REVIEW ARTICLE

Transperineal laser ablation in the management of benign prostatic hyperplasia: an updated systematic review and pooled analysis

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INTRODUCTION: Standard surgical options for Benign Prostatic Hyperplasia [BPH], despite their excellent functional outcomes, are associated with multiple side effects and require general/spinal anesthesia and hospitalization. In this scenario, Transperineal Laser Ablation of the Prostate [TPLA] emerged as an ultra-minimally invasive ejaculation-sparing procedure, showing promising functional results, with a good safety profile. This systematic review aimed to provide an overview of the current role of TPLA in clinical practice, focusing on operative setting, safety, and efficacy.

EVIDENCE ACQUISITION: Literature search was performed on June 12th, 2024 using PubMed, Embase, and Cochrane Central databases, following the EAU Guidelines Office and the PRISMA statement recommendations. All studies reporting outcomes after TPLA procedures were included.

EVIDENCE SYNTHESIS: Seventeen studies were included in this systematic review, of which 2 RCTs compared TPLA with TURP, 12 prospective and 3 retrospective non-randomized studies (of which 1 comparing TPLA and Prostatic Artery Embolization [PAE]). All procedures were performed using the same EchoLaser™ system (SoracteLite™) (Elesta s.r.l., Calenzano (FI), Italy), however great heterogeneity exists considering inclusion criteria, peri- and post-operative management. Mainly low-grade complications (Clavien-Dindo [CD] Grade ≤ II) were reported, while no major adverse events (CD grade > III) occurred. In all studies TPLA led to a great improvement in urinary function, up to 5 years after the procedure, while not significantly impacting erectile and ejaculatory functions.

CONCLUSIONS: TPLA showed promising results both in the short- and mid-term, improving urinary function while preserving sexual function and keeping a good safety profile. Since the evidence available is still limited, larger prospective comparative studies are warranted to confirm the efficacy of TPLA and to adequately compare it to standard endoscopic techniques and other minimally invasive surgical treatments.

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INTRODUCTION

A conservative approach based on behavioral/dietary modifications (since BPH showed a correlation with metabolic syndrome [1, 2]) and medical therapy is currently recommended by European Guidelines as first-line treatment for male LUTS due to Benign Prostatic Hyperplasia [BPH] [3, 4]. However, since the pharmacological treatment has an impact on sexual function (especially on ejaculatory functions for α-blockers and on sexual desire and erectile function for PDE5-I) [5–7], it may lead many patients to have poor compliance and discontinue the therapy [7]. Moreover, while classical surgical procedures proved excellent functional outcomes, they are also associated with multiple possible side effects (sexual dysfunction, mainly retrograde ejaculation/anejaculation, bleeding, urethral strictures, infections, bladder neck contracture, etc.) [8], and they require general/spinal anesthesia and hospitalization.

Over the last decade, to obtain effective relief of LUTS trying to have a lesser impact on QoL and the sexual sphere in selected patients, a wide number of Minimally Invasive Surgical Techniques [MISTs] for BPH have emerged [9–13]. Although these procedures proved to achieve slightly inferior functional outcomes compared with standard treatments, they have the advantage of being performed as day-surgery procedures using local anesthesia or intravenous/oral sedation, ensuring rapid recovery and a limited impact on sexual function, with a low risk of complications [11, 14].

In this scenario, TPLA is an ultrasound-guided minimally-invasive and ejaculation-sparing procedure, using a low-power laser with 4 independent channels for multi-fiber lasing approach

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connected to small needles inserted transperineally, to produce an area of irreversible coagulative necrosis of prostatic cells, obtaining a volume reduction of the gland while allowing the preservation of the urethra [15]. TPLA proved to be an innovative minimally invasive treatment option for BPH, showing promising results in terms of function improvement, while preserving ejaculation and erectile function and maintaining a good safety profile with a low rate of complications [16–18].

This systematic review aims to provide an updated summary of the existing evidence on TPLA and a comprehensive overview of its current role in clinical practice, focusing on the operative setting, on its safety, and its efficacy in terms of functional outcomes and sexual function preservation.

EVIDENCE ACQUISITION

Literature search

This systematic review was performed according to the European Association of Urology [EAU] Guidelines Office [19] and the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA] statement recommendations [20].

The protocol has been registered in the International Prospective Register of Systematic Reviews database (PROSPERO ID: CRD42024549332).

The literature search was performed on June 12th, 2024, using PubMed, Embase and Cochrane Central databases. The complete research strategy is available in section 1 of the Appendix.

Selection criteria

The PICOS (Patient, Intervention, Comparison, Outcome, Study type) model was used to frame and answer the clinical question:

P: Adult (>18 years old) male patients with Benign Prostatic Hypertrophy [BPH]
I: Transperineal Laser Ablation [TPLA]
C: No comparison
O: Technique, safety profile, and functional outcomes of TPLA
S: Prospective and retrospective studies

Study screening and selection

Studies were included based on PICO eligibility criteria. Reviews, letters to the editor, commentaries, and meeting abstracts were excluded. Only English papers were accepted.

In case of multiple articles written by the same author/group on similar patient cohorts, only the most recent study with the largest cohort was included.

All retrieved studies were independently screened by two authors (F.S., B.G) based on title and abstract. A third author solved discrepancies through discussion. The same two authors (F.S., B.G) independently screened the full text of the papers that were found pertinent to the aim of this review and selected those for data extraction.

All prospective and retrospective studies reporting outcomes after TPLA procedures were included.

Data extraction and analysis

A priori-developed Excel data extraction form was used to collect information on study design, participant demographics, intervention characteristics, and outcome measures. Two authors (M.L., and E.C.) independently extracted data relating to the prespecified outcomes. In case of discrepancies, a third author revised the data and solved the conflict through discussion.

In case of studies reporting comparisons with other treatments (e.g., TPLA vs. TURP), only data regarding the TPLA procedure were considered for the analysis.

Descriptive statistics were used to summarize baseline characteristic data.

Two authors (A.A. and R.N.) independently evaluated the study quality and assessed the risk of bias. Discrepancies were solved through discussion. The Cochrane Handbook for Systematic Reviews of Interventions risk-of-bias tool was used for RCTs [21] (Fig. 1), while the Risk of Bias in Non-randomized Studies of Interventions [ROBINS-I] tool was used for prospective studies [22] (Fig. 2). The possible confounders were considered by consensus of the authors from review of the literature.

Statistical analyses were performed by Spyder IDE 5.4.3 (conda), using Pandas, Numpy, Matplotlib, and Scipy modules and R Version 4.2.2. Descriptive statistics were used to summarize baseline characteristic data. We calculated and depicted forest plots with a 95% CI. Cochrane's Q test and the I2 test were used to evaluate the heterogeneity. Significant heterogeneity was indicated by a $p < 0.05$ in the Cochrane's Q-tests and $I^2 > 50\%$. A random effect model was used to calculate pooled results. Considering the observational nature of the present systematic review, in case of significant heterogeneity between the studies we did not investigate the underlying causes. Due to the aim of our review, we decided not to perform Egger's test for publication bias. Due to the paucity of comparative studies, it was not feasible to perform a formal meta-analysis. Statistical significance was established at $p < 0.05$.

EVIDENCE SYNTHESIS

Literature search and characteristics of included studies

The literature search identified 112 papers. After removal of duplicates and title/abstract screening, 28 full-text papers were screened for appropriateness. Of these, 11 papers were further excluded as they did not fit the purpose of our review (5 studies did not report results regarding the TPLA procedure, 3

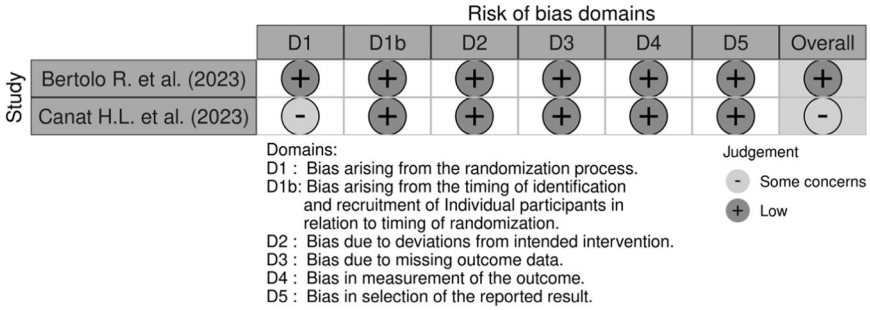

Fig. 1 The Cochrane Handbook for Systematic Reviews of Interventions risk-of-bias tool for RCTs. A risk-of-bias judgement is assigned to each domain possibly affecting the results of RCTs ("Low risk"/"Some concerns"/"High risk" of bias). Judging a result to be at a particular level of risk of bias for an individual domain implies that the result has an overall risk of bias at least this severe. A "traffic light plot" graphically displays the risk of bias judgment for each domain.

were meeting abstracts, 1 was a systematic review, 1 was an expert's comment, and 1 study by Cai et al. [23] had the same cohort of another trial carried on by the same group). As a result, 17 papers were considered for the results and analyzed [15, 24–39]. Figure 3 shows the PRISMA flow diagram of the review.

