European Review for Medical and Pharmacological Sciences 2021; 25: 4527-4534

Efficacy and efficiency of Green-Light XPS 180-watt laser system for benign prostatic enlargement in patients treated with 5α-reductase inhibitors

J. GHAHHARI[1], C. DE NUNZIO[1], R. LOMBARDO[1], A. TUBARO[1], A. BRASSETTI[2], P. DE FRANCESCO[3], L. SCHIPS[3], L. CINDOLO[4]

[1]Department of Urology, "Sant'Andrea" Hospital, Sapienza University, Rome, Italy
[2]Department of Urology, IRCCS Regina Elena, Rome, Italy
[3]Department of Urology, "G. D'Annunzio" University, Chieti, Italy
[4]Department of Urology, Villa Stuart Hospital, Rome, Italy

Abstract. – OBJECTIVE: Aim of the study was to evaluate efficacy and efficiency of 180-watt Green-Light XPS (GL-XPS) laser photoselective vaporization of the prostate (PVP) in patients under 5-Alpha-Reductase Inhibitors (5ARI) treatment.

PATIENTS AND METHODS: A consecutive series of patients with lower urinary tract symptoms due to benign prostatic enlargement treated by PVP with the GL-XPS were enrolled. Patients were divided in two groups according to the chronic use (>6 months) of 5ARI. These two groups were compared on lasing density (kilojoules per prostate volume), vaporization efficiency (prostate volume per lasing time), vaporization power (kilojoules per lasing time), Prostate Specific Antigen (PSA) reduction from baseline, symptom score change from baseline and uroflowmetry parameters improvement. Follow-up was performed at 3, 6 and 12 months with International Prostate Symptom Score, Uroflowmetry parameters and PSA.

RESULTS: Overall 193 patients were enrolled. Out of them 87/193 (45%) were on 5ARI treatment. No significant differences were recorded between the two groups at baseline. Median age was 68 years old and median prostate volume was 60 ml. In terms of laser efficiency, no statistically significant differences were recorded in terms of lasing time (25 min *vs*. 24.5 min; *p*>0.05); energy used (250 kJ *vs*. 221 kJ; *p*>0.05), lasing density (6.8 kJ/ml *vs*. 6.6 kJ/ml, *p*>0.05), vaporization efficiency (1.4 ml/min *vs*. 1.3 ml/min, *p*>0.05) and vaporization power (9.6 kJ/min *vs*. 9.4 kJ/min; *p*>0.05). Finally, no significant differences were also recorded postoperatively in the two groups in terms of PSA reduction, improvement in symptom score and uroflowmetry parameters (*p*>0.05).

CONCLUSIONS: Thirty-seven efficacy and efficiency outcomes were not statistically different between the two groups. 5ARI does not reduce the performance and ability of the 180-watt Green-Light XPS laser system.

Key Words:
GreenLight, Photoselective vaporization prostatectomy, Benign prostatic hyperplasia, BPH, Dutasteride, Finasteride, 5 alpha-reductase inhibitors.

Introduction

Lower urinary tract symptoms (LUTS) represent one of the most common clinical complaints in adult men. The European Association of Urology (EAU) guidelines suggest Green Light (GL) approach as an alternative to transurethral resection of the prostate (TURP) in patients with moderate to severe LUTS[1-4]. GL physics show high absorption rates for hemoglobin (absorption coefficient 10^2/cm) and low absorption for water (absorption coefficient 10^{-4}/cm). This characteristic is perfect to treat hyperplastic prostate tissue[5]. In a comparative functional and pathologic study in living and cadaver canine prostatic tissue, Kuntzman et al[6] proved that bloodless cadaver parenchyma was less susceptible to laser vaporization than living tissue. Kuntzman et al[6] demonstrated that cadaveric prostate needed twice as much energy per cubic centimeter cavity vaporization when compared to vital tissue[6].

