2017. Association between dependent variables (delivered energy and operating time) and independent variables (adenoma volume and experience) were estimated with regression analysis. The experience was calculated as the time interval between the date of the first operation of the series and the date of the operation being considered.
Results: A total of 100 patients were registered for the study. Median operative time was 56.5 min (interquartile range [IQR]: 40–85 min). Median enucleation time was 17.4 min (IQR: 15–21.5 min). Median enucleation index (enucleation time per adenoma gram) was 0.3 min/g (0.2–0.3 min/g). The overall operative time is not influenced by experience, but we registered a significant trend towards a reduction in the total amount of energy delivered energy normalized per adenoma gram ($p = 0.0148$).

* Corresponding author.
E-mail address: gmo.pirola@gmail.com (G.M. Pirola).
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Conclusion: We believe that further attention is needed for these new "*en bloc*" prostatic enucleation techniques, which can facilitate some surgical steps, leading to a widespread use of laser technology for BPH surgical treatment.

1. Introduction

Transurethral laser endoscopic enucleation of the prostate (EEP) techniques is becoming the standard of care for benign prostatic hyperplasia (BPH) surgical treatment. This statement has been proven by a recent randomized controlled trial comparing those endoscopic techniques with open prostatectomy, showing similar outcomes with the advantages of reduced hospitalization, catheter period and morbidity [1].

Thulium laser enucleation of the prostate (ThuLEP) is recognized to be a valid alternative to transurethral resection of the prostate (TURP) and Holmium laser enucleation of the prostate (HoLEP) in men with moderate to severe lower urinary tract symptoms (LUTS), leading to immediate and mid-term objective and subjective improvements [2].

Moreover, a recent editorial comment by Herrmann [3], points out the fact that EEP techniques achieve similar results independently from the different type of energy adopted.

The classical laser enucleation technique for HoLEP and ThuLEP consisted in a three-lobe enucleation of the adenoma with a separate enucleation of the median and lateral lobes. Scoffone and Cracco [4] developed an "*en bloc*" enucleation technique for HoLEP in 2016, showing a potential role of this alternative technique to ease some difficult intraoperative steps of enucleation and to improve the learning curve of HoLEP.

In October 2017, we published the first depiction of "*en bloc*" ThuLEP, showing the capacity of this technique to shorten enucleation time and to reduce the amount of laser energy delivered to achieve a complete adenoma enucleation, compared to the classical "three-lobe" technique [5].

However, those initial results were not confirmed by a larger casistic and only medium-sized prostates were considered. Herein, we present the results obtained from our updated single-surgeon prospective analysis of a 100-patient casistic.

2. Methods

2.1. Patient population

After receiving institutional review board approval (DGEN 421/2017), from May 2015 to November 2017, we prospectively recruited 100 patients suffering from symptomatic BPH who were treated with "*en bloc*" ThuLEP in our institution (Department of Urology, Ospedale di Circolo e Fondazione Macchi, Varese, Italy). All patients underwent a previous complete clinical and symptomatic evaluation, by administering the International Prostate Symptom Score (IPSS) questionnaire and the Quality of Life (QoL) index. Uroflowmetry, prostatic-specific antigen (PSA), postvoid residual urine evaluation, urine culture test and ecographic estimation of prostate and adenoma volume were always performed before giving surgical indication. Inclusion criteria were Q_{max} less than 15 mL/s, IPSS greater than 8, or patients with medical therapy failure. Patients who had undergone previous urethral/prostatic surgery, or with prostate cancer, urethral strictures, or urodynamically diagnosed detrusor underactivity were not considered in this study. Written informed consents were always collected from all participants and patients' data were progressively collected in an unidentified Microsoft Excel® database. Table 1 lists all the main patients' baseline characteristics.

2.2. Instrumentation

The surgical procedure performed in our institution has been fully standardized. The same laser machine (Cyber TM® 200 W; Quanta System, Solbiate Olona, Varese, Italy)

Table 1 Baseline patients'characteristics.