Among the 17 papers included in this review, 2 reported data from RCTs comparing TPLA with TURP [30, 31], 11 were prospective

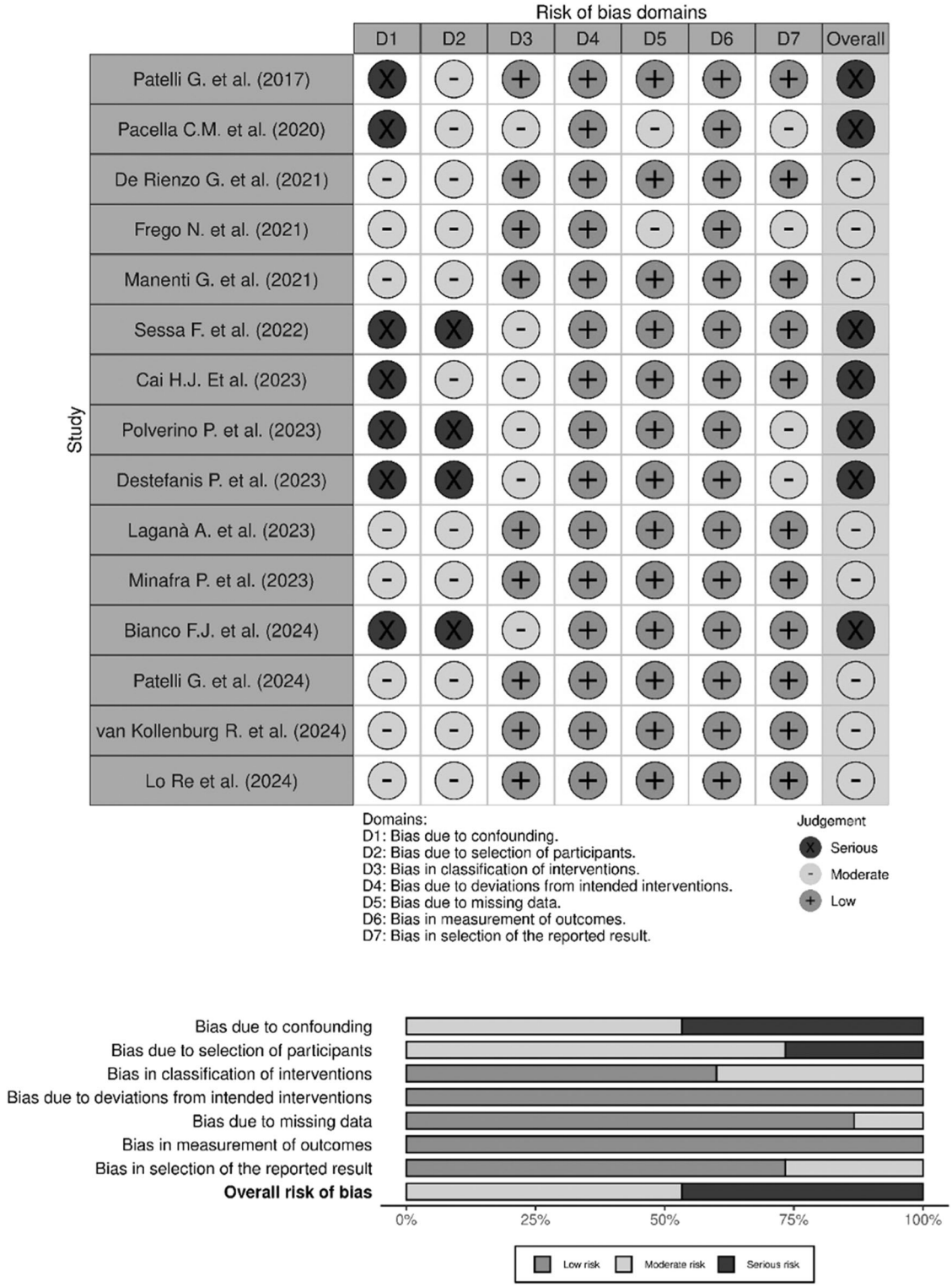

Fig. 2 The Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool for prospective studies. A risk-of-bias judgement is assigned to each of the seven domains through which bias might be introduced into a non-randomized study ("Low risk"/"Moderate risk"/"Serious risk"/"Critical risk" of bias). Judging a result to be at a particular level of risk of bias for an individual domain implies that the result has an overall risk of bias at least this severe. A "traffic light plot" graphically displays the risk of bias judgment for each domain.

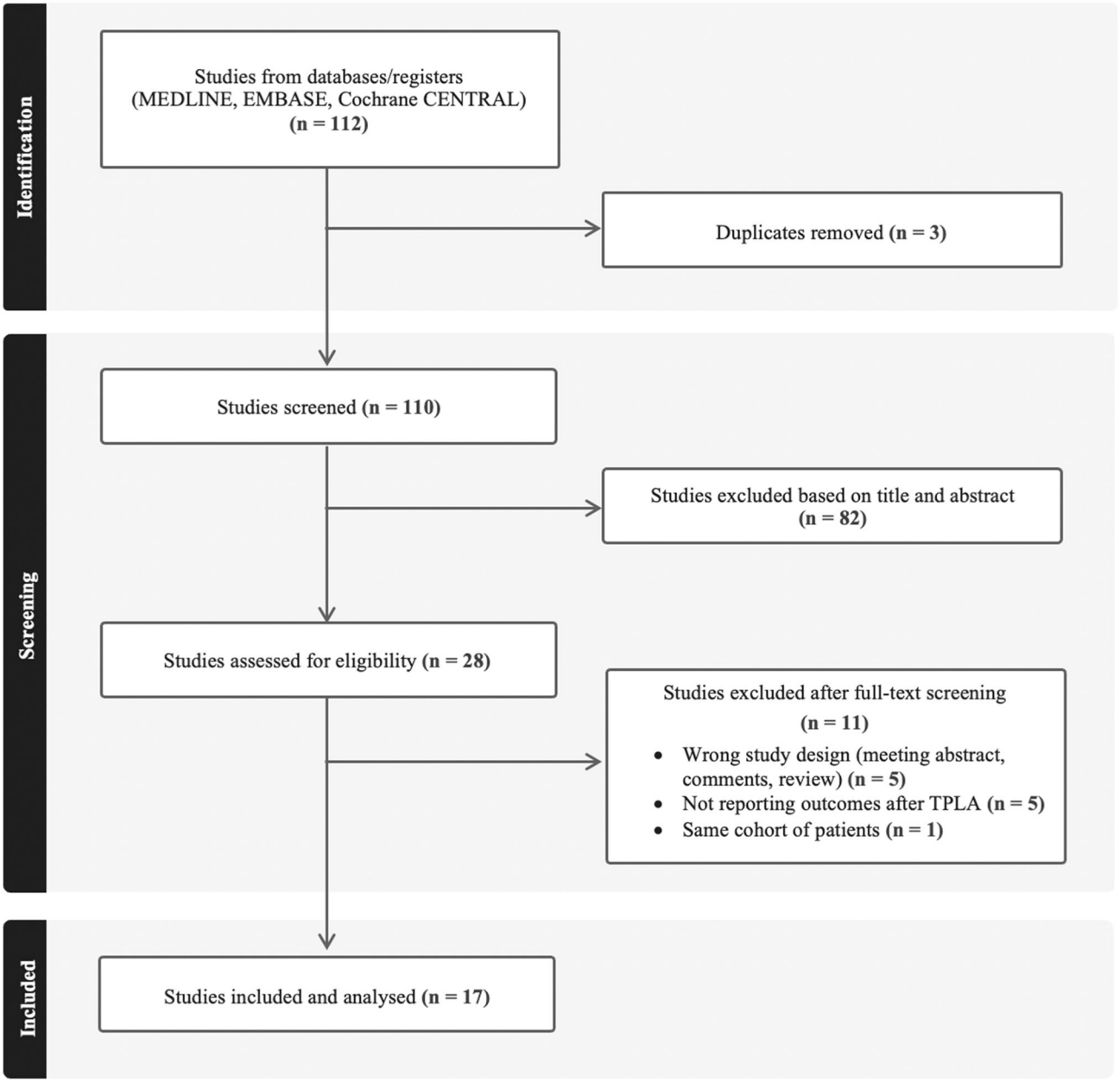

Fig. 3 Preferred reporting items for systematic review and meta-analysis (PRISMA) flowchart. The flow diagram depicts the flow of information through the different phases of the systematic review. It maps out the number of records identified and screened, included and excluded, and the reasons for exclusions.

non-randomized single-center studies [15, 24, 26–28, 32–35, 37, 38], 1 was a prospective non-randomized multi-center study [36], 2 were retrospective single-center studies (of which one comparing TPLA and Prostatic Artery Embolization [PAE]) [29, 39], and 1 was a retrospective multi-center study [25].

The complete list of studies included is available in section 2 of the Appendix.

Overall, data on 702 patients treated with TPLA were reported.

Median follow-up was ≤12 months for most of the studies, while only 3 authors (Minafra et al. [34], Bianco et al. [38], and Patelli et al. [35]) reported results up to 36 months after the procedure.

Mean/median prostate volumes were very heterogeneous across the included studies, ranging from 38 mL (30.5–73) to 102.4 ± 36.3 mL, reflecting large differences in terms of inclusion criteria and characteristics of the different cohorts analyzed.