Several studies have demonstrated the role of 5 alpha reductase inhibitors (5ARI) in reducing

Corresponding Author: Jamil Ghahhari, MD; e-mail: jamil.ghahhari@gmail.com

microvesicle density in the prostate. They also showed an important reduction in intraoperative and perioperative bleeding[7] in TURP series. These considerations have opened the way to the debate concerning the possible impact of the 5ARI therapy on surgical and clinical outcomes of patients treated with GL. Nevertheless, previous works[5,8,9] have proved that 5ARI does not reduce efficacy and efficiency of the GL laser. These studies were performed with the outdated 80-watt KTP and 120-watt HPS systems. To date, the impact of 5ARI on the efficacy of the 180-watt LBO crystal Green Light Xcelerated Performance System (XPS) ™ with a 532 nm wavelength, metal-capped and liquid cooled irrigated fiber (Moxy™ fiber) have not been studied. With this knowledge in mind, aim of the study was to evaluate efficacy and efficiency of 180 watt Green-Light XPS (GL-XPS) laser PVP in patients under 5ARI treatment.

Patients and Methods

After an internal Review Board approval, all patients undergoing GL-XPS PVP between February 2017 and September 2019 were prospectively enrolled. All patients signed informed consent and all the procedures were performed in accordance to the Declaration of Helsinki. Patients were divided in two groups according to the chronic use (>6 months) of 5 ARI *vs.* no treatment. Any patient with a prior history of prostatic or urethral surgery, urethral stricture, neuro-vesical dysfunction and/or prostate cancer was excluded from the study.

Patients with bothersome LUTS were offered surgery if preoperative IPSS ≥12 points and/or quality of life (QoL) ≥ 4 and/or maximal urinary flow rate (Qmax) <15 mL and/or not-responding to medical therapy and/or not willing to undergo medical therapy. All operations were performed by one single expert surgeon (L.C).

Clinical data including age, BMI, hemoglobin levels, International Prostate Symptom Score (IPSS), QoL score, prostate specific antigen (PSA), prostatic volume (PV) and post-void residual volume, maximum urinary flow (Qmax) were retrospectively collected. Prostate volume was measured using transrectal 7.5 MHz ultrasound probe, volume was calculated using the ellipsoid formula: $\pi/6 \times$ with x height $\times$ depth of prostate.

Surgical Procedure

Procedures started with evaluation of striated sphincter, ureteral orifices and exclusion of tumors or any suspicious areas in the bladder. *Standard* PVP was carried out by creation of a working space at 5 and 7 o'clock position, the gland was then vaporized in a centrifuge way from prostatic urethra towards prostatic capsule. When an *anatomical* technique was implemented, the procedure started with the identification of the capsular plan at the apex of the gland; then, the surgeon proceeded by the tip of the resectoscope to sunder the adenoma from prostatic capsule. Finally, vaporization was performed in a out-in manner, pointing the laser fire from the outer border of the adenoma to the prostatic urethra.

General or spinal anesthesia was used for the procedures. The antibiotic prophylaxis was adopted according to local practice guidelines.

Laser Efficiency Outcomes

Energy density, vaporization efficiency and vaporization power were recorded. *Lasing density* was defined as kilojoules of energy applied per cm^3 of prostate volume, *vaporization efficiency was* defined as cm^3 of prostate volume per lasing time (minute) and *vaporization power* was defined as kJ of energy applied per lasing time (min).

Safety Outcomes

Early and late complications (within 30 post-operative days and after 90 days, respectively) were noted and reported according to Clavien-Dindo classification[10,11]. In the evaluation of complications following surgical procedure, we reported frequency and urgency when they justified a change in post-operative management and/or showed a serious impact on the patient's quality of life.

Pollakiuria, dysuria, urgency were counted as storage symptoms. Re-intervention in case of urethral stenosis, bladder neck contracture or prostatic fossa sclerosis was also marked. Presence of urinary incontinence was rated as urine loss of any type (stress or urge) and degree if troublesome and wearing for patient activity and life.

Efficacy Outcomes

Patients were assessed at 3, 6, and 12 months after surgery. At each follow-up stage, IPSS, Qmax, and PSA were marked. The Patient Global Impression of Improvement (PGI-I) was elaborated with PGI-I scale[12].

