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ARTICLE

Clinical Research

Transperineal laser ablation for percutaneous treatment of benign prostatic hyperplasia: a feasibility study. Results at 6 and 12 months from a retrospective multi-centric study

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Abstract

Purpose To investigate the effectiveness and safety of SoracteLite™—transperineal percutaneous laser ablation (TPLA) in the treatment of patients with symptomatic benign prostatic hyperplasia (BPH) at 6 and 12 months follow-up.

Methods Patients with urinary symptoms secondary to BPH underwent TPLA under local anesthesia in four centers. Under US guidance, up to four 21G applicators were inserted in the prostatic tissue. Each treatment was performed with diode laser operating at 1064 nm changing the illumination time according to prostate size. The primary end-points of this study were change in IPSS, PVR, Qmax, QoL, and prostatic volume at 6 an 12 months from SoracteLite™ TPLA treatment. Secondary end-point was the assessment of complications.

Results Analysis was performed on data 160 patients (mean age 69.8 ± 9.6 years) with at least 6 months follow and of 83 patients (mean age 67.9 ± 8.7 years) with at least 12 months follow-up. At 6 months, IPSS improved from 22.5 ± 5.1 to 7.7 ± 3.3 ($P < 0.001$), PVR from 89.5 ± 84.6 to 27.2 ± 44.5 ml ($P < 0.001$), Qmax from 8.0 ± 3.8 to 14.3 ± 3.9 ml/s ($P < 0.001$), QoL from 4.5 ± 1.1 to 1.8 ± 1.0 ($P < 0.001$), volume from 75.0 ± 32.4 to 60.3 ± 24.5 ml ($P < 0.001$). At 12 months, IPSS improved from 22.5 ± 4.5 to 7.0 ± 2.9 ($P < 0.001$), PVR from 71.7 ± 93.9 to 17.8 ± 51.0 ml ($P < 0.001$), Qmax from 8.6 ± 5.2 to 15.0 ± 4.0 ml/s ($P < 0.001$), QoL from 4.2 ± 0.6 to 1.6 ± 0.9 ($P < 0.001$), volume from 87.9 ± 31.6 to 58.8 ± 22.9 ml ($P < 0.001$). 7/160 (4.3%) grade I and 1/160 (0.6%) grade III complication occurred.

Conclusions SoracteLite™ TPLA allows significant improvement of IPSS, Qol, Qmax, PVR, and reduction of prostatic volume at 6 and 12 months.

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Introduction

Bladder outlet obstruction is a common condition affecting patients at varying severity. It affects 70% of the male population between 60 and 69 years and 80% of those aged 80 years or older [1]. In this population approximately 70% of men with benign prostatic hyperplasia (BPH) exhibit coexisting lower urinary tract symptoms (LUTS) and/or erectile dysfunction (ED) [2]. The standard medical strategies for patients with LUTS/BPH is based on alpha-blockers and/or 5-alpha reductase inhibitors. However, often these treatments do not achieve the desired results and some patients later require surgical treatments [3]. In the case that surgical treatment is required, transurethral resection of the prostate (TURP) is still the most widely applied treatment option [4]. Prostatectomy might be required for patients with very a large prostate or complicating factors. These options, though, can be

associated with a non-negligible rate of side effects and complications [5].

The flourishing of minimally invasive therapies (MITs) also arises from the need to offer options personalized based on patients and pathological factors. The available armamentarium today includes thermal therapies such as conductive transurethral needle ablation of the prostate (TUNA) [6], transurethral microwave thermotherapy (TUMT) [7], mechanical therapies such as prostatic urethral lift (PUL) [8, 9], intraoperative stents [10], intraoperative injection [11–14], and many other emerging therapies such as Rezum Convective Water Vapor Energy (WAVE) ablation [15], prostatic artery embolization (PAE) [16, 17], Aquablation™ [18, 19], and histotripsy [20]. Some of the use of these therapies are in decline while others remain experimental, some of which seem to provide promising results.