The general characteristics of the studies included in this review (study design, follow-up period, number of patients, and baseline characteristics of the patients) are summarized in Table 1.

A summary of the inclusion/exclusion criteria as reported in the different studies included in this systematic review is reported in Supplementary Table 1.

Technical aspects of TPLA and peri-operative management

All the included studies used EchoLaser^{TM} system (SoracteLite^{TM}) (Elesta s.r.l., Calenzano (FI), Italy), consisting of a multisource diode laser with 4 independent laser sources operating at 1064 nm wavelength, and a biplanar transrectal ultrasound [TRUS] probe, to perform TPLA. Additionally, a planning tool with simulation

Table 1. Baseline characteristics of the included studies.

Reference [year]	Study design	Patients [*n*]	Follow-up [months]	Age [years]	PSA [ng/mL]	Previous medical therapy for BPH *n* (%) (type)	Antiplatelet/ Anticoagulants *n* (%)	Charlson comorbidity index	Indwelling catheter *n* (%)
Patelli G. [24]	Prospective single-center pilot study	18	3	71.7 ± 9.4	NR	NR	NR	NR	NR
Pacella C.M. (2020)	Retrospective multi-centric study	160	12	69.8 ± 9.6	NR	NR	NR	NR	36 (22.5%)
De Rienzo G. [26]	Prospective single-center study	21	12	62 (54–69)	2 (1.33–3)	14 (66.7%) (α-blocker); 10 (47.6%) (5-ARI); 8 (38.1%) (combined)	NR	2 (1–2)	None
Frego N. [27]	Prospective single-center pilot study	22	12	61.9 (55–65.5)	2.2 (1.4–4.5)	22 (100%) (α-blocker); 6 (27.3%) (combined)	NR	1 (1–2)	2 (9%)
Manenti G. [28]	Prospective single-center study	44	12	72 ± 6.6	7.3 ± 1.8	NR	NR	NR	None
Sessa F. [19]	Prospective single-center study	40	3	72 (64–79)	1.64 (0.6–2.4)	16 (53.3%) (α-blocker); 6 (20%) (5-ARI); 4 (13.3%) (combined)	11 (36.7%)	2 (1–2)	4 (13.3%)
Cai H.J. (2023)	Retrospective single-center comparative study	20	6	73.9 ± 9.2	NR	NR	NR	ASA 2: 16 (80%); ASA 3: 4 (20%)	NR
Polverino P. [29]	Retrospective single-center study	23	12	77 (68–84)	NR	NR	11 (48%) antiplatelet; 4 (17%) NOACs; 3 (13%) Warfarin	5 (3–6)	6 (26%)
Bertolo R. [30]	Prospective single-center randomized trial	26	6	63 (57–70.5)	3 (1.1–4)	23 (88.5%)	10 (38.5%)	0 (0–1)	NR
Canat H.L. (2023)	Prospective single-center randomized trial	25	12	65.6 ± 6.6	4.8 ± 4.6	NR	NR	ASA score: 2.33 ± 0.62	None
Destefanis P. [32]	Prospective single-center study	40	6	80 (72.5–84)	2.2 (0.8–3.8)	12 (30%) (α-blocker); 4 (10%) (5-ARI); 15 (37.5%) (combined)	22 (55%)	6 (5–7)	23 (57.5%)
Laganà A. [33]	Prospective single-center study	63	12	72.3 ± 10.0	4.8 ± 1.8	27 (42.9%) (α-blocker); 6 (9.5%) (5-ARI)	NR	3 (2–5)	10 (15.9%)
Minafra P. [34]	Prospective single-center study	20	36	63 (55–70)	NR	13 (65%) (α-blocker); 10 (50%) (5-ARI);	NR	NR	None

Table 1. continued

Reference [year]	Study design	Patients [*n*]	Follow-up [months]	Age [years]	PSA [ng/mL]	Previous medical therapy for BPH *n* (%) (type)	Antiplatelet/ Anticoagulants *n* (%)	Charlson comorbidity index	Indwelling catheter *n* (%)
						8 (40%) (combined)			
Bianco F.J. (2024)	Prospective single-center study	20	24	66.1 (8.4)	1.8 (1.1)	NR	NR	NR	None
Patelli G. [35]	Prospective single-center study	40	57 (36–76)	65.1 ± 8.3	NR	NR	NR	NR	16 (40%)
van Kollenburg R. [36]	Prospective multi-centric pilot study	20	12	70.3 ± 7.3	5.0 ± 3.3	12 (60%) (α-blocker); 8 (40%) (5-ARI); 1 (5%) (β3-agonist)	NR	NR	None
Lo Re M. [37]	Prospective single-center study	100	12	66.5 (60–75)	NR	60 (60%) (α-blocker); 4 (4%) (5-ARI); 17 (17%) (combined)	24 (24%)	1 (0–2)	14 (14%)

BPH benign prostatic hyperplasia, *5-ARI* 5-alpha reductase inhibitors, *NOACs* non-vitamin K antagonist oral anticoagulants, *ASA score* American Society of Anesthesiologists score.

software was included, enabling the users to safely place the needles and plan the treatment.

Sixteen authors [15, 23–29, 31–38] performed TPLA under local anesthesia of the perineal region and periprostatic block using 2% Lidocaine/Bupivacaine, eventually supplemented by conscious sedation with benzodiazepines, while only Bertolo et al. [30] performed the procedure under spinal anesthesia.

After catheter placement, anesthesia, and antibiotic prophylaxis (fluoroquinolones or third-generation broad-spectrum cephalosporins, with no clear preference for one over the other, while only Destefanis et al. [32] reported antibiotic prophylaxis-based on urine culture and antibiogram results), according to prostate volume, up to two 21 G Chiba needles for each lobe were transperineally inserted under ultrasound guidance, allowing the subsequent positioning of the laser fibers. More than one fiber per lobe was used if prostate volume was ≥40 mL [24, 25], ≥45 mL [28], ≥55 mL (and/or if presence of median lobe) [26], ≥60 mL [27, 31], or ≥80 mL [15], according to the different included studies. A step-by-step guide for patient positioning, needle/fiber placement, and treatment administration was previously reported elsewhere [15].

As reported in the technical sheet of the EchoLaser^{TM} device, a minimum safety distance from the fiber tip and local anatomical structures was respected by all studies: 15 mm from the bladder neck, 8–10 mm from the prostatic capsule, and 8–10 mm from the urethra. Some authors also reported a minimum distance kept between the different fibers, in case of large prostates needing more than one fiber per lobe, widely ranging from 8–10 to 15–20 mm.

The number of fibers consequently reflects the total energy delivered, which was reported to be 1800 J per fiber by most of the included studies. The total power delivered to the gland ranged from 3 to 5 Watts, with the majority of the authors setting a fixed power of 3 W all along the procedure [23–25, 27, 33, 36], while others starting with 4.5–5 W and then decreasing to 3–3.5 W after few minutes [15, 28, 30, 37].

Ablation time ranged from a mean of 8.6 [38] to 23.4 [25] min, with an overall mean procedural time variable between 26.5 [38] and 60.9 [23] min. Depending on prostate size, one to two consecutive illumination cycles and a pull-back maneuver followed by a second ablation were usually performed during the same session.

The length of hospital stay varied a lot among the different studies. Many authors reported same-day discharge for all patients, after a short post-operative observation period [15, 28, 29, 31–33, 36–38], while in other studies patients were hospitalized for 1–2 days (median hospital stay ranging from 6.4 h [15] to 1.8 days [25]).

Almost all patients were discharged with an indwelling catheter, kept in place for a period widely ranging from 4 [30] to 22.8 [35] days, while Bianco et al. [38] reported a 60% (12/20 patients) catheter-free discharge, evaluating post-operative voiding and not placing a catheter if PVR < 250 mL.

Just few studies reported data on medical therapy at discharge: most of these agree on the continuation of antibiotic therapy (fluoroquinolones or third-generation cephalosporins, as for prophylaxis), in combination with corticosteroids (Prednisone or Dexamethasone,) for at least 5–7 days [26–28]; Manenti et al. [28], De Rienzo et al. [26], Bianco et al. [38], and Destefanis et al. [32] also recommended to keep alpha-blockers for 1 month or until catheter removal.

Tables 2 and 3 summarize the technical aspects and peri-operative data of TPLA procedures as reported in the included studies.

Safety profile of TPLA

All the studies included in this systematic review but one reported complication rates after TPLA procedures [15,

Table 2. Technical aspects of TPLA procedures in the included studies.