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS v.24, IBM Corp., Armonk, NY, USA). Evaluation of data distribution using the Kolmogorov-Smirnov test showed a non-normal distribution of the study data set. The study involved two groups: Group I consisted of patients on chronic 5ARI (minimum 6-month duration) therapy at the time of operation and Group II included patients who had never taken 5ARI in the last 3 years. Differences between groups of patients in medians for quantitative variables and differences in distributions for categorical variables were tested with the Kruskal Wallis one-way analysis of variance and chi-square test, respectively. Post-hoc power calculation according to Levine resulted in a power >80% for all laser efficiency outcomes. A *p*-value of 0.05 was considered as threshold of significance.

Results

Overall, 193 patients were eligible for the study analysis. Out of them 87/193 (45%) were under 5ARI treatment (Group I) while 106/193 were not under 5ARI treatment (Group II) before surgery.

At baseline no statistically significant differences were recorded in terms of age, symptoms, QoL, prostate volume, PSA levels and baseline Qmax (Table I). In terms of laser efficiency, no statistically significant differences were recorded in terms of lasing time (25 min *vs.* 24.5 min; $p>0.05$); energy used (250 kJ *vs.* 221 kJ; $p>0.05$). lasing density (6.8 kJ/ml *vs.* 6.6 kJ/ml, $p>0.05$), vaporization efficiency (1.4 ml/min *vs.* 1.3 ml/min, $p>0.05$) and vaporization power (9.6 kJ/min *vs.* 9.4 kJ/min; $p>0.05$) (Table II).

Catheterization time, hospital stay and post-operative acute urinary retention were similar between groups (Table I).

No statistically significant differences were recorded postoperatively in the two groups regarding PSA decrease, and improvement in symptom score (Table III). Furthermore, no statistically significant differences were found for Qmax and IPSS between groups (Table III). All three parameters (PSA, Qmax and IPSS) improved over time (Table III).

Moreover, Patient Global Impression of Improvement (PGI-I) assessed according to PGI-I scale(12) showed that most patients in the post-operatory period, reported their condition as "very much better" and "much better".

Finally, according to Clavien-Dindo classification, the most common early complications were Grade I in both groups (33% Group I *vs.* 36% Group II) and similar rates between groups were recorded (Table IV). The most frequent early complication was burning urination (overall 35%, 16% in Group I *vs.* 19% in Group II), while the most frequent late complication was storage symptoms with *de novo* urgency (Table IV).

Table I. Patients demographics.

Variable	Overall	5αRI+	5αRI-	*p*-value
Number of patients, n (%)	193	87 (45)	106 (55)	NA
Age (Years), median (range)	68.3 (63/74)	69 (75-64)	67 (73.2-62)	0.132
ASA Score, median (range)	2 (2-2)	2 (2-2)	2 (2-2)	0.243
TRUS volume (mL), median (range)				
Prostate volume (mL)	60 (84-50)	60 (80-50)	60 (90-43.5)	0.653
Adenoma volume (mL)	30 (42-25)	30 (47.5-20.7)	30 (40-25)	0.541
PSA (ng/mL), median (range)	2.4 (4.3-1.1)	2.8 (5.8-1.2)	2.3 (3.6-0.9)	0.326
αAntagonists, n (%)	142 (73.5)	77 (40)	65 (33.6)	
Urinary retention, n (%) (Indwelling catheter history)	27 (14)	14(7)	13 (6.7)	0.520
Urethral stenosis, n (%)	20 (10.3)	6 (3.1)	14 (7.2)	0.334
Antiplatelet/anticoagulant				0.965
None	111 (57.5)	49 (25.3)	62 (32.1)	
Antiplatelet	53 (27)	25 (12.9	28 (14.5)	
Anticoagulant	12 (6.2)	6 (3.1)	6 (3.1)	
Unknown	17 (8.8)	7 (3.6)	10 (5.1)	
Hemoglobin (g/dl), median (range)	14.9 (15.5-14)	14.6 (15.7-14)	14.7 (15.5-13.9)	0.125
Hematocrit (g/dl), median (range)	44.9 (47.2-42.9)	44.8 (47-43)	44.6 (47.6-42.6)	0.569

Table II. Intraoperative and perioperative data.

