ORIGINAL PAPER

FUNCTIONAL UROLOGY

# Thulium laser transurethral incision of the prostate with ejaculation-sparing intent: 2-year follow-up outcomes from a high-volume centre

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Citation: Carilli M, Vittori M, Iacovelli V, et al. Thulium laser transurethral incision of the prostate with ejaculation-sparing intent: 2-year follow-up outcomes from a high-volume centre. Cent European J Urol. 2024; 77: 235-242.

Article history
Submitted: Nov. 23, 2023
Accepted: Jan. 23, 2024
Published online: April 7, 2024

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**Introduction** Several 'ultra-minimally-invasive' surgical treatments (uMISTs) have been developed, aiming to relieve benign prostatic obstruction (BPO) and spare ejaculatory function; however, such techniques do not always ensure substantial improvements in uroflowmetry parameters. The aim of the present study was to evaluate the 2-year functional outcomes of thulium laser transurethral incision of the prostate (ThuIP) as an alternative to uMISTs.

**Material and methods** Data of consecutive patients affected by BPO with indication to surgical intervention and a strong will to spare ejaculatory function were collected on a dedicated prospectively maintained database. A specific "trifecta" was identified as the contemporary presence of: (1) post-operative Qmax ≥15 ml/s; (2) absence of early (within 90 days) complications; and (3) preserved antegrade ejaculation.

**Results** 120 patients underwent ThuIP and were analysed. Median catheterisation time was 2 days (IQR 2-2). Significant improvements in IPSS and IPSS-QoL scores and uroflowmetry parameters were observed at all follow-up times. At the last follow-up visit (24 months) the median ΔIPSS was -12 (-17; -9), median ΔIPSS-QoL was -3 (-4; -2), median ΔQmax was +7.7 ml/s (+5.2; +11.0), and median ΔPVR was -50 ml (-100; 0) (all p-values <0.001). Fourteen patients reported postoperative absence of antegrade ejaculation (11.7%). Overall, trifecta was achieved in 86 patients (71.7%) at 6 months, in 79 patients (65.8%) at 12 months, and in 75 patients (62.5%) at 24 months.

**Conclusions** ThuIP allows for a significant improvement in uroflowmetry parameters and patient-reported outcomes at 2-year follow-up. Moreover, antegrade ejaculation is preserved in approximately 90% of cases.

Key Words: ejaculation sparing ‹› thulium laser ‹› TUIP ‹› benign prostatic obstruction ‹› lower urinary tract symptoms

## INTRODUCTION

Over the years, endoscopic treatment of benign prostatic obstruction (BPO) secondary to benign prostatic hyperplasia (BPH) with different energy sources has become the standard of care, despite its impact on sexual well-being: in fact, post-operative ejaculatory dysfunction is often considered an "inevitable" consequence of prostatic surgery (occurring in over 70% of the cases) [1], with a non-negligible impact on quality of life, especially in younger and sexually-active patients [2]. For this reason, several so-called 'ultra-minimally invasive surgical treatments' (uMISTs) have been developed, aiming to both relieve from BPO and spare the ejaculatory function. These techniques have been reported to preserve antegrade ejaculation in a high percentage of patients, but they do not always ensure

substantial improvement in uroflowmetry parameters [3, 4].
Transurethral incision of the prostate (TUIP) was described almost 50 years ago [5], showing a similarly low risk of loss of antegrade ejaculation, beyond being equivalent to transurethral resection of the prostate (TURP) in relieving from BPO in men with lower urinary tract symptoms (LUTS) and prostate size <30 ml [6].
We analysed the outcomes of this procedure in its modern laser declination, on a large cohort of patients, with less stringent inclusion criteria than those proposed by the European Association of Urology (EAU) guidelines (LUTS with absolute indications for surgery or non-responders to medical treatment or those who do not want medical treatment but request active treatment, and prostate volume <30 ml) [7]. The aim of the present study was to evaluate the mid-term functional outcomes of thulium laser transurethral incision of the prostate (ThuIP).

## MATERIAL AND METHODS

### Patients

Data of consecutive patients affected by BPO and LUTS refractory to medical treatment or intolerance to medical therapy with indication to surgical intervention (maximum flow rate (Qmax) <15 ml/s and International Prostate Symptom Score (IPSS) >12 [8]) and strong will to spare the ejaculatory function were collected on a dedicated, prospectively maintained database between September 2018 and April 2021.
The study was conducted in accordance with the Declaration of Helsinki and its later amendments. The study was approved by the local institutional Ethics Committee of San Camillo Forlanini Hospital, Rome (approval no. STS CE Lazio 1/N-840). Informed consent was taken from all the patients.
Exclusion criteria were prostate volume >80 ml; previous prostate surgery; urethral strictures; bladder stones; history of prostate or bladder cancer; indwelling catheter; neurogenic bladder dysfunction or urinary incontinence; and absent/compromised ejaculatory function.