Reference [year]	Laser system	Fibers	Minimum distance of fibers [mm]				Anesthesia	Antibiotic prophylaxis	Energy and power setting
			Bladder neck	Prostate capsule	Urethra	Between fibers			
Patelli G. [24]	EchoLaser XVG (Elesta)	1 fiber per lobe if prostate <40 mL (4/18) (22.2%); 2 fibers per lobe if prostate >40 mL (14/18) (77.8%)	15	NR	8	15–20	Conscious sedation (Midazolam IV, 3 mg) + local anesthesia of the perineal region and periprostatic block (Lidocaine 2%, 20 mL)	NR	Power: 3 W Energy: 1200–1800 J per fiber
Pacella C.M. (2020)	EchoLaser X4 (Elesta)	2 fibers per lobe if prostate >40 mL	15	10	8–10	8–10	Conscious sedation (Midazolam IV, 3 mg) + local anesthesia of the perineal region and periprostatic block (Lidocaine 2%, 20 mL)	Ciprofloxacin 500 mg	Power: 3 W Energy: 1800 J per fiber
De Rienzo G. [26]	EchoLaser XVG (Elesta)	2 fibers per lobe if prostate >55–60 mL; additional fiber if mid lobe Mean: 2.2 ± 0.5 (range 2–4)	15	8	8	10–15	Conscious sedation (Midazolam IV) + local anesthesia of the perineal region and periprostatic block (Lidocaine 2%, 20 mL)	NR	Energy: 1800 J per fiber
Frego N. [27]	EchoLaser X4 (Elesta)	1 fiber per lobe if prostate <60 mL (12/22) (54.5%); 2 fibers per lobe if prostate >60 mL (10/22) (45.5%)	15	10	10	10–15	Conscious sedation (Midazolam IV, 3 mg) + local anesthesia of the perineal region (Lidocaine 2%, 10 mL) and periprostatic block (Lidocaine 2%, 10 mL)	Levofloxacin 500 mg the day before the procedure	Power: 3 W Energy: 1800 J per fiber
Manenti G. [28]	EchoLaser X4 (Elesta)	1 fiber per lobe if prostate <45 mL 2 fibers: 3 (6.8%); 3 fibers: 4 (9.1%); 4 fibers: 37 (84.1%)	15	10	10	8–10	Local anesthesia of the perineal region and periprostatic block (Lidocaine 2%, 20 mL)	Levofloxacin 500 mg 1 h before the procedure	Power: 5 W reduced to 3 W after 2 min Energy: 1800 J per fiber
Sessa F. [19]	EchoLaser X4 (Elesta)	2 fibers per lobe if prostate >80 mL Median: 2 (2–2)	15	NR	8	NR	Local anesthesia of the perineal region and periprostatic block (Lidocaine 2%, 20 mL)	Cephazolin 2 g IV 1 h before the procedure	Power: 5 W reduced to 3.5 W after 2 min
Cai H.J. (2023)	EchoLaser X4 (Elesta)	2 fibers per lobe	15	NR	8–10	15–20	2% Lidocaine injected layer by layer from skin to prostatic capsule	NR	Power: 3 W Energy: 1800 J per fiber
Polverino P. [29]	EchoLaser (Elesta)	Median n° of fibers: 2 (2–2)	NR	NR	NR	NR	Local anestesia (20 mL Lidocaine 2%) + low-dose oral Benzodiazepine	NR	NR
Bertolo R. [30]	EchoLaser EVO (Elesta)	NR	15	8	8	10–15	Spinal anesthesia	NR	Power: 4.5 W reduced to 3.5 W after 1–2 min Energy: 1800 J
Canat H.L. (2023)	EchoLaser X4 (Elesta)	2 fibers per lobe if prostate >60 mL	15	8	8	NR	Conscious sedation (Midazolam IV, 3 mg) + local anesthesia of the perineal region (Lidocaine 2%, 10 mL) and periprostatic block (Lidocaine 2%, 10 mL)	NR	Energy: 1800 J per fiber

Table 2. continued

Reference [year]	Laser system	Fibers	Minimum distance of fibers [mm]				Anesthesia	Antibiotic prophylaxis	Energy and power setting
			Bladder neck	Prostate capsule	Urethra	Between fibers			
Destefanis P. [32]	EchoLaser X4 (Elesta)	Median n° of fibers: 2 (2–2.5)	NR	NR	NR	NR	Local anesthesia with Lidocaine/ Bupivacaine (periprostatic blockade) ± light intravenous sedatives (optional)	According to pre-operative urine culture	NR
Laganà A. [33]	EchoLaser X4 (Elesta)	Mean n° of fibers per lobe: 1.82 ± 0.4	15	8–10	8–10	10	Conscious sedation + local anesthesia of the perineum and periprostatic block	Cephazolin 2 g IV	Power: 3 W Energy: 1800 J per fiber
Minafra P. [34]	EchoLaser X4 (Elesta)	NR	15	8	8	NR	Periprostatic local anesthesia (Lidocaine 2%, 20 mL) + IV sedation + analgesia	NR	NR
Bianco F.J. (2024)	EchoLaser X4 (Elesta)	NR	NR	NR	NR	NR	Local anesthesia of the perineal region and periprostatic block (Lidocaine 2%, 20 mL)	Ceftriaxone 250 mg IM	Power: variable energy: 1800 J
Patelli G. [35]	EchoLaser XVG (Elesta)	Mean n° of fibers: 3.5 ± 0.8	15	NR	8	15–20	Conscious sedation (Midazolam IV) + local anesthesia of the perineal region and periprostatic block (Lidocaine 2%, 20 mL)	Levofloxacin before the procedure and continued for 7 days	Power: 3 W
van Kollenburg R. [36]	EchoLaser X4 (Elesta)	2 fibers: 7 (35%); 3 fibers: 7 (35%); 4 fibers: 6 (30%)	15	8	8	NR	Local anesthesia of the perineal region (Lidocaine 2%, 5–10 mL) and periprostatic block (Lidocaine 2%, 20 mL) ± Conscious sedation (Midazolam IV, 3 mg) (optional)	Ciprofloxacin 500 mg 1–2 h before the procedure	Power: 3 W Energy: 1800 J per fiber
Lo Re M. [37]	EchoLaser (Elesta)	Median n° of fibers: 2 (2–2)	15	NR	8	NR	Local anesthesia (20 mL Lidocaine 2%) ± low-dose oral Benzodiazepine (optional)	NR	Power: 5 W reduced to 3.5 W after 2 min

Table 3. Peri-operative data of TPLA procedures in the included studies.

Reference [year]	Energy released [J]	Procedural time [min]	Ablation time [min]	Length of hospital stay [days]	Catheterization time [days]	Therapy at discharge	Complications [Clavien-Dindo]
Patelli G. [24]	10522 ± 3290.5	43.3 ± 8.7	15.9 ± 3.9	1.5 ± 0.4	17.3 ± 10	NR	2 (5%) SIR grade I
Pacella C.M. (2020)	6616.2 ± 3880.4	44.1 ± 12.9	23.4 ± 10.2	1.8 ± 0.4	11.3 ± 11.5	NR	7 (4.3%) grade I 1 (0.6%) grade III
De Rienzo G. [26]	NR	36.0 ± 9.5	NR	20.8 ± 3.6 h	8.7 ± 2.5	Oral Fluoroquinolones/Cephalosporines for 5 days + Prednisone 25 mg for 15 days + Bromelain + BPH tablets for 30 days	1 (4.8%) grade III
Frego N. [27]	1800 J (1800–3200) per fiber	NR	17.2 (10–18.9)	1	7	Levofloxacin 500 mg for 5 days + Dexamethasone 8 mg and Ketoprofen 100 mg for 7 days	8 (36.3%) grade I 5 (22.7%) grade II
Manenti G. [28]	1800 J each fiber (max 7200 J)	28.2 ± 10.6	6.7–10 for each fiber	<1 day	7	Levofloxacin 500 mg and Prednisone 25 mg for 5 days + α-blockers for 30 days	1 (2.3%) grade I 1 (2.3%) grade II 1 (2.3%) grade III
Sessa F. [19]	NR	31.5 (28–37)	NR	6.4 h (5.9–7.2)	7 (7–8)	Cefixime 400 mg + Ibuprofen 600 mg bid + Pantoprazole 20 mg for 1 week	No peri-operative AEs CD ≥ 2
Cai H.J. (2023)	7179.2 ± 2815.7	60.9 ± 10.8	42.6 ± 9.9	1.5 ± 0.5	16.5 ± 4.2	NR	2 (10%) grade I
Polverino P. [29]	2800 (2400–3200)	NR	NR	<1 day	7 (7–9)	NR	2 (8.5%) grade I
Bertolo R. [30]	NR	35 (30–55)	NR	2 (2–3)	4 (2–7)	NR	5 (19%) grade I
Canat H.L. (2023)	NR	NR	16 ± 2.35	0.76 ± 0.49	6.5 ± 1.02	NR	NR
Destefanis P. [32]	7202.5 (3652–7227.5)	42.5 (8.5–18.5)	17.5 (8.5–18.5)	8–12 h	NR	α-blocker continued for 1 month/until catheter removal	16 (40%) grade I 9 (22.5%) grade II 1 (2.5%) grade III
Laganà A. [33]	8261.6 ± 3280.1	48.8 ± 14.3	13.0 ± 1.95	<1 day	14.9 ± 7.5	NR	1 (1.6%) grade I 2 (3.2%) grade III
Minafra P. [34]	NR	NR	NR	NR	NR	NR	No late-onset complications
Bianco F.J. (2024)	3400 (2600–3600)	26.5 (20.2–27.7)	8.6 (7.3–12)	<1 day	12 (60%) catheter-free at discharge; 19 (95%) catheter-free at 30-days	Antibiotic + anti-inflammatory + Tamsulosin for 30 days	12 (80%) CTCAE 1 1 (5%) CTCAE 3
Patelli G. [35]	11214 ± 4097.1	43.3 ± 8.7	17.3 ± 4.4	2	22.8 ± 10.9	Levofloxacin for 7 days	2 (5%) grade II
van Kollenburg R. [36]	8271 ± 3259	59 ± 14.0	17.2 ± 6.3	6.5 ± 5 h	15.2 ± 3.5	Dexamethasone 8 mg for 7 days	15 (75%) grade I 17 (85%) grade II
Lo Re M. [37]	2800 (2400–3100)	NR	NR	<1 day	7 (7–7)	NR	2 (2%) grade II

SIR Society of Interventional Radiology classification system, *CD* Clavien Dindo classification, *AEs* Adverse Events, *NR* Not Reported, *CTCAE* Common Terminology Criteria for Adverse Events.