Variable	Overall	5αRI+	5αRI-	*p*-value
Energy usage (kJ), median (range)	237 (326-150)	250 (329-150)	221 (318-150)	0.640
Lasing time (min), median (range)	25 (35-16)	25 (35-16)	24.5 (34.7-17)	0.747
Operation time (min), median (range)	55 (67-40)	55 (65-40)	55 (70-41)	0.518
Lasing Density (kJ/gr), median (range)	6.7 (8-5)	6.6 (9.1-4.7)	6.8 (8.4-5)	0.976
Vaporization Efficiency (gr/min), median (range)	1.3 (1.6-1.0)	1.4 (1.6-1.0)	1.3 (1.6-1.0)	0.678
Vaporization Power (kJ/min), median (range)	9.5 (9.9-9)	9.6 (10-9.2)	9.4 (9.8-8.9)	0.192
Surgical technique				0.990
Anatomic PVP	82 (42)	37 (19)	45 (23.3)	
Standard PVP	111 (58)	50 (25.9)	61 (31.6)	
Hospital stay (h)	48	48	48	0.958
Catheterization time (h)	43	45	38	0.324
Post-operative acute urinary retention, n (%)	18 (9.3)	8 (4.1)	10 (5.1)	0.824

Discussion

The present study indicates the efficacy of the GL XPS in treating patients with LUTS due to BPE independently of the 5ARI treatment. Our cohort patients treated with GL-XPS presented statistically significant improvements in symptoms, urinary flow and quality of life up to 1 year after surgery[13]. As well, GL-XPS is a safe procedure with minor complications. These data are in line with the peer-reviewed literature and show the internal validity of our results[3].

Several studies have evaluated the histological effects of 5ARI: finasteride and dutasteride. They act not only by decreasing prostate volume, but also work by reducing bleeding through alteration of sub urethral micro vessel density. 5ARI drugs act through lowering intraprostatic 5α-dihydrotestosterone which consequently produces a reduction of stromal cell hypertrophy, expression of sub urethral vascular endothelial growth factor and angiogenesis process[14-21]. Hochberg et al[14] showed that there was a significant reduction in sub urethral prostatic micro vessel density in

Table III. Clinical outcomes.

Variable	Overall	5αRI+	5αRI-	*p*-value
PSA (ng/mL)				
Baseline	2.4 (4.3-1.1)	2.3 (3.6-0.9)	2.8 (5.8-1.2)	0.326
Follow up period				
• 3 mo	1.7 (3.2-1.2)	2.7 (4-0.6)	1.7 (2.9-1.4)	0.447
• 6 mo	2 (5.5-0.3)	1.2 (3-0.2)	1.9 (6.7-2.8)	0.121
• 12 mo	1 (3.4-0.5)	0.8 (3.6-0.5)	0.7 (2.3-1.6)	0.341
Qmax (mL/sec)				
Baseline	9 (10-7)	8 (10-7)	9 (11-7)	0.085
Follow up period				
• 6 mo	19 (21-18)	19 (21-17.5)	19 (21-17.7)	0.496
• 12 mo	20 (23-18)	21 (24-18)	20 (22.7-18)	0.372
IPSS				
Baseline	25 (27-23)	25 (27-23)	25 (27-23)	0.714
Follow up period				
• 6 mo	8 (9-7)	8 (9-7)	8 (9-7)	0.190
• 12 mo	7 (8-7)	7 (8-7)	7 (8-7)	0.881
Patient global impression of improvement				
Very much better	106 (54.9)	49 (25.3)	57 (29.5)	0.839
Much better	36 (18.6)	17 (8.8)	19 (9.8)	
A little better	9 (4.6)	5 (2.6)	4 (2)	
No change	6 (3.1)	4 (2)	2 (1)	
A little worse	/	/	/	
Much worse	3 (1.5)	1 (0.5)	2 (1)	
Very much worse	/	/	/	
Unknown	34 (17.6)	11 (5.7)	23 (11.9)	

Table IV. Complications.