Based on recommendations for innovations in surgery [21] among various therapies, SoracteLite™—transperineal laser ablation (TPLA) has been recently proposed as a potential effective treatment modality [22]. Due to the very thin caliber of the applicators used and high precision of the energy delivery, percutaneous laser ablation has been demonstrated to be a safe and effective treatment in several pathological conditions [23, 24]. Particularly, this technique appears to be promising for the application in BPH treatment because the transperineal route avoids damage to the urethral channel. This technique has been reported to be feasible in a small preliminary study [22]. To the best of our knowledge, there is no study investigating the safety and clinical results of SoracteLite™ TPLA in a large multicentric cohort of patients. Thus, the aim of the present paper is to investigate the effectiveness and safety of SoracteLite™ TPLA in the treatment of patients with symptomatic BPH in a large series of patients as well as the evaluation of results of this treatment at 6 and 12 months follow-ups.

Materials and methods

Centers performing transperineal laser ablation for the treatment of BPH in their routine clinical practice were contacted and asked to participate in this multi-centric retrospective study. Three centers agreed to participate, and a common database was shared for data entry among centers. Institutional review board approval was obtained.

Patients were eligible for transperineal laser treatment following criteria previously established [22]. Inclusion criteria: >50 years old with International Prostate Symptoms (IPSS) ≥12, maximum urinary flow rate (Q_{max}) <15 ml, estimated prostate volume >30 ml on transrectal ultrasonographic (TRUS) images, and post-void residual urine volume (PVR) of <400 ml. Patients with any history of urethral stricture or prostatic surgery, confirmed prostate cancer and with known neurological disorders (neurogenic bladder) were excluded from the study. The use of anticoagulants or indwelling urinary catheters for urinary retention was not a criterion for exclusion. Also, the presence of a large median lobe was not a contraindication to the treatment. All procedures were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All patients signed a dedicated informed consent. Before treatment, patients completed the International Prostate Symptoms Score (IPSS) and Quality of Life (QoL) questionnaire. They underwent pressure-flow urodynamics to evaluate Qmax, trans abdominal ultrasound to determine post voiding residue (PVR), and transrectal ultrasound to determine the volume of the prostate.

Transperineal laser ablation technique

The patient was placed in the radiological intervention suite in lithotomy position. A three-way Foley 18-F catheter was inserted with continuous irrigation of a saline solution during and after the maneuver. The technique has been described in detail previous literature [22]. In practice it consists of positioning up to 4 applicators (one to two per lobe, depending on prostate volume and shape) consisting of a 21-gauge Chiba needle (Sterylab, Rho, Milano, Italy) as introducer in whose lumen is inserted a bare optic fiber of quartz of 300-μm until it protrudes by 10 mm from the tip of the thin introducer which was done under ultrasound guidance. The needle insertion and positioning is performed using a dedicated guidance device of the biplanar probe that allows to insert regularly spaced multiple parallel needle simultaneously. The optic fibers were connected to a multisource laser system operating at 1.064 nm (EchoLaser X4, Elesta srl, Calenzano, Italy). A support planning tool device (ESI, Echolaser Smart Interface, Elesta srl, Calenzano, Italy), can be connected to a general US scanner and used for treatment planning. In the case of volumes less than or equal to 40 ml, a single applicator per lobe can be inserted; while in the case of a prostate with a volume greater than 40 ml two applicators per lobe are used. The tip of the fiber should be placed 8–10 mm away from the outer wall of the urethra, 15 mm from the bottom of the bladder and 10 mm from the outer edge of the prostate capsule. The position of the applicators must be carefully controlled using a biplanar ultrasound probe. In the case of two applicators, these must be positioned one after the other at a mutual distance of 8–10 mm. More generally, applicators must be positioned along a path that is as parallel as possible to the longitudinal plane of the prostate. Each treatment is

performed with patient under conscious sedation by IV of midazolam (3 mg) and with local anesthesia of the superficial tissues of the perineal region and prostate anesthesia by transrectal prostatic block with lidocaine solution 2% (20 mL). Ciprofloxacin 500 mg is used as antibiotic prophylaxis. This last maneuver has not always been followed by some operators who have started using this method to treat patients with LUTS/BPH in the light of the fact that the patients tolerate the treatment well even without the local anesthesia.