23–30, 32–38]. Of them, 14 used the Clavien Dindo [CD] classifications of Surgical complications [40], while Patelli et al. [24] and Bianco et al. [38] respectively used the Society of Interventional Radiology classification system [41] and the Common Terminology Criteria for Adverse Events v5.0 [CTCAE] to report peri- and post-procedural adverse events [AEs].

Overall, complication rates ranged from 0% [34] to 65% [32]. Among these, only CD grade 1 (1.6% [33] to 36.3% [27]), grade II (2% [37] to 22.7% [27]), and grade III (0.6% (25) to 4.8% [26]) AEs were described, while no major complications (CD grade > III) have been reported. A summary of peri- and post-operative complications as reported in the included studies is reported in Table 3.

The timeframes of the reported AEs varied from 30 days [36] up to 36 months [35] for most of the studies, while only Cai et al. [23] reported intra-operative complications (in particular one case of urethral burn) in their paper.

The most frequently reported low-grade complications were transient dysuria, hematuria, catheter displacement/malfunction, urinary tract infection [UTI], and acute urinary retention [AUR]. As described by Bianco et al. [38], one of the main AE was hematospermia (CTCAE Grade 1), which was reported in their paper by 12 of 15 men (80%) who had intercourse during the 30 days post-TPLA. Other reported AEs were orchitis and three cases of prostatic abscess (treated with percutaneous drainage + antibiotic therapy) [25, 26, 28].

Notably, among all these authors, only Minafra et al. [34] reported no complications after the procedure. However, it is worth noticing that in their paper the absence of late-onset complications is stated to be patients-reported, with no mention on peri- and early post-operative adverse events.

Urinary function and QoL after TPLA procedures

Sixteen papers included in this review assessed urinary function using the International Prostate Symptom Score [IPSS] and reported uroflowmetry results in terms of peak urinary flow rate [Q_{max}] and post-void residual volume [PVR]. All 17 studies reported Patient Reported Outcome Measures [PROMs] on QoL using the IPSS-QoL questionnaire.

According to the studies included in this systematic review, PROMs on urinary function and QoL were reported at baseline, and at short to mid-term follow-up (varying between 1 month and 3 years), as summarized in Table 4. The effect of TPLA on functional outcomes and pooled analysis is depicted in Fig. 4.

All studies demonstrated a great improvement in IPSS scores from baseline at each specified time point, reaching statistical significance in the majority of included studies. In fact, as reported by De Rienzo et al. [26], already at 1-month follow-up TPLA showed a significant effectiveness in improving urinary function, with IPSS values going from 18.3 ± 3.9 to 12.0 ± 5.6 ($p < 0.01$). This subjective improvement in urinary function seems to even increase over time, with IPSS values decreasing as time goes by in most of these studies, maintaining statistically significant differences up to 12 months compared to the baseline. Only a few authors reported mid-term results, with a median follow-up of respectively 24 (Bianco et al. [38]), 36 (Minafra et al. [34]), and 57 months (range 36–76) (Patelli et al. [35]). In their series, IPSS score remained significantly below baseline values years after the procedure, with a slight and gradual increase over time.

Alongside the decline of IPSS values, patient-reported QoL was significantly improved in most studies, both in the short and mid-term, remaining stable up to 3 years after the procedure.

Regarding uroflowmetric parameters as reported in the included studies, baseline Qmax was generally quite low (mean/median values ranging between 7.6 and 10.2 mL/s), reflecting a moderate-severe degree of urinary obstruction, while baseline PVR values were very heterogeneous (mean/median values ranging between 24.6 and 199.9 mL). All studies reported a great improvement (beyond the threshold of statistical significance for most of them), regarding both Qmax and PVR, showing a progressive improvement over time, up to 12 months. As for IPSS, at 3-years follow-up the improvement in Qmax and PVR remained quite stable and significantly below baseline values, albeit with slightly lower results compared to previous evaluations, as reported by Minafra et al. [34] and Patelli et al. [35].

Sexual function after TPLA procedures

Ten papers included in this review reported pre- and post-operative data on sexual function, in terms of erections and/or ejaculatory function, using the International Index of Erectile Function [IIEF-5] or the Sexual Health in Men score [SHIM], and the Male Sexual Health Questionnaire Ejaculatory Dysfunction 3-items [MSHQ-EjD3], respectively. Six authors [23–25, 29, 33, 35] did not assess either of the aforementioned items, while Destefanis et al. [32] stated that did since a severe pre-operative sexual dysfunction (median IIEF5 score of 0 [0–6] and median MSHQ-SF score of 1 [1–5]) was a common feature for all their patients, it was not feasible to properly evaluate the effect of TPLA on such domain in a sexually inactive population.

As for urinary function, PROMs on sexual function were reported at baseline, and at short to mid-term follow-up (varying between 1 month and 3 years). A summary of post-operative outcomes on erectile function and ejaculatory function is reported in Table 4.

As it emerges from the results, no significant differences ($p > 0.05$) in the IIEF scores were assessed, both considering short- and mid-term follow-up. Furthermore, albeit with non-significant increases, IIEF scores after TPLA were higher than baseline for most of the studies, highlighting how TPLA not only does not affect erections but can also benefit sexual function by improving patients' QoL.

Similarly, while all the studies reported preservation of ejaculatory function after TPLA, post-operative MSHQ-EjD3 values were sometimes not only safeguarded but also statistically improved compared to baseline [26, 34, 37].

DISCUSSION

Treatment options for BPH are rapidly and constantly evolving, with MISTs gaining more and more ground compared to classical endoscopic and other more invasive techniques. In fact, these approaches demonstrated good efficacy in relieving obstructive LUTS, while sparing ejaculation and overall sexual function, with rapid recovery and the possibility of being carried out in outpatient or day surgery regime, at the cost of relatively few and low-grade side effects.

Nowadays, as emerges from most of the studies included in this systematic review and from a recent Delphi consensus [42], Echolaser™ TPLA for the treatment of BPH is usually recommended for prostates with volumes ranging from 30–40 to 80 mL, even if satisfactory outcomes were achieved including glands >80 mL [23, 25, 28, 38]. Even considering the presence of a median lobe, most authors do not place limits in this regard, suggesting the feasibility and the efficacy of the treatment of such cases, while others, such as Manenti et al. [28], Bertolo et al. [30], and Lo Re et al. [37] excluded prostates with large median lobes in their studies (see Supplementary Table 1), since approaching the third lobe transperineally might be challenging for the surgeon and its presence could reduce the effectiveness of the treatment.

Moreover, while there is agreement between the authors in excluding patients with anatomical and/or functional alterations that can impact bladder function (e.g., urethral strictures, neurological disorders, etc.), which could influence the functional tests and the interpretation of the results, there is no consensus on whether patients with indwelling catheters should be included in such studies. In fact, several studies excluded patients with indwelling catheters or performing intermittent catheterization [26, 28, 31, 34, 38], while the majority did not address the topic,

Table 4. Summary of pre-operative features and post-operative outcomes.