Variable	Overall	5αRI+	5αRI-	*p*-value
Early complications				0.558
Fever < 38°C	10 (5.1)	2 (1)	8 (4.1)	
Fever > 38°C	8 (4.1)	1 (0.5)	7 (3.6)	
Burning urination	35 (18.1)	16 (8.2)	19 (9.8)	
Frequency	18 (9.3)	10 (5.1)	8 (4.1)	
De novo urgency	18 (9.3)	10 (5.1)	8 (4.1)	
De novo urge-incontinence	12 (6.2)	5 (2.6)	7 (3.6)	
Stress incontinence	9 (4.6)	3 (1.5)	6 (3.1)	
Capsule perforation	/	/	/	
Haematuria	14 (7.2)	7 (3.6)	7 (3.6)	
Urinary tract infection	5 (2.6)	2 (1)	3 (1.5)	
Blood transfusion	2 (1)	1 (0.5)	1 (0.5)	
Minor cardiovascular event	/	/	/	
MACE*	3 (1.5)	1 (0.5)	2 (1)	
Clavien-Dindo classification of early complication				0.450
I	69 (13.7)	33 (17)	36 (18.6)	
II	4 (2)	3 (1.5)	1 (0.5)	
IIIa	/	/	/	
IIIb	/	/	/	
IVa	3 (1.5)	1 (0.5)	2 (1)	
IVb	/	/	/	
V	/	/	/	
Late complications				0.408
Urethral stenosis	2 (1)	/	2 (1)	
Bladder neck contracture	6 (3.1)	3 (1.5)	3 (1.5)	
Prostatic fossa sclerosis	4 (2)	3 (1.5)	1 (0.5)	
Stress incontinence	7 (3.6)	2 (1)	5 (2.6)	
Re-intervention	5 (2.6)	2 (1)	3 (1.5)	
Storage symptoms/De novo urgency	10 (5.1)	2 (1)	8 (4.1)	

finasteride-treated patients. The downregulation of growth factors that are androgen stimulated are probably the primary target of 5ARI. Vascular endothelial growth factor (VEGF) is an important and powerful promoter of angiogenesis[22,23]. In 2001 Häggström et al[15] found that finasteride significantly decreases expression of sub urethral VEGF. 5ARI also affect glandular/stromal ratio[24] and this modification, in long term period, can increase fibrous content of the gland, making PVP less efficacious.

On this basis, it is postulated that laser PVP, which has a high affinity for hemoglobin, its primary chromophore, would be harder in prostates treated chronically with 5ARI. In 1997 a human and dogs' trial with 60-watt KTP laser proved that there was a need to deliver twice of energy to vaporize a similar cadaveric volume compared to living tissue[25]. In consideration of the effects of 5ARIs treatment on prostate gland vasculature, this drives to the supposition that these drugs can negatively impact the length of the operative time (which gets longer). Araki et al[5] in 2007 tested KTP laser PVP as treatment for benign prostatic hyperplasia in patients on long-term 5ARIs[5]. In this study transurethral PVP was performed with the use of an 80-W KTP side-firing laser system in one hundred sixty BPH-patients (117 were not on a 5ARI and 43 were on either finasteride or dutasteride for a minimum of 6 months). They only rated intra-operative laser time and energy usage. Mean follow up was 52 weeks. They concluded that the drugs do not have a detrimental effect on the efficiency and efficacy of KTP laser PVP. Two years later Bepple et al[8] evaluated the effect of dutasteride on the efficacy of GreenLight PVP[8]. In this prospective, placebo-controlled, randomized, double blind study (DOP trial) 59 subjects were randomized to either dutasteride 0.5 mg daily (n = 30) or placebo daily (n = 29) for 3 months before PVP with the 80-W KTP laser system. Operative endpoints included surgical time, joules used, estimated blood loss, and ease of the procedure. Mean follow up was 12 months. They experienced that patients randomized to dutasteride, compared with patients randomized to placebo, showed a trend toward decreased time, joules used, and blood

loss during surgery. Finally in 2011, Strom et al[9] analyzed the efficacy and efficiency of 120-watt GreenLight HPS laser PVP in patients on chronic 5**α**-reductase inhibitor therapy. The study focused on one hundred eighty-one BPH-patients. Fifty-seven patients (31.5%) comprised group I and were on either dutasteride or finasteride; 124 patients not taking 5ARI (68.5%) comprised group II. Follow up was 12 months. Like the previous study of Akari et al[5], the study group of Strom et al[9] rated the intra-operative variables laser time and energy usage and concluded that the efficacy and efficiency of PVP with the GreenLight HPS laser are not negatively affected in patients on chronic 5ARI therapy.