Each treatment is performed at a fixed power of 3 W changing the illumination time case by case according to prostate size. Depending on the size of the prostate, one to three consecutive illuminations are performed with a "pull-back" technique (retractionof the fibers of ~10–12 mm) during the same treatment session. The treatment ends when 1800 Joules are reached for a single illumination for each single fiber (3600 Joules for two illuminations, 5400 Joules for three illuminations). So the time needed to release maximum energy dose ranged 600–1800 s (total energy 3600–21600 Joules). The number of sources and illuminations (up to three in special cases) for each lobe can vary from the standard model described above in the case of considerable volume at baseline of the prostate greater than 100 ml, marked hypeplasia of the middle lobe and/or of asymmetry of glands' lobes. At the end of treatment, based on the patient's clinical condition, Dexamethasone 4–8 mg can administered to reduce edema. After an observation period of about one hour, the patient underwent transrectal ultrasonography with the administration of an echo-amplifier contrast agent to evaluate the extent of the coagulation zone. The coagulation area can best be evaluated in its actual extension, when possible, with Magnetic Resonance Imaging. Images of two cases are shown in Figs. 1 and 2. The SoracteLite™ system is shown in Fig. 3. The patient is kept in the hospital for one or two days and the catheter, in the absence of adverse events, is removed at the end of the treatment. In particular clinical conditions, as in the case of patients with a long history of urinary retention and those who have kept urinary catheters permanently for a long time before treatment, urinary catheters could be left in place longer according to the referring urologist.

Variable analysis

The primary end-points of this study were evaluation of change in IPSS, Qol, Qmax, PVR, and prostatic volume at 6 and 12 months from SoracteLite™ TPLA treatment. Secondary end-point was evaluation of complications after SoracteLite™ TPLA. Definition of complications was consistent with the classification of surgical complications according to the modified Clavien system (CCS) [25, 26].

Analysis was performed using GraphPad Prism 5 software (Graph-Pad, La Jolla, CA, USA). Continuous variables were expressed as mean ± SD, and categorical variables displayed as frequencies and compared using the Mann–Whitney U test, χ^2 or Fisher test, as appropriate. A P value < 0.05 was considered statistically significant

Results

Analysis was performed on data of 160 patients (mean age 69.8 ± 9.6 years) with a follow-up of at least 6 months and of 83 patients (mean age 67.9 ± 8.7 years) with a follow-up of at least 12 months. 36/160 (22.5%) of patients were chronic catheter carriers. Mean operation time was 44.1 ± 12.9 min, mean ablation time was 23.4 ± 10.2 min, mean energy deployed was 6616.2 ± 3880.4 J, mean hospital stay was 1.8 ± 0.4 days, and mean catheterization time was 11.3 ± 11.5 days (12.6).

At 6 months, IPSS improved from 22.5 ± 5.1 to 7.7 ± 3.3 ($P < 0.001$), PVR from 89.5 ± 84.6 to 27.2 ± 44.5 ml ($P < 0.001$), Qmax from 8.0 ± 3.8 to 14.3 ± 3.9 ml/s ($P < 0.001$), QoL from 4.5 ± 1.1 to 1.8 ± 1.0 ($P < 0.001$), volume from 75.0 ± 32.4 to 60.3 ± 24.5 ml ($P < 0.001$). At 12 months, IPSS improved from 22.5 ± 4.5 to 7.0 ± 2.9 ($P < 0.001$), PVR from 71.7 ± 93.9 to 17.8 ± 51.0 ml ($P < 0.001$), Qmax from 8.6 ± 5.2 to 15.0 ± 4.0 ml/s ($P < 0.001$), QoL from 4.2 ± 0.6 to 1.6 ± 0.9 ($P < 0.001$), volume from 87.9 ± 31.6 to 58.8 ± 22.9 ml ($P < 0.001$). Results at 6 months are reported in Table 1, and results at 12 months are reported in Table 2.

