

GREEN LIGHT PHOTOSELECTIVE VAPORIZATION OF THE PROSTATE: ONE LASER FOR DIFFERENT PROSTATE SIZES

GreenLight in prostate less and more than 100 cc

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ABSTRACT

INTRODUCTION

GreenLight laser vaporization of the prostate (PVP) is a safe and effective procedure for Benign Prostatic Hyperplasia. Long term results and advantages of PVP in patients with large and symptomatic prostate are still under evaluation.

MATERIALS AND METHODS

In a multicenter experience, patients who underwent standard or anatomical PVP were retrospectively reviewed. Patients with follow-up >12 months were divided into two groups based on prostate volume (<100cc vs \geq 100cc). Pre- and peri-operative data as well as post-operative results and complications were recorded after 3, 6, 12 months and then annually.

RESULTS

1031 patients were eligible, 916 of these had a prostate volume of <100 cc and 115 \geq 100 cc. Median follow-up period was 25.0 months (IQR 16.5-35.0) and 16.0 months (IQR 12.0-24.0) in \geq 100 and <100 groups, respectively. No difference was found in terms of catheterization time, post-operative stay and post-operative acute urine retention. Patients with prostate \geq 100 required longer operative time (75 versus 55 minutes), lasing time (41.7 versus 24.9 minutes), and higher energy used but lower energy density. Patients with prostate \geq 100 had a higher incidence of early (50.4 versus 35.7%) and late complications (21.7 versus 12.8%) and early urge/incontinence symptoms (40.9 versus 29.3%). No statistically significant differences were found for the Qmax and IPSS results between the two groups. The re-intervention rate in \geq 100 group was 3.5% versus 2.3% in <100.

CONCLUSIONS

In the midterm follow-up, Greenlight PVP guarantees the same results in different prostate volumes groups. Early and late complications are more frequent in large prostates.

GreenLight Laser in prostate less and more than 100 cc

INTRODUCTION

Since 1997, when the prototype of a 60 Watt continuous-wave Very High Power (VHP)TM laser system was first used, two additional Green Laser devices have been introduced, the 80W Potassium Titanyl Phosphate (KTP) and the 120W high-performance system (HPS)TM Lithium Triborate (LBO) [1].

These three laser systems differ in maximum power output and fiber design, and this evolution has been researched to allow higher and faster tissue ablation and lower fiber degradation [1]. Nowadays, Green light laser photoselective vaporisation of the prostate (PVP) is a consolidated and safe technique for Benign Prostatic Obstruction (BPO). Several papers have reported long term results with the 80W KTP and the 120W LBO, documenting lack of inferiority compared to TURP in terms of International Prostate Symptom Score (IPSS) and peak urinary flow rates, with lower transfusion requirements, shorter catheterization time and hospital length of stay in favor of PVP, while re-operation rates and operation time are in favor of TURP [1].

The introduction of the 180W LBO crystal Green Light Xcelerated Performance System (XPS)TM (American Medical System-AMS, Minnetonka, Minnesota) with a new 532 nm wavelength, metal-capped and liquid cooled irrigated fiber (MoxyTM fiber) and the development of different PVP techniques (standard photovaporization- PVP, anatomical PVP and GreenLight enucleation of prostate - GreenLEP) have permitted to vaporize more tissue in a shorter time with less fibers used, aiming to reduce re-treatment rates [1-3]. The European Association of Urology (EAU) guidelines recommend Green light laser vaporisation of the prostate to men with moderate-to-severe lower urinary tract symptoms (LUTS) as an alternative to TURP with a level of evidence (LE) of 1a (evidence obtained from meta-analyses of randomized trials) for short-term results with the 80W KTP laser and for mid-term results with the 120W, and of LE-1b (evidence obtained from at least one randomized trial) with the 180W LBO laser [4]. Conversely, for patients affected by large and symptomatic prostates, long-term functional results and re-operation rates after PVP performed with the 180 W LBO laser are mainly based on retrospective data [1, 5-10].

Based on these considerations, we decided to analyze a large multicenter cohort of 1031 patients in order to evaluate complication rates and functional outcomes in patients with BPO treated by 180W LBO laser according to prostate volume.