Reference (year)	Timepoint	Qmax [mL/min] mean (SD)/ median (range)	PVR [mL] mean (SD)/median (range)	IPSS mean (SD)/median (range)	IIEF-5 mean (SD)/median (range)	MSHQ-EjD3 mean (SD)/ median (range)	QoL mean (SD)/ median (range)	Prostate volume [mL] mean (SD)/median (range)
Patelli G. [24]	Baseline	7.6 ± 2.7	199.9 ± 147.3	21.9 ± 6.2	NR	NR	4.7 ± 0.6	69.8 ± 39.9
	Post-procedural [time from baseline] (*p* value)	3mo: 13.3 ± 7.2 ($p = 0.001$)	3mo: 81.5 ± 97.8 ($p < 0.001$)	3mo: 10.7 ± 4.7 ($p < 0.001$)	NR	NR	3mo: 2.1 ± 1.2 ($p < 0.001$)	3mo: 2.1 ± 1.2 ($p < 0.001$)
Pacella C.M. (2020)	Baseline	8.0 ± 3.8	89.5 ± 84.6	22.5 ± 5.1	NR	NR	4.5 ± 1.1	75.0 ± 32.4
	Post-procedural [time from baseline] (*p* value)	6mo: 14.3 ± 3.9 ($p < 0.001$) 12mo: 15.0 ± 4.0 ($p < 0.001$)	6mo: 27.2 ± 44.5 ($p < 0.001$) 12mo: 17.8 ± 51.0 ($p < 0.001$)	6mo: 7.7 ± 3.3 ($p < 0.001$) 12mo: 7.0 ± 2.9 ($p < 0.001$)	NR	NR	6mo: 1.8 ± 1.0 ($p < 0.001$) 12mo: 1.6 ± 0.9 ($p < 0.001$)	6mo: 60.3 ± 24.5 ($p < 0.001$) 12mo: 58.8 ± 22.9($p < 0.001$)
De Rienzo G. [26]	Baseline	9.2 ± 3.4	81.8 ± 62.6	18.3 ± 3.9	17.9 ± 6.9	5.7 ± 4.5	4.1 ± 1.0	40 (40–50)
	Post-procedural [time from baseline] (*p* value)	1mo: 12.1 ± 6.4 ($p < 0.01$) 3mo: 13.3 ± 6.7 ($p < 0.01$)6mo: 13.9 ± 6.2 ($p < 0.01$)	1mo: 37.4 ± 25.7 ($p < 0.05$) 3mo: 18.7 ± 21.2 ($p < 0.01$) 6mo: 14.0 ± 16.7 ($p < 0.01$)	1mo: 12.0 ± 5.6 ($p < 0.01$) 3mo: 8.3 ± 3.8 ($p < 0.01$) 6mo: 6.1 ± 2.6 ($p < 0.01$)	1mo: 17.4 ± 5.0 ($p > 0.05$) 3mo: 17.7 ± 6.7 ($p > 0.05$) 6mo: 18.3 ± 5.7 ($p > 0.05$)	1mo: 9.6 ± 4.1 ($p < 0.01$) 3mo: 6.8 ± 3.5 ($p < 0.01$) 6mo: 8.6 ± 3.1 ($p < 0.01$)	1mo: 2.4 ± 1.6 ($p < 0.01$) 3mo: 1.4 ± 0.9 ($p < 0.01$) 6mo: 1.7 ± 0.8 ($p < 0.01$)	NR
Frego N. [27]	Baseline	9 (5–12.5)	60 (25–107.5)	22 (19.5–25.25)	22 (16.5–24)	NR	4 (4–5)	65 (46.5–81)
	Post-procedural [time from baseline] (*p* value)	3mo: 12 (9–16.5) ($p = 0.025$) 6mo: 15 (11.5–20.5) ($p < 0.001$) 12mo: 20.5 (14.3–23.8) ($p < 0.001$)	3mo: 39 (10–87.5) ($p = 0.43$) 6mo: 40 (16–63) ($p = 0.46$) 12mo: 30 (5–50) ($p = 0.052$)	3mo: 8 (4.5–11) ($p < 0.001$) 6mo: 5 (3–8.5) ($p < 0.001$) 12mo: 6 (4.25–7) ($p < 0.001$)	3mo: 22 (19.5–24) ($p = 0.342$) 6mo: 23 (20.5–24) ($p = 0.141$) 12mo: 21.5 (17.3–23.8) ($p = 0.151$)	NR	3mo: 1 (0.5–2) ($p < 0.001$) 6mo: 1 (0–2) ($p < 0.001$) 12mo: 1 (1–2) ($p < 0.001$)	3mo: 46 (28.4–69) ($p = 0.058$) 6mo: 42.3 (39.5–59) ($p = 0.003$) 12mo: 41.5 (36.3–55) ($p = 0.001$)
Manenti G. [28]	Baseline	7.6 ± 4.2	138.4 ± 40.8	18.5 ± 5.5	21 ± 4	4.9 ± 3.7	5.8 ± 1.4	102.4 ± 36.3
	Post-procedural [time from baseline] (*p* value)	12mo: 16.2 ± 4.9	12mo: 18.8 ± 8.5	12mo: 6.2 ± 3.8	12mo: 22 ± 3	12mo: 7.7 ± 3.2 ($p = 0.030$)	12mo: 2.1 ± 1.1	12mo: 48.1 ± 19.2
Sessa F. [19]	Baseline	9.5 (7.6–11.2)	100 (70–150)	21.5 (18–27.8)	16.0 (7.5–23.5)	5.0 (3–7.4)	4.0 (4.0–5.0)	42 (40–53)
	Post-procedural [time from baseline] (*p* value)	1mo: 10.5 (8–16) 3mo: 14.2 (11.2–16.3)	1mo: 50 (20–100) 3mo: 40 (25–70)	1mo: 14.5 (12–17.8) 3mo: 13.0 (11.3–16.4)	1mo: 18.0 (15–24) 3mo: 23.0 (17.5– 25)	1mo: 7.5 (4.0–13.1) 3mo: 8.9 (7–16.4)	1mo: 3.0 (2–3.75) 3mo: 2.0 (1.75–2.25)	NR
Cai H.J. (2023)	Baseline	8.5 ± 3.0	78.7 ± 58.8	22.7 ± 5.3	NR	NR	4.9 ± 1.7	70.8 ± 23.8
	Post-procedural [time from baseline] (*p* value)	6mo: 15.2 ± 4.8 ($p < 0.001$)	6mo: 30.3 ± 34.2 ($p < 0.05$)	6mo: 9.1 ± 3.2 ($p < 0.001$)	NR	NR	6mo: 2.3 ± 1.3 ($p < 0.001$)	6mo: 54.7 ± 20.9 ($p < 0.05$)
Polverino P. [29]	Baseline	NR	NR	NR	NR	NR	4 (3–5)	42 (39–70)

Table 4. continued

Reference (year)	Timepoint	Qmax [mL/min] mean (SD)/ median (range)	PVR [mL] mean (SD)/median (range)	IPSS mean (SD)/median (range)	IIEF-5 mean (SD)/median (range)	MSHQ-EjD3 mean (SD)/ median (range)	QoL mean (SD)/ median (range)	Prostate volume [mL] mean (SD)/median (range)
	Post-procedural [time from baseline] (*p* value)	NR	NR	NR	NR	NR	12mo: 2 (1–3)	NR
Bertolo R. [30]	Baseline	10.2 (8.7–12.0)	70 (20–100)	24.0 (16.0–29.0)	17.0 (15.0–21.0)	29.0 (25.0–30.0)	5 (3–5)	49 (37–65)
	Post-procedural [time from baseline] (*p* value)	6mo: 15.2 (13.3–18.3) ($p < 0.001$)	0 (0–5)	6mo: 11 (8–15) ($p = 0.01$)	1mo: 18 (14–23) ($p = 0.5$)	1mo: 29 (25–30) ($p = 0.2$)	6mo: 2 (2–4) ($p = 0.002$)	NR
Canat H.L. (2023)	Baseline	8.7 ± 3.8	125 ± 68.5	20.1 ± 6.0	14.8 ± 3.9	10.8 ± 2.4	4.8 ± 0.8	66.8 ± 25.3
	Post-procedural [time from baseline] (*p* value)	12mo: 14.3 ± 3.7 ($p < 0.01$)	12mo: 46.9 ± 32.4 ($p < 0.01$)	12mo: 10.1 ± 3.2 ($p < 0.01$)	12mo: 14.7 ± 3.9 (p = 0.83)	12mo: 10.3 ± 2.3 ($p = 0.54$)	12mo: 1.5 ± 0.9 ($p < 0.01$)	12mo: 47.3 ± 13.6 ($p < 0.01$)
Destefanis P. [32]	Baseline	8 (5.5–10)	50 (15–180)	25 (19–30)	0 (0–6)	MSHQ-SF: 1 (1–5)	6 (5–6)	38 (30.5–73)
	Post-procedural [time from baseline] (*p* value)	3mo: 12.5 (9.5–14) ($p = 0.056$) 6mo: 12 (10–13) ($p = 0.044$)	3mo: 30 (0–60) ($p = 0.090$) 6mo: 30 (0–60) ($p = 0.092$)	3mo: 10.5 (7.5–13) ($p < 0.001$) 6mo: 8 (6–11.5) ($p < 0.001$)	NR	NR	3mo: 3 (0–4) ($p < 0.001$) 6mo: 2 (0–4) ($p < 0.001$)	3mo: 35 (26–49) ($p < 0.001$) 6mo: 34 (28–49) ($p < 0.001$)
Laganà A. [33]	Baseline	8.6 ± 3.5	124.8 ± 115.4	20.8 ± 7.4	NR	NR	4.7 ± 1.4	63.6 ± 29.7
	Post-procedural [time from baseline] (*p* value)	3mo: 13.2 ± 5.7 ($p = 0.083$) 12mo: 16.2 ± 4.3 ($p = 0.014$)	3mo: 43.6 ± 53.6 ($p < 0.001$) 12mo: 40.6 ± 53.6 ($p = 0.003$)	3mo: 11.0 ± 6.6 ($p < 0.001$) 12mo: 8.4 ± 5.9 ($p < 0.001$)	NR	NR	3mo: 1.5 ± 1.2 ($p < 0.001$) 12mo: 1.2 ± 0.8($p < 0.001$)	3 mo: 45.6 ± 21.8 ($p = 0.003$) 12mo: 42.8 ± 14.2($p = 0.071$)
Minafra P. [34]	Baseline	8.8 (7.8–10.8)	70.0 (33–120)	18 (16–21)	17 (15–21)	4 (3–8)	4 (4–5)	41.5 (40.0–54.3)
	Post-procedural [time from baseline] (*p* value)	6mo: 13.9 (5.0–32.0) ($p < 0.01$) 3 y: 11.0 (9.0–12.8) ($p < 0.01$)	6mo: 14.0 (0–50) ($p < 0.01$) 3 y: 15.0 (0–25) ($p < 0.01$)	6mo: 6 (3–12) ($p < 0.01$) 3 y: 12 (10–15) ($p < 0.01$)	6mo: 18 (3–25) ($p > 0.05$) 3 y: 17 (15–20) ($p > 0.05$)	6mo: 9 (5–13) ($p < 0.01$) 3 y: 11 (7–12) ($p < 0.01$)	6mo: 2 (1–3) ($p < 0.01$) 3 y: 2 (1–2) ($p < 0.01$)	3 y: 35.0 (32–38.8) ($p < 0.01$)
Bianco F.J. (2024)	Baseline	9.5 ± 2.2	24.6 ± 14.9	14 (12–17)	SHIM: 23 (18.5–24)	NR	5 (4–6)	48.1 ± 13.7
	Post-procedural [time from baseline] (*p* value)	6 mo: 16.9 ± 5.6 ($p < 0.001$) 12 mo: 20.7 ± 4.6 ($p < 0.001$) 2 y: 22.3 ± 4.2 ($p < 0.001$)	6 mo: 9.7 ± 9.4 ($p = 0.001$) 12 mo: 7.9 ± 5.3 ($p < 0.001$) 2 y: 7.4 ± 4.6 (p < 0.001)	6 mo: 6 (3–8) ($p < 0.001$) 12 mo: 3 (5–2) ($p < 0.001$) 2 y: 3 (2–4) ($p < 0.001$)	6 mo: 21.5 (18.5–24) 12 mo: 22 (18.2–23) 2 y: 22 (19-22.7) (p = 0.15)	NR	6 mo: 2 (2–3) ($p = 0.005$) 12 mo: 2 (1–3) ($p < 0.001$) 2 y: 1 (1–3) ($p < 0.001$)	47.3 ± 13.1
Patelli G. [35]	Baseline	9.8 ± 6.2	108 (38–178)	23 (19–26)	NR	NR	5 (4–5)	66 (48.5–86.5)
					NR	NR		