After the procedure, 7/160 (4.3%) grade I complications and 1/160 (0.6%) grade III complications occurred. Particularly, three patients experienced transient hematuria, three had acute urinary retention, and one had orchitis. The three cases of acute urinary retention were treated with a bladder catheter that was left in place for 15 days. After 15 days, the bladder catheter was removed without further complications. One patient out of one hundred and sixty (0.6%) had prostatic abscess after SoracteLite™ TPLA, which was successfully drained. Six out of one hundred and sixty (3.7%) patients experienced transient dysuria, and 2/160 (1.2%) patients independently reported lost of ejaculatory function at follow-up visit, but this was not measured by questionnaire or directly asked. Disuria and ejaculatory disorders were regarded as sequelae.

Discussion

The results of the present multi-centric study show how SoracteLite™ TPLA can achieve significant improvement of IPSS, Qol, Qmax, PVR, and also the reduction of prostatic volume at 6 and 12 months in patients with BPH. In

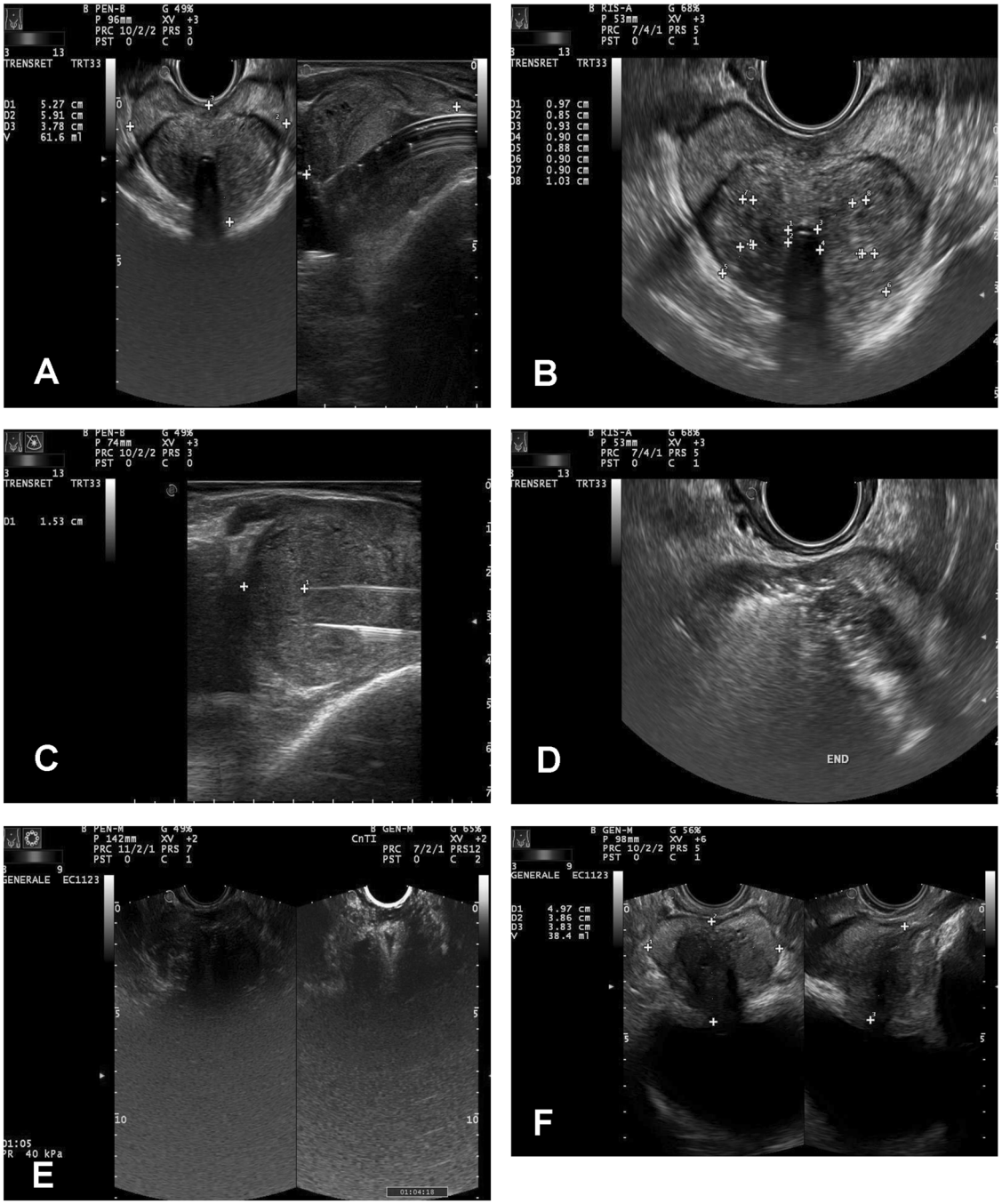

Fig. 1 Case of a patient with benign prostate hyperplasia treated with transperineal laser ablation. a transrectal ultrasound showing an enlarged prostate of 61.6 ml. **b**, **c** axial and longitudinal view of needle and laser fiber positioning. **d** hyperechoic area due to gas formation at the end of the procedure. **e** contrast-enhanced ultrasound showing lack of enhancement in the treated area. **f** transrectal ultrasound showing reduction of prostatic volume to 38.4 ml at 12 months from treatment.

particular, the results obtained in this study with SoracteLite™ TPLA compare favorably with the data reported in studies with a similar follow-up period both with emerging technologies such as Aquablation [27], Rezum WAVE [15, 27], and with other different lasers such as Holmium Laser Enucleation of the Prostate (HoLEP), Green Light Photoselective Vaporization of the Prostate (PVP) [28–30] and Thulium Laser Vapo-enucleation (ThuVEP) [31] as well as results of TURP [6, 32, 33].

In the continuous attempt to provide better results for patients, and reduce the invasiveness of treatment, the technique of prostate artery embolization (PAE) [34] has been developed by interventional radiologists and is achieving great interest. In a recent comparative