### Outcomes measurements

Preoperative variables, including age, American Society of Anesthesiologists (ASA) score [9], serum prostate-specific antigen (PSA), prostate volume, presence of median lobe (defined as intravesical prostatic protrusion >1 cm assessed by preoperative ultrasonography) [10], eventual intaking of medical therapy for BPO, Qmax with post-voiding residual volume (PVR), International Prostate Symptom Score (IPSS) with quality of life (QoL) [11], International Index of Erectile Function (IIEF-5) score [12], and ejaculatory function status, were collected at baseline.
Intra- and perioperative data were collected, including operative time, length of hospital stay, and catheterisation time. Specifically, the rate of postoperative urinary incontinence was recorded (defined as patient requiring >1 pad after surgery). Eventual postoperative complications were recorded and classified according to the Clavien-Dindo system [13]. Readmissions were recorded as well. Post-operative functional outcomes were evaluated at 6, 12, and 24 months by clinical consultation including uroflowmetry (Qmax and PVR) and administration of IPSS, IPSS-QoL, and IIEF-5 questionnaires. Post-operative ejaculatory function re-assessment was performed at one-month follow-up by physician interview: patients were clustered into 2 groups based upon their answer (lost versus maintained antegrade ejaculation). During subsequent follow-up visits, patients were asked whether any change in ejaculatory function occurred from the previous consultation.
For the purpose of the study, we identified a specific "Trifecta" as the contemporary presence of: (1) post-operative Qmax ≥15 ml/s; (2) absence of early (within 90 days) complications; and (3) preserved antegrade ejaculation. Finally, the number of surgical failures (i.e. patients who restarted alpha-blocker therapy or underwent other prostatic surgical procedures) were recorded during follow-up.

### Surgical procedure

All procedures were performed under spinal anaesthesia with a continuous flow 26 F resectoscope (Richard Wolf, Knittlingen, Germany) and a 550 $\mu$m thulium laser end-fire fibre connected to a 200 W Cyber TM laser generator (Quanta System, Samarate (VA), Italy). Cutting and coagulation were set at 70 and 40 W, respectively [14].
In the absence of median lobe, the bladder neck was deeply incised at 5 or 7 o'clock down to the prostatic capsule in a retrograde fashion to the verumontanum (Figure 1A). In the presence of median lobe, it was vapo-resected. In all cases, an ejaculation-sparing intent was pursued by preserving the paracollicular and supramontanal tissue (about 1 cm above the verumontanum, while identifying ejaculatory duct orifices if possible) (Figure 1B).

## Statistical analysis

Continuous variables were summarised using medians and interquartile ranges (IQR); frequencies and proportions were used to report categorical variables. All data were tested for normality using the Shapiro-Wilk test. The Wilcoxon non-parametric test was performed to compare repeated measures of functional results over time. The chi-square test was used for categorical variables. Univariate and multivariate logistic regression models were built to identify predictors of post-operative absence of antegrade ejaculation, trifecta achievement and surgical failure at 24 months. Data analysis was conducted using SPSS 21.0 software (IBM, Armonk, NY, USA). Statistical significance was defined as a p-value <0.05.