MATERIALS AND METHODS

We retrospectively reviewed cases undergoing standard or anatomical PVP in a multi-institutional prospectively collected database between September 2011 and October 2017 using the 180-W XPS GL system for BPO. The study involved several surgeons with consolidated experience in GreenLight. Informed consent was obtained from all individual participants included in the study. This study and all related procedures have been performed in accordance with the Declaration of Helsinki. Patients with history of prostate cancer, neurogenic bladder disease, previous prostate surgery as well as those who underwent GreenLEP or contemporary urethrotomy, treatment of bladder stones, and with incidental bladder tumors were excluded. Surgical procedures were performed according to surgeon's preferences, as previously described [1, 3]. All the procedures start with visualization of the striated sphincter, the ureteral orifices and the exclusion of bladder tumors. In standard PVP, after the creation of a working space at 5 and 7 o'clock, the prostate is vaporized in a centrifuge way from the prostatic urethra towards the prostatic capsule (inside out). Conversely, in anatomical PVP after the localization of the capsule at the apex of the prostate, the surgeon performs a bilateral incision lateral to veru montanum and the tip of the resectoscope is used to find the anatomical plane between the prostatic capsule and the adenoma. The dissection plane is followed towards the bladder neck at 6 o'clock and the dissection is accompanied by vaporization of the enucleated tissue, which is performed by firing the laser in direction of prostatic urethra (outside in). In both techniques, all the tissues were vaporized and morcellation was not necessary [3]. All procedures were performed under general or spinal anesthesia. Antibiotic prophylaxis was administered to all patients according to local practice guidelines.

Examined pre-and post-operative factors and intra- and peri-operative data include: age, American Society of Anesthesiology score (ASA), prostate volume evaluated with trans-rectal ultrasound (TRUS), use of antiplatelet and anticoagulant medications, LUTS therapy and history of catheterization or retention, PSA level, IPSS, maximum urinary flow (Qmax),

operative time, lasing time, energy used, catheterization time, hospital stay and re-treatment rate. Energy density was coded as energy used divided the prostate volume. All the patients were recalled and underwent an outpatient clinic evaluation at least after 3, 6, and 12 months and then annually. Follow-up was calculated as time from surgery to last visit. During follow-up visit, symptoms score (IPSS), maximum urinary flow (Qmax), and PSA level were recorded. Patient Global Impression of Improvement (PGI-I) was evaluated with PGI-I scale [11]. Complications were collected as early (within 30 post-operative days) or late (after 90 days) and classified according to Clavien-Dindo classification [12-13]. We have considered post-operative frequency and urgency as complications when they prompted additional medical examination or bothered patients. Haematuria requiring application of bladder catheter and irrigation or re-intervention or medical examination was also reported. Urinary incontinence was defined as reported incontinence of any degree and type (stress or urge incontinence) if bothersome and impairing patient quality of life.

Statistical methods.

Quantitative variables were summarized as median and interquartile range (IQR). Qualitative data were summarized as frequency and percentage. After stratification according to prostate volume (<100 cc vs \geq 100 cc) the Chi-square and the Mann-Whitney U tests tested the statistical significance in proportions and median differences. We relied on a non-parametric model for repeated measurements [14] to test the effect of prostate volume and time on PSA, Qmax and IPSS. Moreover, we tested the interaction between pre-operative prostate volume and time. Boxplots graphically depicted the distribution of PSA, Qmax and IPSS values at each time points (baseline, 6 and 12 months). Furthermore, univariable and multivariable logistic regression models tested the effect of prostate size on acute urinary retention, early and late complications rates. All the multivariate logistic regression models were adjusted for age, baseline PSA, BPO/LUTS therapy, antiplatelet/anticoagulant therapy, surgery type and history of catheter indwelling prior surgery. All tests were two-sided and the level of statistical significance was set at $p < 0.05$. Analyses were performed using the R software environment for statistical computing and graphics (version 3.5.1; <http://www.r-project.org/>).

RESULTS

A total of 1031 patients were eligible for the study analysis. 916 of these had a prostate volume <100 cc and 115 patients had a prostate volume \geq 100 cc. The median prostate volume in <100 group was 55.0 cc (43.0-70.0) versus 112.0 cc (100.0-130.0) in \geq 100 group ($p < 0.001$). Patients with large prostate volume had more frequently a history of indwelling catheter (27% versus 15%, $p < 0.001$). Patients with prostate \geq 100cc required longer operative times (75 versus 55 minutes, $p < 0.001$), longer lasing times (41.7 versus 24.9 minutes, $p < 0.001$), and higher energy used (390 versus 205 kJ, $p < 0.001$) but lower energy density (3.3 versus 4.1 kJ/mL, $p < 0.001$). Age, catheterization time and post-operative hospital stay were similar between the two groups (Table 1).