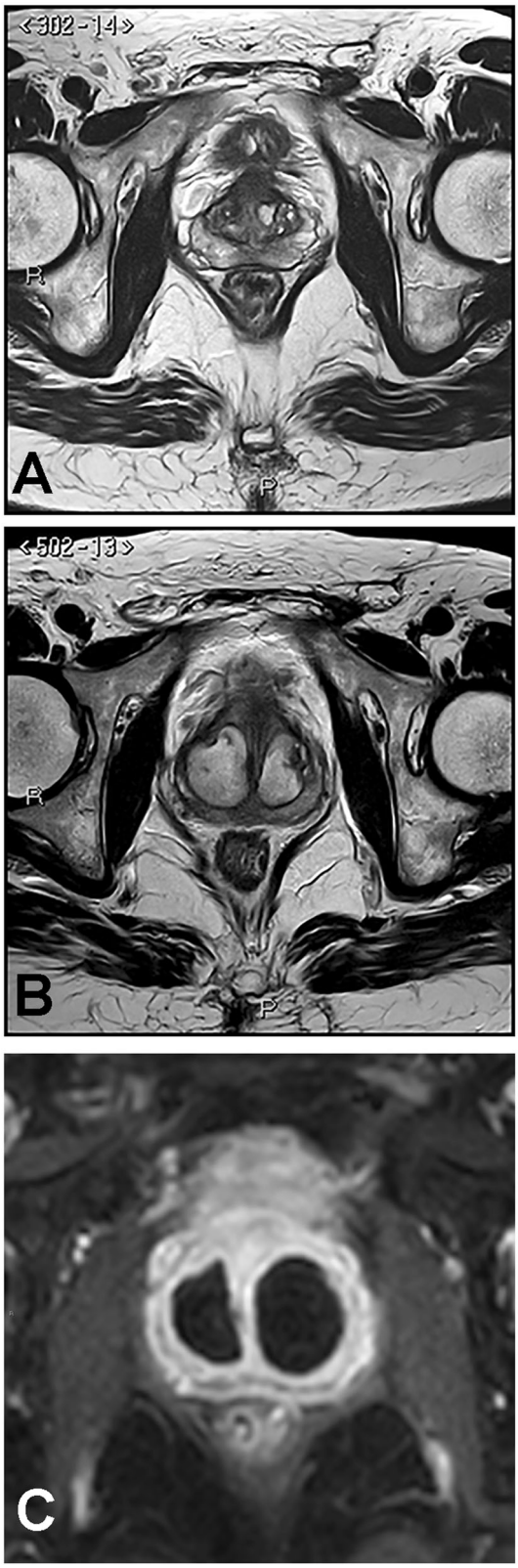

Fig. 2 3 T prostate MRI of a patient with benign prostate hyperplasia treated with transperineal laser ablation. a T2W axial plane medium gland pre-procedural image showing bilateral benign central gland hyperplasia with stromal rich component and pseudo-cystic intra-adenomatous spots. **b** T2W axial plane medium gland post-procedural image showing bilateral central gland thermal coagulative necrosis with almost complete adenoma vaporization and urethral sparing. **c** T1W contrast-enhanced axial plane medium gland post-procedural image showing central gland contrast-enhancement defects as a huge taylored tissue damage with selective urethral sparing.

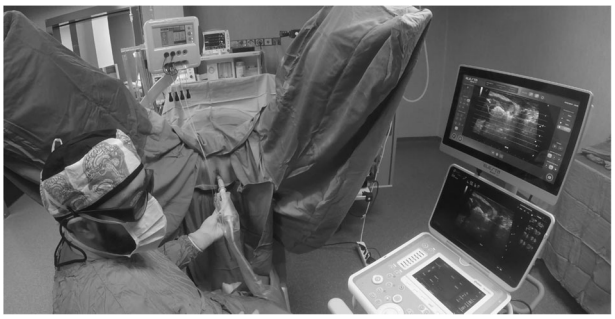

Fig. 3 Picture shows the used devices, Echolaser X4 and ESI (Echolaser Smart Interface), for the SoracteLitetm treatment in the interventional suite.

Table 1 Comparison of Qmax, RPM, IPSS, QoL, and prostate volume before treatment and at 6 months from TPLA of BPH in 160 treated patients.

	Baseline	6 months	% change	*p* value
IPSS	22.5 ± 5.1	7.7 ± 3.3	64.6 ± 17.0	<0.001