Parameter	"*en bloc*" ThuLEP (n = 100)
Age (year)[a]	70.00 ± 7.27
Prostatic adenoma volume (mL)[b]	59 (48, 76)
Prostatic volume in classes, *n* (min–max)	
<60 mL	52 (20–59)
60–79 mL	26 (60–78)
80–99 mL	10 (80–99)
100–120 mL	8 (100–120)
>120 mL	4 (132–167)
Indwelling catheterization, *n* (%)	24 (26)
IPSS score[b]	26 (21, 30)
QoL[b]	4 (4, 5)
PSA (ng/mL)[a]	4.16 ± 8.46
Q_{max} (mL/s)[a]	8.58 ± 2.80
PVR (mL)[a]	70.00 ± 35.00
Preoperative Hb (g/dL)[b]	14.6 (13.3, 15.5)

Hb, hemoglobin; IPSS, International Prostate Symptom Score; PSA, prostatic specific antigen; PVR, postvoid residual urine; Q_{max}, maximum urinary flow rate; QoL, Quality of Life Index; ThuLEP, thulium laser enucleation of the prostate.
[a] Data presented as mean ± SD.
[b] Data presented as median (interquartile range).

was adopted for all patients, using 800 μm calibre end-firing reusable laser fibres. Maximum power setting was 110 W. The resectoscope was a 26 Ch calibre with continuous 0.9% saline irrigation (Karl Storz, Tuttlingen, Germany). A 26 Ch morcellator device (Piranha®; Wolf, Knittlingen, Germany) inserted by means of a nephroscope sheath was utilized in all procedures. Continuous bladder irrigation was left for the first 24 h postoperatively. Bladder catheter was removed on the first day postoperatively in absence of macroscopic haematuria.

2.3. Previous experience

We started to perform "*en bloc*" ThuLEP after a wide experience in "three-lobe" ThuLEP [6], with more than 300 cases performed since June 2012. Moreover, results presented in this study refer to a single expert surgeon (Giovanni Saredi).

2.4. Surgical procedure

The surgical technique has been fully described in a precedent work [5].

"*En bloc*" ThuLEP starts with a single incision from the bladder neck to the veru montanum at 5 o' clock. After identifying the capsular plane at the apex, the left lobe is enucleated counterclockwise from 5 to 11 o'clock; the right lobe, together with the median lobe, is enucleated clockwise from the apex to the prostatic base at 11 o'clock. Enucleation is finally completed with an anterior apical incision from 10 to 2 o'clock of the remaining fan-shaped mucosa. Regarding morcellation, "*en bloc*" ThuLEP is not any different from the classical technique described by Herrmann et al. [7], as the device morcellates the isthmus of the prostate first (being the weakest point), splitting the prostate into two lobes which are then morcellated separately.

2.5. Perioperative evaluation and follow-up

The outcomes evaluated to study the efficacy of this technique are listed in Table 2.

Energy index and consequently the enucleation time are the main parameters of this analysis.

Table 2 Intraoperative characteristics and outcomes of the whole patients' series presented in the study.

Parameter	"*en-bloc*" ThuLEP (n = 100)
Total surgical time (min)[a]	56.5 (40, 85)
Enucleation time (min)[a]	17.4 (15, 21.5)
Delivered energy (J)[a]	108 652 (88 473, 125 835)
Enucleation index (min/g)[a]	0.3 (0.2, 0.3)
Energy index (J/g)[a]	6202.5 (5903.2, 6519.4)
Hemoglobin drop (g/dL)[a]	-1.4 (-1.9, -0.7)
Catheterization (day)[a,b]	1 (1, 12)
Hospital discharge (day)[a,b]	1 (1, 2)

ThuLEP, thulium laser enucleation of the prostate.
[a] Results are expressed as median (interquartile range).
[b] Day in which the bladder catheter was kept in place after the intervention.

Perioperative and postoperative complications were reported according to the modified Clavien–Dindo System [8].

2.6. Statistical analysis

Continuous variables are presented as mean ± SD. Not normally distributed variables are presented as median and interquartile ranges (IQR).

Association between dependent variables (delivered energy and operating time) and independent variables (adenoma volume and experience) were estimated with regression analysis. Experience was calculated as the time interval between the date of the first operation of the series and the date of the operation being considered. Energy was divided into high and low delivered energy, above or below the median value respectively, and experience was divided into tertiles (low, medium, and high experience). The odds ratio (OR) between high delivered energy and tertile of experience was calculated.

Comparisons between the results among the three tertiles of experience were achieved through the ANOVA (Analysis of Variance) test.

Receiver operating characteristic (ROC) curves were calculated and the areas under the ROC curves (AUC) with 95% confidence intervals (CI) were used to measure the ability of the considered variables. Results are presented as OR with 95%CI.

All calculations were computed with the aid of the SAS software package (Version 9.4, SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Patient characteristics

A total of 100 patients were registered for the study. The complete patients' baseline characteristics are presented in Table 1. Mean age was 70.00 ± 7.27 years. Twenty-four patients underwent the intervention after acute urinary retention, so they were under indwelling catheterization. Median prostatic volume was 59 mL (IOR: 48–76 mL). Table 1 also reports the distribution of prostatic volume in classes.