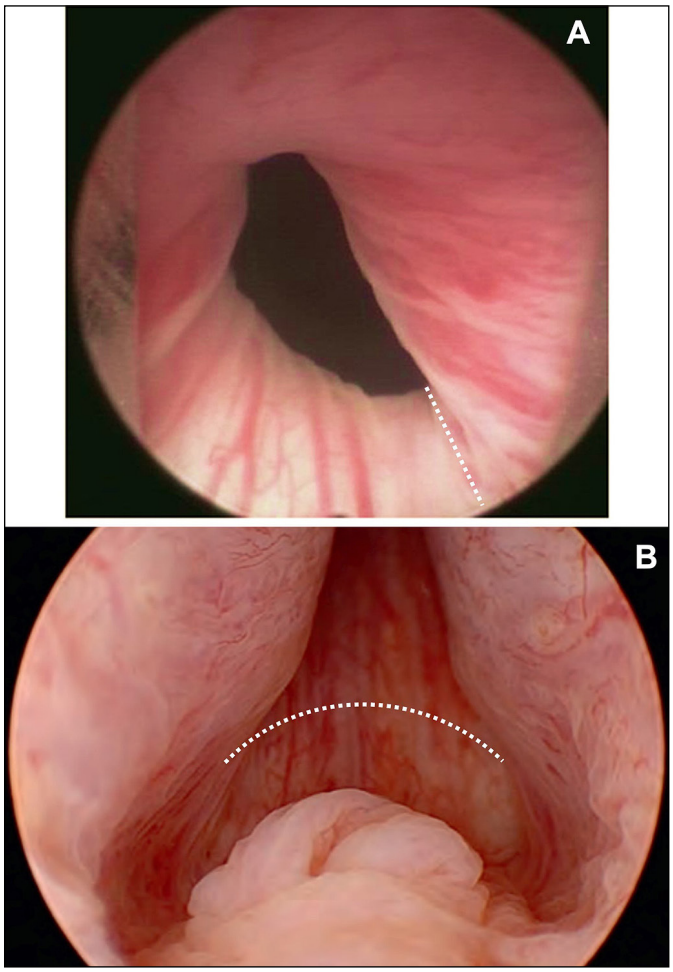


**Figure 1. A:** *Incision of the bladder neck;* **B:** *Paracollicular and supramontanal tissue (about 1 cm above the verumontanum).*

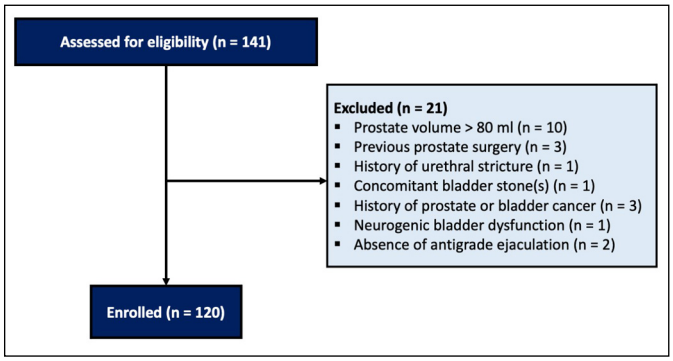


**Figure 2.** *Flow chart.*

**Table 1.** *Baseline characteristics*

| | n = 120 |
|---|---|
| Age (years), median (IQR) | 55 (49–63) |
| Prostate volume (ml), median (IQR) | 35 (29–50) |
| Median lobe, n (%) | |
| No | 88 (73.3) |
| Yes | 32 (26.7) |
| ASA score, n (%) | |
| ASA I | 37 (30.8) |
| ASA II | 72 (60.0) |
| ASA III | 11 (9.2) |
| PSA (ng/ml), median (IQR) | 1.4 (0.7–2.2) |
| BPH medical therapy, n (%) | |
| No therapy | 21 (17.5) |
| Alpha-blocker | 94 (78.3) |
| Alpha-blocker + 5-ARI | 5 (4.2) |
| IPSS, median (IQR) | 21 (17–24) |
| IPSS-QoL, median (IQR) | 5 (4–5) |
| IIEF-5, median (IQR) | 19 (17–21) |
| Qmax (ml/s), median (IQR) | 9.8 (7.7–12.0) |
| PVR (ml), median (IQR) | 50 (23–100) |

ASA – American Society of Anesthesiologists; PSA – prostate-specific antigen; 5-ARI – 5-alpha reductase inhibitor; IPSS – International Prostate Symptoms Score questionnaire; IPSS-QoL – IPSS quality of life score; IIEF-5 – International Index of Erectile Function; Qmax – maximum flow rate; PVR – post-void residual

**Table 2.** *Perioperative outcomes*

| | n = 120 |
|---|---|
| Operative time (min), median (IQR) | 15 (15–30) |
| Surgical technique, n (%) | |
| Incision | 88 (73.3) |
| Incision + median lobe vaporesection | 32 (26.7) |
| Catheter time (days), median (IQR) | 2 (2–2) |
| Length of hospital stay (days), median (IQR) | 3 (2–3) |
| Post-operative complications, n (%) | |
| Clavien-Dindo I-II | 6 (5.0) |
| Transient AUR requiring re-catheterisation | 4 (3.4) |
| UTI with fever >38°C requiring intravenous antibiotics | 1 (0.8) |
| Macrohematuria requiring blood transfusion and bladder irrigation | 1 (0.8) |
| Clavien-Dindo IIIa-V | 1 (0.8) |

AUR – acute urinary retention; UTI – urinary tract infection; IQR – interquartile range

## RESULTS

After accounting for the exclusion criteria (Figure 2), 120 patients underwent ThuIP at our Institution. Table 1 shows the distribution of baseline patient's characteristics. Preoperatively, 99 patients (82.5%) were receiving at least one medical treatment for BPO.