PVR (ml)	89.5 ± 84.6	27.2 ± 44.5	74.8 ± 26.6	<0.001
Qmax (ml/s)	8.0 ± 3.8	14.3 ± 3.9	87.1 ± 72.0	<0.001
QoL	4.5 ± 1.1	1.8 ± 1.0	56.2 ± 26.4	<0.001
Volume (ml)	75.0 ± 32.4	60.3 ± 24.5	27.2 ± 14.9	<0.001

Qmax maximum urinary flow rate, *PVR* post void residual, *IPSS* International Prostate Symptom Score, *QoL* Quality of Life

Table 2 Comparison of Qmax, RPM, IPSS, QoL, and prostate volume before treatment and at 12 months from TPLA of BPH in 83 treated patients.

	Baseline	12 months	% change	*p* value
IPSS	22.2 ± 4.5	7.0 ± 2.9	68.0 ± 12.9	<0.001
PVR (ml)	71.7 ± 93.9	17.8 ± 51.0	88.2 ± 22.9	<0.001
Qmax (ml/s)	8.6 ± 5.2	15.0 ± 4.0	88.8 ± 72.6	<0.001
QoL	4.2 ± 0.6	1.6 ± 0.9	60.7 ± 23.5	<0.001
Volume (ml)	87.9 ± 31.6	58.8 ± 22.9	33.0 ± 19.4	<0.001

Qmax maximum urinary flow rate, *PVR* post-void residual, *IPSS* International Prostate Symptom Score, *QoL* Quality of Life

randomized controlled trial of TURP vs PAE the difference between change in mean value of IPSS, PVR, Qmax, QoL, and Prostate Volume were 78%, 89%, 179%, 80%, and 43% vs 49%, 51%, 44%, 53%, and 19%, respectively [32, 35, 36].