Compared to previous works, our study is the first that assesses the efficacy and efficiency of 180-watt GreenLight XPS (GLXPS) laser photoselective vaporization prostatectomy in patients receiving 5ARI in an Italian population. Our results evaluated two homogeneous groups with no significant differences at baseline. Data from our study add important evidence on the efficacy of GL XPS in patients under 5ARI treatment and are in line with the available literature. Our results agree the previous of Strom, Bepple and Araki that do not support the hypothesis that the efficacy and the efficiency of the GreenLight laser is compromised in patients taking 5ARI therapy[5,8,9].

Our study is the first that evaluated also the subjective impression of improvement with the use of PGI-I scale. Most patients revealed their perception regarding the postoperative condition as "very much better" and "much better", without differences between groups.

Concerning safety profile, burning urination emerged as the most frequent early complication with an overall rate of 35%. Reporting complications after 90 days from procedure, storage symptoms with de novo urgency showed the highest frequency (overall rate 10%). Martín Way et al[26] analyzing efficacy of oral anticholinergics in postoperative period of GL-XPS concluded that using these drugs is not an effective preventive strategy for storage symptoms and incontinence associated with this surgery, which seem to self-limit over time. Di Pasquale et al[27] studied the role of Cernilen-flogo® (OMEGA PHARMA Srl, Cantù (CO), Italy) therapy (Graminex G6, Quercetin, Bromelain, Valerian and Mallow) after PVP procedure, in reducing irritative LUTS, pelvic discomfort and postoperative pain. The study group proved that postoperative treatment with Cernilen-flogo® is effective in reducing pelvic discomfort and improving the quality of life.

We have to acknowledge some limitations to the present study. Our research is single center and therefore our results strictly depend on the enrolled population. The retrospective analysis may be considered a possible limitation. However, our database was prospectively collected limiting possible biases. Moreover, the post-hoc power calculation confirmed a power >80% for all efficiency endpoints. In reporting pre- and post-operative events, we did not use questionnaires to score urinary incontinence (such as International Consultation on Incontinence Questionnaire-short form –ICIQ-SF– and OverActive Bladder questionnaire-short form –OABq-SF). This is maybe a further possible limitation. Lastly there is a lack of long-term follow-up. However, a study to evaluate long term outcomes is ongoing.

Despite the limitations, the proposed retrospective designed comparative study proved and confirmed that neither the efficacy nor efficiency and power of the 180 watt Green Light XPS laser system PVP are compromised in patients on 5ARI-therapy.

Conclusions

Our data demonstrate that 5ARI-therapy does not have a negative effect on the efficacy and efficiency of the 180-watt Green Light XPS laser system PVP. PVP can be therefore safely proposed to patients under 5ARI treatment.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) Cindolo L, De Nunzio C, Greco F, Destefanis P, Bergamaschi F, Ferrari G, Fasolis G, Palmieri F, Divan C, Oriti R, Ruggera L, Tubaro A, Dadone C, De Rienzo G, Frattini A, Mirone V, Schips L; Members of Green Laser Italian Group. Standard vs. anatomical 180-W GreenLight laser photoselective vaporization of the prostate: a propensity score analysis. World J Urol 2018; 36: 91-97.

2) Leonardo C, Lombardo R, Cindolo L, Antonelli A, Greco F, Porreca A, Veneziano D, Pastore A, Dalpiaz O, Ceruti C, Verze P, Borghesi M, Schiavina R, Falabella R, Minervini A; AGILE

Group. What is the standard surgical approach to large volume BPE? Systematic review of existing randomized clinical trials. Minerva Urol Nefrol 2020; 72: 22-29.