Table 2 summarises the perioperative outcomes. Eighty-eight patients received a pure incision of the bladder neck (73.3%), while 32 patients (26.7%) required an additional vaporesection of the obstructing median lobe. Median catheterisation time was 2 days (IQR 2-2). No patient had incontinence at catheter removal. Forty-three patients (35.8%) reported mild-to-moderate dysuria and/or pelvic pain (transient and self-limiting within 14 days). Six low-grade Clavien-Dindo complications (5%) occurred. One patient had higher-grade complication (Clavien-Dindo IIIa) and underwent endoscopic re-intervention on the second post-operative day due to arterial bleeding and clot retention.

Fourteen patients reported postoperative absence of antegrade ejaculation (11.7%) at the one-month interview. During subsequent follow-up visits (6, 12, and 24 months) no patients reported any variation in ejaculatory function from the previous visit.

A significant improvement in IPSS and IPSS-QoL scores and uroflowmetry parameters compared to baseline values was observed at all follow-up times (Table 3). At last follow-up visit (24 months), median ΔIPSS was -12 (-17; -9), median ΔIPSS-QoL was -3 (-4; -2), median ΔQmax was +7.7 ml/s (+5.2; +11.0), and median ΔPVR was -50 ml (-100; 0) (all p-values <0.001). Erectile function as assessed by IIEF-5 did not show any significant variation during the follow-up (p >0.05).

Overall, trifecta was achieved in 86 patients (71.7%) at 6 months, in 79 patients (65.8%) at 12 months, and in 75 patients (62.5%) at 24 months.

Twelve patients experienced surgical failure at 12 months (7 patients had to re-start alpha-blocker therapy, one patient underwent TURP, and 4 patients underwent thulium-laser enucleation of prostate), while another 4 patients experienced failure at 24 months (one patient had to re-start alpha-blocker therapy, and 3 patients underwent TURP). Overall, the cumulative incidence of failure was 13.3% (16/120) at 24 months.

Univariate logistic regression model identified age (odds ratio [OR] 1.08, p = 0.01), prostate volume >30 ml (OR 5.56, p = 0.03), presence of median lobe (OR 3.24, p = 0.04), and each one-minute increase in operative time (OR 1.06, p = 0.01) as predictors

**Table 3.** *Differences in functional outcomes during follow-up*

| | Δ T1-T0* (n = 120) | p-value | Δ T2-T0* (n = 120) | p-value | Δ T3-T0* (n = 108) | p-value |
|---|---|---|---|---|---|---|
| ΔIPSS, median (IQR) | -11 (-16;-6) | <0.001 | -12 (-17;-8) | <0.001 | -12 (-17;-9) | <0.001 |
| ΔIPSS-QoL, median (IQR) | -3 (-4;-1) | <0.001 | -3 (-4;-2) | <0.001 | -3 (-4;-2) | <0.001 |
| ΔIIEF-5, median (IQR) | 0 (-1; +1) | 0.3 | 0 (0; 0) | 0.6 | 0 (0; +1) | 0.08 |
| ΔQmax (ml/s), median (IQR) | +8.3 (+6.4; +11.8) | <0.001 | +7.7 (+5.3; +11.7) | <0.001 | +7.7 (+5.2; +11.0) | <0.001 |
| ΔPVR (ml), median (IQR) | -50 (-79; 0) | <0.001 | -50 (-90; 0) | <0.001 | -50 (-100; 0) | <0.001 |

* T0 = preoperative; T1 = 6 months; T2 = 12 months; T3 = 24 months
IPSS – International Prostate Symptoms Score questionnaire; IPSS-QoL – IPSS quality of life score; IIEF-5 – International Index of Erectile Function; Qmax – maximum flow rate; PVR – post-void residual