Table 4. continued

Reference (year)	Timepoint	Qmax [mL/min] mean (SD)/ median (range)	PVR [mL] mean (SD)/median (range)	IPSS mean (SD)/median (range)	IIEF-5 mean (SD)/median (range)	MSHQ-EjD3 mean (SD)/ median (range)	QoL mean (SD)/ median (range)	Prostate volume [mL] mean (SD)/median (range)
	Post-procedural [time from baseline] (*p* value)	1 y: 12.8 ± 7.4 2 y: 10.8 ± 6.9; 3 y: 10.4 ± 4.8 Last: 12.0 ± 6.6	1 y: 13.5 (0–40.5) ($p < 0.001$) 2 y: 23 (5–54); 3 y: 21 (5–49) Last: 28.5 (15–50) ($p = 0.031$)	1 y: 5 (4–9) ($p < 0.001$) 2 y: 5 (4–10); 3 y: 7 (3–10) Last: 8.5 (4–12) ($p < 0.001$)			1 y: 1 (0–1) ($p < 0.001$) 2 y: 1 (0–1); 3 y: 1 (0–2) Last: 1 (0–2) ($p < 0.001$)	1 y: 46 (36–65) ($p < 0.001$) 2 y:48 (31–84);3 y:49.5 (31–79) Last: 61 (37–89) ($p < 0.001$)
van Kollenburg R. [36]	Baseline	9.7 ± 3.5	61.8 ± 58.3	21.3 ± 5.2	IIEF-15: 35.4 ± 23.6	NR	4.9 ± 0.9	65.5 ± 23.0
	Post-procedural [time from baseline] (*p* value)	3mo: 12.8 ± 6.1 6mo: 12.1 ± 6.1 12mo: 14.9 ± 6 ($p = 0.015$)	3mo: 64.8 ± 70.4 6mo: 74.2 ± 87.4 12mo: 44.2 ± 55.8 ($p = 0.755$)	3mo: 12.8 ± 6.0 6mo: 11.7 ± 5.2 12mo: 10.9 ± 5.5 ($p < 0.001$)	3mo: 36.9 ± 24.8 6mo: 40.5 ± 23.3 12mo: 31.1 ± 24.4 ($p = 0.57$)	NR	3mo: 2.6 ± 1.7 6mo: 1.8 ± 1.0 12mo: 1.9 ± 1.1 ($p < 0.001$)	12mo: 63.2 ± 20.6 ($p = 0.251$)
Lo Re M. [37]	Baseline	9.1 (6.9–12)	90 (50–150)	18 (15–23)	NR	6 (2–11)	4 (3–4)	50 (40–70)
	Post-procedural [time from baseline] (*p* value)	3mo: 11 (8.8–14.8) ($p < 0.001$) 6mo: 11 (8.5–16.0) ($p < 0.001$) 12mo: 13 (8.5–16.9) ($p < 0.001$)	3mo: 45 (20.77.5) ($p < 0.001$) 6mo: 50 (20–90) ($p < 0.001$) 12mo: 45 (1.2–87.5) ($p < 0.001$)	3mo: 10 (6–13) ($p < 0.001$) 6mo: 10 (5.7–14) ($p < 0.001$) 12mo: 10 (5–16.5) ($p < 0.001$)	NR	3mo: 10 (5–13) ($p < 0.001$) 6mo: 11 (5–14) ($p < 0.001$) 12mo: 9 (5–13) ($p < 0.001$)	3mo: 2 (1–3) ($p < 0.001$) 6mo: 2 (1–3) ($p < 0.001$) 12mo: 2 (1–3) ($p < 0.001$)	NR

Qmax maximum urinary flow rate, *PVR* post-void residual, *IPSS* International Prostatic Symptoms Score, *IIEF-5* International Index of Erectile Function Questionnaire, *MSHQ-EjD3* male sexual health questionnaire for ejaculatory dysfunction, *QoL* quality of life.

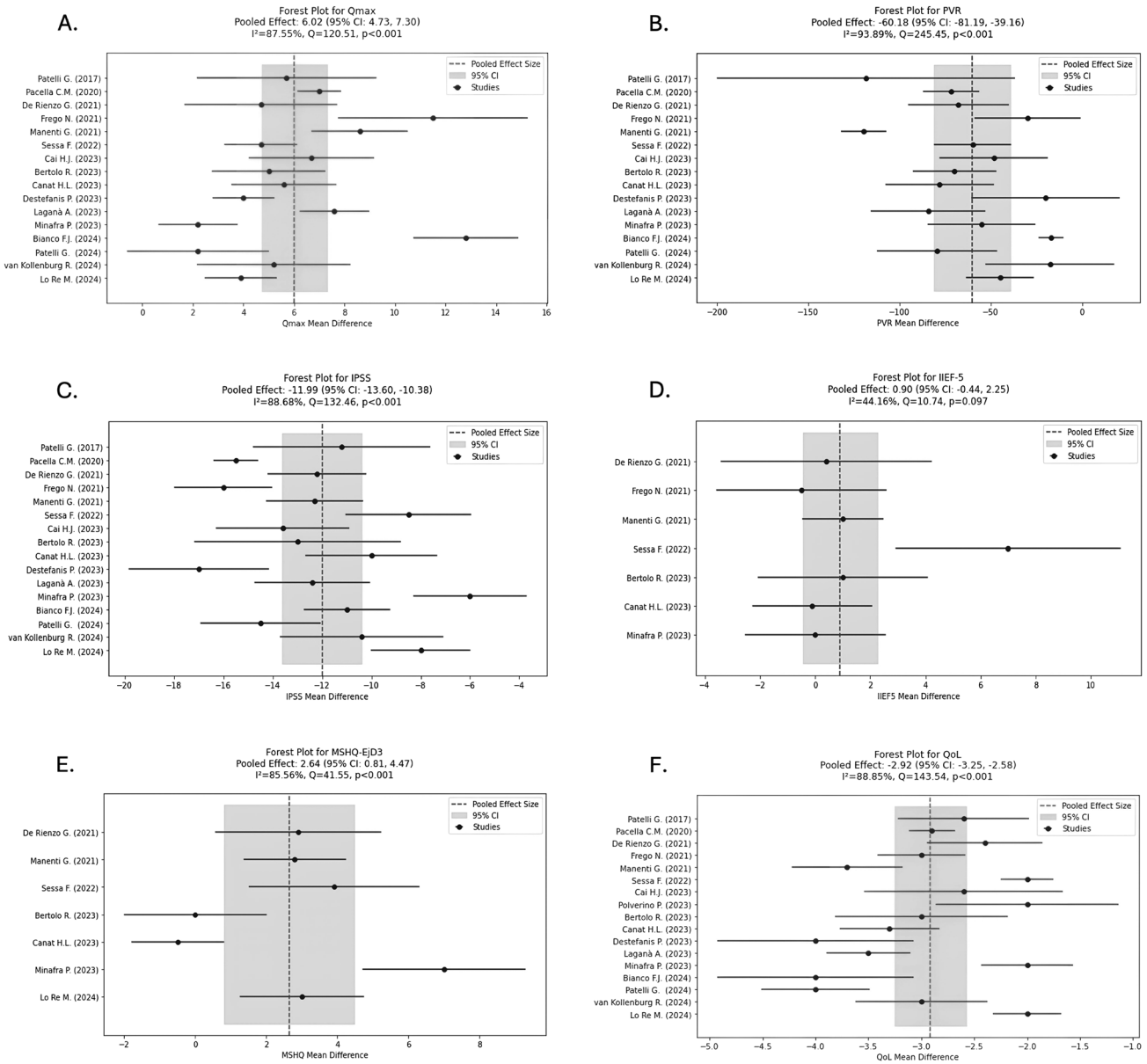

Fig. 4 Forest plot displaying the pooled effect on functional outcomes after TPLA. A Forest plot for Qmax. **B** Forest plot for Post-Void Residual (PVR). **C** Forest plot for IPSS. **D** Forest plot for IIEF-5. **E** Forest plot for MSHQ-EjD3. **F** Forest plot for QoL.

suggesting that such patients could also be included and treated with good functional results, as confirmed by two trials by Pacella et al. [25] and Frego et al. [27], demonstrating the possibility of successfully removing the catheter after the procedure.