3) Reale G, Marchioni M, Altieri V, Greco F, De Nunzio C, Destefanis P, Ricciardulli S, Bergamaschi F, Fasolis G, Varvello F, Voce S, Palmieri F, Divan C, Malossini G, Oriti R, Tuccio A, Ruggera L, Tubaro A, Delicato G, Laganà A, Dadone C, De Rienzo G, Ditonno A, Frattini A, Pucci L, Carrino M, Montefiore F, Germani S, Miano R, Schips L, Rabito S, Ferrari G, Cindolo L. Operative profile, safety and functional outcomes after GreenLight laser prostate surgery: results from a 12 months follow-up multicenter Italian cohort analyses. Minerva Urol Nefrol 2020; 72: 622-628.
4) Speakman MJ, Cornu JN, Gacci M, Gratzke C, Mamoulakis C, Herrmann TRW, Omar MI, Rieken M, Tikkinen KAO, Gravas G. What Is the Required Certainty of Evidence for the Implementation of Novel Techniques for the Treatment of Benign Prostatic Obstruction? Eur Urol Focus 2019; 5: 351-356.
5) Araki M, Lam PN, Culkin DJ, Wong C. Decreased Efficiency of Potassium-Titanyl-Phosphate Laser Photoselective Vaporization Prostatectomy with Long-Term 5 alpha-Reductase Inhibition Therapy: Is it True? Urology 2007; 70: 927-930.
6) Kuntzman RS, Malek RS, Barrett DM, Bostwick DG. Potassium-titanyl-phosphate laser vaporization of the prostate: A comparative functional and pathologic study in canines. Urology 1996; 48: 575-583.
7) Bansal A, Arora A. Transurethral resection of prostate and bleeding: A prospective randomized, double blind, placebo controlled trial to see efficacy of short term use of Finasteride and Dutasteride on operative blood loss and prostatic micro-vessel density. J Endourol 2017; 31: 910-917.
8) Bepple JL, Barone BB, Eure G. The Effect of Dutasteride on the Efficacy of Photoselective Vaporization of the Prostate: Results of a Randomized, Placebo-controlled, Double-blind Study (DOP Trial). Urology 2009; 74: 1101-1104.
9) Strom KH, Gu X, Spaliviero M, Wong C. The effects of 5α-reductase inhibition on benign prostatic hyperplasia treated by photoselective vaporization prostatectomy with the 120 watt greenlight HPS laser system. J Am Coll Surg 2011; 212: 244-250.
10) De Nunzio C, Lombardo R, Autorino R, Cicione A, Cindolo L, Damiano R, De Sio M, Falsaperla M, Franco G, Gacci M, Leonardo C, Presicce F, Tubaro. Contemporary monopolar and bipolar transurethral resection of the prostate: Prospective assessment of complications using the Clavien system. Int Urol Nephrol 2013; 45: 951-959.
11) Mamoulakis C, Efthimiou I, Kazoulis S, Christoulakis I, Sofras F. The modified Clavien classification system: A standardized platform for reporting complications in transurethral resection of the prostate. World J Urol 2011; 29: 205-210.
12) Hossack T, Woo H. Validation of a patient reported outcome questionnaire for assessing success of endoscopic prostatectomy. Prostate Int 2014; 2: 182-187.
13) Thomas JA, Tubaro A, Barber N, D'Ancona F, Muir G, Witzsch U, Grimm MO, Benejam J, Stolzenburg JU, Riddick A, Pahernik S, Roelink H, Ameye F, Saussine C, Bruyère F, Loidl W, Larner T, Gogoi NK, Hindley R, Muschter R, Thorpe A, Shrotri N, Graham S, Hamann M, Miller K, Schostak M, Capitán C, Knispel H, Bachmann A. A Multicenter Randomized Noninferiority Trial Comparing GreenLight-XPS Laser Vaporization of the Prostate and Transurethral Resection of the Prostate for the Treatment of Benign Prostatic Obstruction: Two-yr Outcomes of the GOLIATH Study. Eur Urol 2016; 69: 94-102.
14) Hochberg DA, Basillote JB, Armenakas NA, Vasovic L, Shevchuk M, Pareek G, Fracchia JA. Decreased suburethral prostatic microvessel density in finasteride treated prostates: A possible mechanism for reduced bleeding in benign prostatic hyperplasia. J Urol 2002; 167: 1731-1733.
15) Häggström S, Tørring N, Møller K, Jensen E, Lund L, Nielsen JE, Bergh A, Damber JE. Effects of finasteride on vascular endothelial growth factor - A placebo-controlled randomized study in BPH patients. Scand J Urol Nephrol 2002; 36: 182-187.
16) Puchner PJ, Miller MI. The Effects of Finasteride on Hematuria Associated with Benign Prostatic Hyperplasia: A Preliminary Report J Urol 1995; 154: 1779-1782.
17) P Pirozzi L, Sountoulides P, Castellan P, Presicce F, Lombardo R, Romero M, De Nunzio C, Tubaro A, Schips L, Cindolo L. Current Pharmacological treatment for male LUTS due to BPH: dutasteride or finasteride? Curr Drug Targets 2015; 16: 1165-1171.
18) Cindolo L, Alvarez-Maestro M, Castellucci R, Schips L. Efficacy and safety of dutasteride for the treatment of symptomatic benign prostatic hyperplasia (BPH): a systematic review and meta-analysis. World J Urol 2015; 33: 441-442.
19) Cindolo L, Fanizza C, Romero M, Pirozzi L, Autorino R, Berardinelli F, Schips L. The effects of dutasteride and finasteride on BPH-related hospitalization, surgery and prostate cancer diagnosis: A record-linkage analysis. World J Urol 2013; 31: 665-671.
20) Busetto GM, Del Giudice F, D'Agostino D, Romagnoli D, Minervini A, Rocco B, Antonelli A, Celia A, Schiavina R, Cindolo L, Chung BI, Kim JH, Maggi M, Sciarra A, De Berardinis E, Porreca A. Efficacy and safety of Finasteride (5 alpha-reductase inhibitor) monotherapy in pa-