**Table 4.** *Logistic regression model predicting postoperative absence of antegrade ejaculation*

| Variable | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | OR (95% C.I.) | p-value | OR (95% C.I.) | p-value |
| Age | 1.08 (1.02–1.14) | 0.01 | 1.08 (1.01–1.16) | 0.03 |
| Prostate volume >30 ml | 5.56 (1.19–26.07) | 0.03 | 4.36 (0.76–25.04) | 0.09 |
| Presence of median lobe | 3.24 (1.04–10.13) | 0.04 | 0.26 (0.02–3.62) | 0.31 |
| Preoperative Qmax | 1.02 (0.89–1.02) | 0.89 | – | – |
| Preoperative PVR | 0.99 (0.98–1.00) | 0.36 | – | – |
| Operative time | 1.06 (1.01–1.10) | 0.01 | 1.07 (0.97–1.17) | 0.14 |

OR – odds ratio; C.I. – confidence interval; Qmax – maximum flow rate; PVR – post-void residual

of post-operative absence of antegrade ejaculation. Preoperative Qmax was found as a predictor of trifecta achievement (OR 1.22, p = 0.01). Prostate volume >30 ml was found as predictor of surgical failure (OR 4.01, p = 0.04). At multivariate analysis, age was confirmed as an independent predictor of absence of antegrade ejaculation (OR 1.08, p = 0.03) (Table 4).

## DISCUSSION

The present study suggests that, at a mid-term follow-up, ThuIP can be a viable transurethral alternative to uMISTs in paring the relief from BPO to the preservation of ejaculatory function.

Historically, urologists have focused on uroflowmetry parameters and patient-reported outcomes as yardsticks for the efficacy of a surgical treatment for BPO.

However, clinical practice of more recent years witnessed how sexual function, particularly ejaculation, is sometimes even more important for the patient. Indeed, new devices and technologies have been developed looking for a balance between deobstruction and incidence of post-operative ejaculatory dysfunction [15, 16].

In the setting of endoscopic treatments for BPO, preservation of ejaculatory function seems to be strictly related to the preservation of the paracollicular and supramontanal prostatic tissue, rather than to the integrity of the bladder neck [17, 18]. Based on these findings, several ejaculation-sparing modifications to "standard" endoscopic procedures have been described while taking into account the above-mentioned anatomical landmarks [19].

Decades ago, some authors were performing TUIP while bearing in mind its potential for a higher likelihood of preserving the ejaculatory function compared to TURP [5]. In 1997, Cornford et al. first described the use of a holmium laser to perform TUIP (Ho-TUIP) in patients with prostate volume <30 ml. They reported a significant improvement in Qmax, PVR, and IPSS, with an 11% rate of post-operative retrograde ejaculation [20]. However, contradicting these initial encouraging results, a recent review by Rapisarda et al. pointed out that retrograde ejaculation after Ho-TUIP can occur in up to 80% of the cases [21].

It is in this setting that we thought about thulium as a better laser source for duplicating the TUIP technique. Specifically regarding thulium laser endoscopic procedures, there are anecdotal reports about the application of this energy in the ejaculation-sparing setting, mainly regarding enucleation techniques [22-24].

We developed the ThuIP technique, taking advantage of the versatility of the thulium laser. In fact, the thulium laser allows the surgeon to adapt the surgical technique case-by-case, choosing an effect rather than another (incision vs vaporization vs vaporesection) depending on the anatomy of the prostate [25, 26]. We believe that the surgical technique must adapt to the patient, not vice versa, to tailor the treatment of BPO. Furthermore, it is our opinion that the physical features of thulium lasers (continuous wave, tissue penetration of about 0.25 mm) are most suitable to preserve the structures involved in the ejaculatory function and avoid the poor outcomes reported in the Ho-TUIP series [27].

Results from our study showed that antegrade ejaculation was preserved in 88% of the cases, with a significant improvement both in the uroflowmetry parameters and the patient-reported outcomes. Namely, we observed a median raw point improvement in Qmax of 8.3 ml/s and a decrease in IPSS of 12 points at 6 months. Durability was satisfactory within a 2-year follow-up.

We believe that these results are at least non-inferior to those obtained post uMISTs. These procedures are progressively catching on, but as highlighted in the systematic review by Checcucci et al., the benefit from uMISTs in terms of Qmax ranges from +3.6 ml/s to +4.1 ml/s at 12 months [3]. Probably, Qmax is not the best outcome measure for an accurate evaluation of the efficacy of uMISTs; nevertheless, in our hands, ThuIP seemed to provide a much better uroflowmetry improvement. Regarding the preservation of antegrade ejaculation, comparison with uMISTs offers conflicting results: our 90% rate of preserved ejaculation is similar to that observed with some uMISTs, but worse than that observed with others. Finally, we underline that the catheterisation time averaged 2 days, which is shorter than observed after different uMISTs [3]. We acknowledge that this protocol best fits with our regional healthcare system, and probably it is not generalisable. Although we have no experience in performing ThuIP as a one-day surgery procedure, we are aware that it could be feasible and is probably uneventful in most cases, as described by reports relative to holmium laser endoscopic procedures [28, 29].