3.2. Perioperative data

Median operative time was 56.5 min (IQR: 40–85 min). Median enucleation time was 17.4 min (IQR: 15.0–21.5 min). Median enucleation index (enucleation time per adenoma gram) was 0.3 min/g (IQR: 0.2–0.3 min/g). These results are reported in Table 2.

Regarding perioperative complications, according to the modified Clavien–Dindo System [8], only one early reintervention for hemostasis and clot evacuation (clavien grade IIIb) was necessary. Table 3 sums up all the surgical complications occurred in our series.

3.3. Influence of operator's experience on surgical results

Table 4 presents the same outcomes of Table 2 but is divided between the three tertiles of experience. After a

Table 3 Analysis of the surgical complications occurred in our series within 30-day perioperative period. Results are reported according to the modified Clavien Grade [8].

Complication, grade	Description	*n*	Management
Clavien Grade I	- Early urinary retention	3	Prolonged bladder catheterization
	- Clot retention without surgical revision	3	Prolonged bladder irrigation
Clavien Grade II	- Massive hematuria	2	Transfusions
	- Urinary tract infection	4	Antibiotic treatment
Clavien Grade IIIb	- Remnant bladder stone	1	Reintervention for endoscopic cystolitholapaxy
	- Hemorrhage/ clot retention	1	Cystoscopy, clot evacuation, monopolar coagulation
Total		14	

careful statistical analysis of our case series, we can state that overall operative time ($p = 0.361$) is not influenced by experience as well as in the enucleation index ($p = 0.325$). However, there is a significant trend towards a reduction in the total amount of delivered energy ($p = 0.054$) and consequently in the energy index (energy delivered normalized per adenoma gram) ($p = 0.005$) with increasing experience.

The OR shows that there is 80% less probability of a high energy delivery for medium and high experience compared to the first tertile (low experience) (Fig. 1).

Fig. 2 provides ROC curves of the statistical model utilized to describe the effect of experience on the reduction of the total amount of energy, and consequently on the enucleation efficacy. The AUC is significatively high (0.783).

3.4. Postoperative data

Table 5 summarizes our 6-month follow-up data. These results are satisfactory, with a clear improvement in both functional and symptomatic parameters. No late complications such as urethral strictures or bladder neck narrowing occurred in our series.

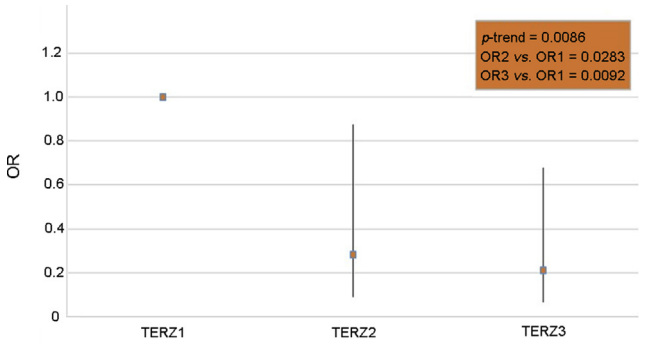

Figure 1 The odds ratio (OR) shows that there is 80% less probability of a high energy delivery for medium and high experience compared to the first tertile (low experience). TERZ, tertile; OR1, first tertile of experience; OR2, second tertile of experience; OR3, third tertile of experience.

4. Discussion

During the last decade, there has been growing interest for laser EEP techniques. HoLEP has been fully recognized to be the standard of reference; however, ThuLEP has progressively reached a comparable success rate and many papers show the equal effectiveness of these two techniques, both in terms of perioperative and follow-up outcomes [9].

Potential advantages of ThuLEP over HoLEP are represented by the shorter learning curve, the higher coagulation power and, probably, the shorter operative time needed to complete the procedure. However, a recent matched-pair comparison study between HoLEP and ThuLEP showed that despite a shorter operative time in favor of ThuLEP, the outcomes between those techniques are comparable [10].

Netsch et al. [11] validated the efficacy of Thulium VapoEnucleation of the prostate (ThuVEP) in 2014, with their 124-patient series, showing excellent results at early and late follow-up, without reporting significative complications.

Those satisfactory results were also confirmed in a systematic review from the same working group, in which

Table 4 Intraoperative characteristics and outcomes comparison between the three tertiles of experience (low, medium and high experience).