tients with benign prostatic hyperplasia: A critical review of the literature. Arch Ital Di Urol e Androl 2019; 19: 205-211.

21) Cindolo L, Berardinelli F, Fanizza C, Romero M, Pirozzi L, Tamburro FR, Pellegrini F, Neri F, Pitrelli A, Schips L. Clinical effects and economical impact of dutasteride and finasteride therapy in Italian men with LUTS. Arch Ital Di Urol e Androl 2013; 85: 200-206.

22) Lekas AG, Lazaris AC, Chrisofos M, Papatsoris AG, Lappas D, Patsouris E, Deliveliotis C. Finasteride effects on hypoxia and angiogenetic markers in benign prostatic hyperplasia. Urology 2006; 68: 436-441.

23) Memis A, Ozden C, Ozdal OL, Guzel O, Han O, Seckin S. Effect of finasteride treatment on suburethral prostatic microvessel density in patients with hematuria related to benign prostate hyperplasia. Urol Int 2008; 80: 177-180.

24) Steers WD. 5A-Reductase Activity in the Prostate. Urology 2001; 58: 17-24.

25) Kuntzman RS, Malek RS, Barrett DM, Bostwick DG. High-power (60-Watt) potassium-titanyl-phosphate laser vaporization prostatectomy in living canines and in human and canine cadavers. Urology 1997; 49: 703-708.

26) Martin Way DA, Barrabino Martin R, Puche Sanz I, Vicente Prados FJ, Cozar Olmo JM. The Effect of Anticholinergics for Prevention of Storage Symptoms After Prostate Photovaporization. Urol J 2019; 16: 598-602.

27) Di Pasquale AB, Cassani A, Masciovecchio S, Zasa G, Ranieri G, Romano G, Di Clemente L. Postoperative treatment with phytotheraphy Graminex G63 (CERNILEN-Flogo®) after greenlight laser XPS (180W) photovaporization of the prostate (PVP), can affect patient's quality of life? Eur Rev Med Pharmacol Sci 2020; 24: 9116-9120.