To the best of our knowledge, this is the first ever report about thulium laser TUIP. When necessary, our technique included a selective vaporesection of the median lobe because the median lobe itself is often mainly responsible for the BPO [30].

Someone could criticise our approach because the technique described seems to be halfway between

incision and laser vaporesection. Probably, using more stringent inclusion criteria as per the EAU guidelines, our outcomes would have been even better, particularly in preserving the ejaculatory function. However, thanks to the versatility and the physical features of the thulium laser, we obtained satisfactory results notwithstanding the heterogeneity of the population treated.

In our patients, median prostate volume was 35 ml (IQR 29–50), with the presence of median lobe in about a quarter of the cases. We believe that the baseline characteristics of prostate are paramount at counselling. Indeed, in our experience, prostate volume >30 ml and presence of median lobe were identified as predictors of postoperative absence of antegrade ejaculation.

Regarding the effectiveness in relieving from BPO, the cumulative 2-year failure rate (we remark that failure included either re-start of medical therapy or surgical treatment) was around 13%.

As shown by univariate analysis, failure seemed to be again related to prostate volume >30 ml. This is not surprising because previous reports about Ho-TUIP showed that postoperative outcomes and reoperation rates were significantly associated with prostate volume >30 ml [31].

Moreover, the studied population had a median age of 55 years (IQR 49–63). In line with the literature, multivariate analysis identified age as an independent predictor of postoperative absence of antegrade ejaculation. In fact, ejaculatory dysfunction seems to be more common among patients aged >50 years [32]. Probably we still lack full knowledge of the pathophysiology of postoperative ejaculatory dysfunction, but similarly to what was observed in the post-radical prostatectomy setting, age could be considered as a major risk factor [33].

Recently, the concept of trifecta has been extended to laser treatments for BPO, but its application is still controversial [34]. According to our results, Trifecta was achieved in about 72% of the patients at 6 months, dropping to about 63% at 24 months, confirming a certain durability of the results over time. Qmax at baseline was found as the only predictor of trifecta achievement. Perhaps, the composite outcome trifecta is a somewhat pitiless way of evaluating the patient's actual satisfaction with treatment, and we need to improve the quality of our assessment.

We acknowledge several limitations of the study. First, the lack of randomisation or a control group: a comparison to TUIP with other energy sources, as well as a comparison to other uMISTs, in a well-designed prospective study might have underlined the good results of ThuIP regarding ejaculatory function. Second, our results could be not fully generalised for several reasons: the heterogenous population treated (patients with and without median lobes, prostate volume up to 80 ml), various techniques used (about 27% required an additional vaporesection of the obstructing median lobe), and the number of surgeons involved (although all of them had consolidated surgical experience in endoscopic treatment of BPO before the study start, because our centre is a referral institution for BPH surgery). Third, we did not record the actual energy delivered (in joules) for each procedure: nevertheless, operative time could be considered a "surrogate" of this variable. Therefore, it is plausible to state that longer operative time translated into greater energy delivered to the prostatic tissue, with proportionally increased likelihood of damage to anatomical landmarks involved in the preservation of antegrade ejaculation, explaining our findings in the logistic regression model. Finally, ejaculatory function was assessed by patients' perception and physician interview, rather than by means of dedicated questionnaires. In a real-life scenario, it is our opinion that the administration of a dedicated questionnaire is not always feasible: accordingly, the assessment of postoperative ejaculatory function as a "binary outcome" (lost vs maintained antegrade ejaculation) is common practice in clinical research, and we believe it is a reliable indicator [35, 36].

Notwithstanding these limitations, this study is the first investigating the use of a thulium laser to duplicate TUIP as a viable alternative to pare the deobstructive effect of the procedure to a high chance to preserve the ejaculation. Although our study does not allow us to establish any strong conclusion, we believe that ThuIP represents a simple way to balance between deobstruction and preservation of antegrade ejaculation, even in relatively large and obstructing prostates. We underline the paramount importance of adequate preoperative counselling, explaining to the patient the potential predictors of worse outcomes.

## CONCLUSIONS

If the patient seeks uMISTs, ThuIP can be offered as a viable alternative, with short catheterisation time, consistent and durable relief from BPO combined with the 90% chance of preserving ejaculatory function.

### CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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