Parameter	Low experience ($n = 33$)	Medium experience ($n = 33$)	High experience ($n = 33$)	*p*-Value
Total surgical time (min)	61.5 (46.5, 89.5)	55 (41.5, 67.5)	56.5 (39, 85)	0.361
Enucleation time (min)	18.4 (16, 22.7)	16.4 (12.3, 20.5)	17.4 (13.8, 20.3)	0.299
Delivered energy (J)	117 039.5 (102 230, 138 037)	100 867 (80 053, 118 264)	102 719.5 (82 284.5, 112 029.5)	0.054
Enucleation index (min/g)	0.3 (0.3, 0.3)	0.3 (0.2, 0.4)	0.3 (0.2, 0.4)	0.325
Energy index (J/g)	6476.2 (6054.5, 6594.9)	6117.4 (5910.9, 6497.8)	6005.7 (5754.7, 6312.5)	0.005
Hemoglobin drop (g/dL)	−1.5 (−2.5, −0.6)	−1.3 (−1.7, −0.7)	−1.4 (−1.8, −0.5)	0.723

Results are expressed as median (interquartile range). The statistic comparison has been performed with the Analysis of Variance (ANOVA) test.

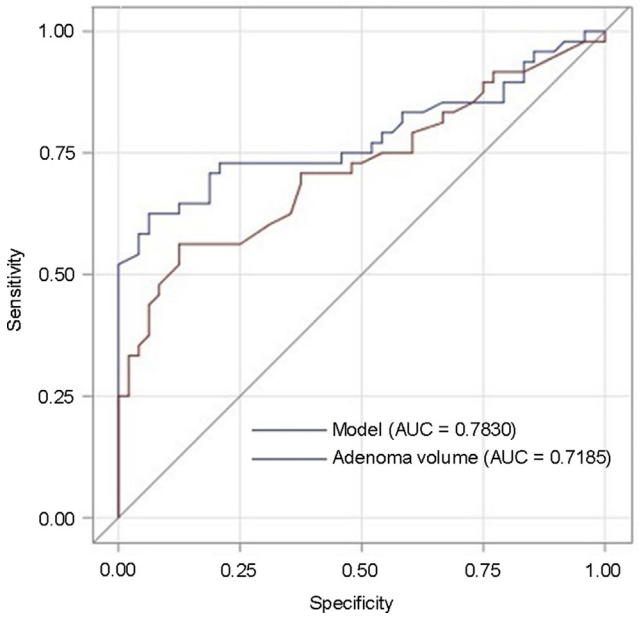

Figure 2 ROC curves of the statistical model utilized to describe the effect of experience on the reduction of the total amount of energy, and consequently on the enucleation efficacy. The area under the curve (AUC) is significatively high (0.783). ROC, receiver operating characteristic.

Tm:YAG enucleation was confirmed to be a safe, effective and size-independent technique for EEP [12].

During the last 2 years, some authors described alternative enucleation techniques and attention has been focused on "*en bloc*" adenoma removal, both for HoLEP and ThuLEP.

In 2015, Kim et al. [13] described an "All-in-One" technique for adenoma enucleation in a 47-patient series with medium-sized prostates, using Thulium laser, with which the adenoma was progressively dissected circumferentially, departing from the apex toward the prostatic base. Results were encouraging, showing a low complication rate and a significative improvement in IPSS score results and Q_{max} at the 3-months follow-up.

Scoffone and Cracco [4] also described an "*en bloc*" procedure for HoLEP, with a precise depiction of all surgical passages of the enucleation, emphasizing the potential of this technique to ease some difficult intraoperative steps of HoLEP and to improve the surgical learning curve.

Several papers discussed the learning curve for EEP techniques. An interesting work by Robert et al. [14] analyzed the learning curve for HoLEP in different centers in France, involving a total of nine surgeons without previous HoLEP experience, showing that several problems and complications were encountered during the first cases. In fact, only five of them arrived to perform the first 20 cases alone. Authors highlighted the need of dedicated training programs with direct tutorship for the first cases. Another work by Shah et al. [15] showed that 50 cases are needed for a single surgeon to be confident with the HoLEP procedure and therefore being considered expert. The same finding is shown in a single surgeon series of 253 patients [16].

Regarding the other EEP techniques, Peyronnet et al. [17] compared a prospective series of 100 HoLEP and green laser enucleation of the prostate (GreenLEP), showing shorter enucleation time and less energy delivered in favor of GreenLEP, a similar complication rate and an inferior catheterization time in the HoLEP group. The learning curves purposed by those authors ranged from 14 to 30 cases for GreenLEP and 22 to 40 cases for HoLEP [17]. Hirasawa et al. [18] presented a wide single surgeon series of 603 patients undergoing bipolar enucleation of the prostate. Authors noticed a clear improvement of surgical efficiency after the first 50 cases [18].