In this scenario, SoracteLite™ TPLA offers some theoretical advantage over other techniques. TPLA can be

performed using the smallest available applicators on the market, thus minimizing the invasiveness related to applicators insertion. Particularly, no blood transfusions were required in our series, which are often are necessary after other procedures, such as TURP. Also, the transperineal route is extremely safe, and already widely used for prostate procedures, such as biopsies, also using larger devices. Notably, the transperineal route avoids damage to the urethra, which is often involved in other kinds of treatments, such as TURP, thus theoretically reducing post-treatment irritative voiding complaints due to urothelial damage and the risk of post-treatment infections. Furthermore, the extreme precision of laser, together with the very simple system of guidance, allows for a very controlled and safe energy delivery and predictable area of ablation, thus minimizing the risk of damage on surrounding structures. The constant monitoring in real time of all the phases of the treatment allows avoidance of severe damage to the adjacent structures. Due to the particular technique, and the possibility of using multiple applicators and perform multiple ablations, it is possible also to treat effectively large prostates with initial volume larger than 100 ml. Finally, due to the minimal invasiveness of this treatment, can be easily performed under conscious sedation and with only local anesthesia, differently from other techniques which often require general or spinal anesthesia.

Complications have been reported at various incidences in the different techniques for minimally invasive treatment of patients with BPH [5, 6, 15, 27, 29, 30, 33, 37–40]. In the series reported in this study, complications were infrequent (4.3%) and according to modified CCS they were mainly grade 1 and only one (0.6%) of treated cases was grade III [26]. Six out of one hundred and sixty (3.7%) patients experienced transient dysuria, and 2/160 (1.2%) patients lost ejaculatory function; these were regarded as sequelae [25, 41]. Notably, the present data includes the initial experience with a new technique, which always requires a learning curve. Thus, the already low rate of complications reported may be even lower in the future with the increase in experience of operators. Particularly, few cases of acute transitory retention have been observed in a few patients. At the beginning of the experience, very ill patients were treated, some of whom were carrying a bladder catheter for an extended period of time before treatment. Consequently, in the first patients, the bladder catheter was kept in place for 15 days after the procedure. Increased operator experience and the adoption of treating less complicated patients, determined a change in the clinical practice; nowadays, in several patients, the bladder catheter is removed immediately after the procedure. Thus, the ideal time for bladder catheter removal is still under evaluation and clinical decision is made according to referring urologist. The preservation of sexual function is a key determinant in the surgical pathway for patients with LUTS secondary to BPH, especially in younger men. Noteworthy is that patients treated with HoLEP or TURP had a retrograde ejaculation in over 70% [5, 42] of cases and incontinence rate ~1–2% [43]. Regarding costs of the procedure, at the time of writing this article the listed price of a single laser fiber in Europe is 600€.

Some limitations of the present work should be taken into account. First of all, this is the retrospective analysis, and no comparison with patients treated with other techniques has been performed. Prospective studies are necessary for further validate the technique, possibly comparing SoracteLite™ TPLA with other techniques such as TURP. Also, patients were treated in separate centers with a novel technique, thus results can be affected by the initial experience of the operators. Particularly, the complication rate is expected to be lowered by an increase in the experience of operators. Furthermore, only a selected subgroup of patients with at least 6 months of follow-up data available has been included in the present analysis. Studies with longer follow-up are necessary to better understand if results are sustained in the midterm and long-term period. Furthermore, ejaculatory function was not evaluated with a specific questionnaire, and thus the rate of ejucalotary complications in our series might be underestimated.

In conclusion, SoracteLite™ TPLA seems to be a safe and effective technique in the treatment of patients with BPH, demonstrating significant results sustained up to 12 months. SoracteLite™ TPLA is well tolerated by patients, does not require general anesthesia, has a low morbidity and requires short hospitalization; therefore, SoracteLite™ TPLA is rightfully taking part of the array of new techniques susceptible to wide application in patients with a long life expectancy. In order to verify the long-term durability of the results of the technique an international registry has been established by AMC-UvA (clinicaltrial.gov https://clinicaltrials.gov/ct2/show/NCT03776006) to recruit a large sample of patients for a broader multicentric study.

Compliance with ethical standards

Conflict of interest GM, CMP and CR: consultant for Elesta SrL. All other authors have nothing to disclose.

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