Being a minimally invasive procedure, TPLA can be safely performed in an outpatient setting with low-grade anesthesia (namely local anesthesia of the perineal region and periprostatic block with Lidocaine 2%), as confirmed by almost all of the studies analyzed (except for Bertolo et al. [30] who performed the procedures under spinal anesthesia to limit potential confounders, being a RCT comparing TPLA and TURP). Moreover, as it requires short operative time and length of hospital stay, it emerges as an option for high-risk comorbid patients with significant anesthesiologic risks.

According to available literature, the Delphi Consensus project on TPLA [42] confirmed it as an "antiplatelet and anticoagulant-friendly treatment" due to its low invasiveness, even if a temporary suspension of such medications should be recommended in the peri-operative period considering the balance between the patient-specific hemorrhagic and thrombotic risk.

Even if there is currently no standardization of inclusion criteria and no consensus on which patients would benefit the most from this procedure, TPLA proved exclusive advantages compared to other treatments for BPH in two main groups of patients. On one hand, young patients with medium-sized prostates (40–60 cc), who are strongly interested in maintaining ejaculation, may benefit from a minimally invasive treatment relieving obstructive symptoms without compromising their sexual life. On the other hand, elderly multimorbid patients may benefit from a desobstructive treatment in an outpatient setting, thus avoiding the risks associated with general anesthesia and hospitalization.

When considering functional results, all the included studies showed how TPLA led to a great improvement in urinary function, up to 3 years after the procedure as reported by Minafra et al. [34] (median Qmax increased by 25%, median PVR decreased by

78.6%, and median IPSS reduced by 33.3% at 3 years follow-up) and Patelli et al. [35] (mean Qmax increased by 22.5%, median PVR decreased by 73.6%, and median IPSS reduced by 63% at last follow-up of median 57 (36–76) months) In fact, most of the authors reported a statistically significant improvement from baseline at each specified timepoint for both Q_{max}, QoL, IPSS, and PVR (see Table 4). Moreover, a progressive improvement as time goes by was reported by several authors [15, 25–27, 32, 33, 36, 37] up to 12 months, with a sudden slight gradual decline (however maintaining statistically significant benefits compared to baseline), as highlighted in studies with longer follow-up [34, 35]. As discussed by De Rienzo et al. [26], this progressive improvement might be explained by the inflammatory effect of lasing and coagulative necrosis, which can temporarily partially hide the beneficial effects of the procedure.

The analysis of the pooled effects across various functional parameters (including Qmax, PVR, IPSS, IIEF-5, MSHQ-EjD3, and QoL), highlighted the significant efficacy of TPLA. In fact, the pooled effect on Qmax was a substantial improvement by 6.02 mL/s (95% CI: 4.73–7.30), with a concomitant reduction in PVR by −60.18 mL (95% CI: −81.19 to −39.16) and a decrease in IPSS score by −11.99 points (95% CI: −13.60 to −10.38), reflecting a notable improvement in urinary flow and voiding while alleviating LUTS. Improvements in QoL (−2.92, 95% CI: −3.25 to −2.58) and MSHQ-EjD3 scores (2.64, 95% CI: 0.81–4.47) further emphasize the positive impact of these treatments on patient well-being.

However, high heterogeneity ($I^2 > 85\%$ for most outcomes) suggests considerable variability in the effects across studies, warranting further investigation into patient-specific or intervention-related factors contributing to this variability.

While this positive effect on urinary function is achieved, none of the studies reported urinary incontinence after the treatment, unlike what is reported for the classic transurethral resective/enucleative techniques [8, 43].

Considering sexual function, TPLA did not significantly impact IIEF-5 scores at short- and mid-term follow-ups. Furthermore, albeit with non-significant increases, post-operative IIEF scores were higher than baseline for most of the studies, making TPLA a good option for patients who have strong will of preserving sexual function. The ejaculatory function was not only preserved but also improved, as shown by De Rienzo et al. [26], Manenti et al. [28], Minafra et al. [34], and Lo Re et al. [37], reporting a significant increase post-operative MSHQ-EjD3 scores at each specified time point. Nevertheless, De Rienzo et al. [26] reported ejaculatory discomfort at 1 month after the procedure (MSHQ-EjD bother item: $+0.5 \pm 1.0$ ($p < 0.01$) compared to baseline), no longer observed at 3 and 6 months. This data is probably due to some grade of post-procedural inflammatory response, which is why several authors agree with a protocol based on anti-inflammatory and anti-oedemigen therapy after the procedure.

Finally, the safety of TPLA was confirmed by both expert consensus [42] and literature. In fact, all the included studies mainly reported low-grade complications (Clavien-Dindo Grade ≤ II), such as transient dysuria and hematuria, hematospermia, UTIs, and few cases of AUR. Overall, three cases of prostatic abscess (CD grade III), treated with percutaneous drainage and antibiotic therapy, were reported [25, 26, 28], while no major complications (CD grade > III) occurred.

A recent systematic review by Lambertini et al. [44] confirmed the good safety profile of TPLA, reporting a lower occurrence of major complications with this technique, compared to other minimally invasive treatments and to standard treatments (TURP). It is worth mentioning that, as reported by Lambertini et al. [44], there seems to be a relationship between the learning curve and complication rate, as complications significantly decreased with a wider sample size.

Although its promising results, the spreading of TPLA seems to be limited since there are only a few studies supporting its safety and effectiveness (especially in the medium-long term) and comparing it to gold standard resective or enucleative techniques. While the clinical improvements achieved with this technique seem slightly lower than those reported by standard resective/enucleative treatments, the preservation of erectile and ejaculatory function, the low rate of complications, and the possibility to perform it in an outpatient setting with same-day discharge, make TPLA extremely attractive and promising.

The main limitations of this systematic review are related to the small amount and the design of included studies (mainly retrospective or prospective single-center observational studies with small sample size and short-term follow-up), as highlighted by the moderate-severe risk of bias assessed for non-randomized studies, reflecting inadequacy to provide high-level evidence. Moreover, due to the paucity of comparative studies (2 RCTs with small sample size comparing TPLA and TURP and one retrospective study comparing TPLA and PAE), no meta-analysis could be performed.

This systematic review updates those previously published by Sessa et al. [16], Tzelves et al. [17], and Tafuri et al. [18], in light of new evidence and studies with longer follow-up. Nevertheless, larger comparative studies with longer follow-ups are still warranted to confirm the benefits of TPLA for the treatment of LUTS due to BPH, as compared to standard techniques and other MISTs.

CONCLUSIONS

TPLA showed promising results in improving urinary function and relieving obstructive symptoms while preserving erectile and ejaculatory function, both at short- and mid-term follow-ups. This procedure also proved to be safe, with an acceptable rate of low-grade complications (CD ≤ II) and no major adverse event (CD > III) reported by any of the included studies. Moreover, compared to other existing MISTs, TPLA is currently the only urethral-sparing technique and could be performed in a complete outpatient setting.

Great heterogeneity exists considering inclusion criteria and post-operative management, suggesting how TPLA will require careful patient selection and decision-making to offer the techniques to the most suitable candidates and to achieve the best postoperative outcomes according to patients' characteristics and expectations. Although there is currently no consensus, the best results may be observed both in young patients strongly interested in maintaining ejaculation, and in elderly, multimorbid patients who may benefit from a minimally invasive treatment in an outpatient setting, thus avoiding the risks associated with general anesthesia and hospitalization.

Although the reported data confirm the effectiveness of the technique, larger prospective comparative studies with longer follow-up are warranted to compare the efficacy of TPLA to standard endoscopic techniques and other minimally invasive surgical treatments and to assess how TPLA could become a common practice for the treatment of obstructive LUTS.

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AUTHOR CONTRIBUTIONS

AA, MLR, RN, and PP were responsible for interpreting data, editing and revising the tables, and writing the paper. EC, FS, and BG were responsible for collecting and reviewing journal articles, editing summary tables, and editing the manuscript. AA and AC were responsible for data analysis. MG was responsible for designing the review protocol, coordinating the group, and supervising the project. FS, AR, RC, AS, and SS provided feedback on the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

As this is a systematic review, institutional review board or patient consent was not required. As for all systematic reviews, the patients presented in this systematic review have been previously reported.

ADDITIONAL INFORMATION

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