In several studies, ThuLEP appeared to have a reduced learning curve compared with HoLEP. In fact, we already demonstrated that 20 cases are enough to be confident with the procedure also without a direct tutor assistance [6] and the same number of procedures were indicated to be enough to complete a learning curve in a recent study by Herrmann et al. [19]. A recent paper from our working group [5] showed that "*en bloc*" ThuLEP reduces operative time, blood loss and overall energy required to perform the enucleation in comparison with the classical "three lobes" technique. This is made possible by a single identification of the plane between the adenoma and the peripheric prostate, starting the enucleation at the prostatic apex at 5 o'clock and ascending, counterclockwise for the left lobe and then clockwise for the right and median lobes, which are dissected together, towards the bladder neck. This technique is now the standard of care in our institution. Previously cited technical advantages were demonstrated comparing 50 initial cases with another 50 similar cases performed using the classical "three-lobe" technique. Herein we show the results obtained from a large prospective series of patients treated with "*en bloc*" ThuLEP performed by a single surgeon (Giovanni Saredi) evaluating the learning curve in the first 100-patient series.

The key result of this study is the high enucleation efficacy, which leads to a reduction of operative time, with an excellent improvement of urinary symptoms after the procedure. The further statistical analysis performed shows how the enucleation efficiency was improved with the increasing experience, by means of a significative reduction

Table 5 Follow-up on functional results at 6 months after surgery.

Parameter	"*en bloc*" ThuLEP ($n = 100$)	*p*-Value*
IPSS score[a]	3 (1, 6)	<0.001
Delta IPSS[a]	−28.0 (−30.5, −21.0)	—
QoL[a]	1 (1, 2)	<0.001
Q_{max} (mL/s)[a]	19 (17, 21)	<0.001
Delta Q_{max} (mL/s)[b]	14.55 ± 4.6	—
Postoperative PSA (ng/mL)[a]	1.0 (0.6, 1.5)	<0.001

IPSS, International Prostate Symptom Score; PVR, postvoid residual urine; Q_{max}, maximum urinary flow rate; QoL, Quality of Life Index. The *p*-Value refers to a comparison with baseline characteristics (Table 1) utilizing the paired *t*-test. PSA, prostate-specific antigen; ThuLEP, thulium laser enucleation of the prostate; —, not available.

[a] Results are expressed in median (min, max).

[b] Results are expressed in mean ± SD.

of delivered energy in the different tertiles (OR) of experience (OR1 *vs.* OR2, $p = 0.0283$; OR2 *vs.* OR3, $p = 0.0092$, respectively, Fig. 1).

The important PSA drop proves the complete enucleation of the adenoma performed with this technique. As we showed in a precedent study, energy delivered to the prostatic capsule is lower than in conventional "three lobes" ThuLEP and this could explain the relative absence of irritative symptoms during early follow-up. Moreover, results are in line with the widest case series for ThuLEP.

These encouraging results, in line with the beginning of our casistic, show that the procedure is safe and effective, and it can be performed by endourologists who are experienced in "three-lobe" ThuLEP, without the need of a specific learning curve, also for large adenomas. As the technique is still recent, there are no similar studies in literature that can confirm these statements and we hope that our results will enhance a debate about the most correct indications for each EEP technique. A main limitation of the results here presented is that they refer to a single surgeon, already experienced in "three-lobe" ThuLEP, so this experience cannot be considered as a reference for a novice surgeon facing this technique. Moreover, this is a non-randomized series without a strict inclusion criterion for prostate volume, so that we present only few cases with prostate volumes of more than 80 g (22/100 cases in total). However, we did not appreciate any technical limitation during the enucleation step due to the volume of the adenoma. Further studies involving both experienced and novice surgeons are needed to clarify the feasibility of this technique and to determine if this approach is superior to the "three lobes" technique.

5. Conclusion

This study provides a large and single-surgeon case series of patients treated with "*en bloc*" ThuLEP. Results show that the technique is safe, feasible and effective in treating prostatic adenomas of all sizes with a low complication rate. We believe that further attention is needed for these new "*en bloc*" prostatic enucleation techniques, which can facilitate some surgical steps, leading to a widespread use of laser technology for BPH surgical treatment, for both ThuLEP and HoLEP.

Author contributions

Study design: Giovanni Saredi, Giacomo Maria Pirola.
Manuscript drafting and editing: Giacomo Maria Pirola, Francesca Ambrosini.
Data analysis: Simone Barbieri, Francesca Ambrosini, Andrea Pacchetti.
Data acquisition: Lorenzo Berti, Domenico Iovino, Giuseppe Ietto, Letizia Libassi.
Critical revision of the manuscript: Giulio Carcano, Giovanni Saredi.

Conflicts of interest

The authors declare no conflicts of interest.

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