According to Clavien-Dindo classification, the most common early complications were Grade I in both groups (93.1% in \geq 100cc and 87.8% in <100cc) and similar rates between groups were recorded (Table 2). The most frequent early complication was burning urination (13.2%), while the most frequent late complication was storage symptoms with de novo urgency (Table 3). Patients in \geq 100 group had a higher risk of developing early (OR: 1.8, 95% CI: 1.2-2.9, $p=0.009$) and late complications (OR: 2.2, 95% CI: 1.3-3.9, $p=0.004$) (Table 4).

When analyzing functional results after surgery, no statistically significant differences were found for the Qmax and IPSS between the two groups (Table 5). All three parameters (PSA, Qmax and IPSS) improved over time (Fig 1-2-3). However, despite PSA was higher in patients with large prostate, the magnitude of decrease overtime was similar in the two groups (p -value for interaction = 0.089). Conversely, even if Qmax and IPSS improved over time in both groups, the Qmax increase and IPSS decrease were larger in patients with large prostates (p -values for interaction = 0.022 and 0.013, respectively).

DISCUSSION

In general, patients with prostate volumes higher than 100cc undergo either simple prostatectomy (open-laparoscopic or robotic) or endoscopic enucleation procedures [4]. Simple prostatectomy is the most invasive procedure to treat BPO but it has longer functional results and it does not require dedicated instruments. Management of large prostate volumes with laser offers the major advantages of this technology (shorter catheterization and hospitalization time, fewer blood transfusion rates) [4, 7]. However,

the approach to large prostate volumes requires experience and relevant endoscopic skills. The long learning curve of the enucleation technique and the requirement of further materials for morcellation are some of the arguments to explain the slow dissemination of this procedure in urological practice. In contrast with other laser techniques (Holmium and Thulium), the Green Light Laser allows to adapt the surgical strategy (pure enucleation versus standard or anatomical vaporization) during a single procedure without modifying the functional outcomes and the complication rates [3, 15, 16]. In this study no difference were made between patients underwent standard PVP (sPVP) or anatomical PVP (aPVP) based on our previous multicentre experience in which we did not find any difference in terms of functional results and complication rates between the two techniques [15]. In the last years several retrospective studies evaluated the safety and outcomes of Green Laser in large prostate volumes [7, 17-26]. The commonest criticisms against the use of XPS in this clinical scenario are the lack of long-term follow-up, the retrospective nature of the available literature data and the reportedly higher re-treatment rates compared to Holmium laser enucleation of the prostate (HoLEP). Our series, with a mean follow-up of 25.0 months (IQR 16.5-35.0) for prostate with a volume ≥ 100 cc is one of the longest so far reported in the literature. The re-intervention rate in the ≥ 100 group was 3.5% versus 2.3% in prostate less than 100cc. These data are slightly better than those reported by the Goliath study with a 24 months re-treatment rate of 9% [27] and worse than those reported by Ajib et al [10] with a re-treatment rate of 1.1% in a series of 370 patients with a mean follow-up of 59.4 months and a mean prostate volume of 48.6 and 78.8 cc, respectively. If we consider only large prostate series, re-treatment rates range from the no re-treatment at 12 months reported by Altay [18], 1.2% at 24 months by Hueber [19], 2.9% by Stone [20], up to 13.2% by Meskawi [22] and 6% for 200cc prostate and 9% for 100-200 cc (mean follow-up: 15.9 months) of the same reviewed multi-institutional series [24]. Only five studies compared the results of photoselective vaporization in large prostate cases: < 80 vs ≥ 80 cc [19], ≥ 200 cc vs 100-200 cc [24], PVP versus en bloc enucleation (GreenLEP) [21], sPVP vs aPVP [25] and simple prostatectomy versus PVP [26]. Despite the different results of re-treatment rates reported in these papers, all the authors (including us) agree with the greater operative and lasing time in large prostate undergoing PVP. Similarly, there are no differences in hospital stay and midterm functional

results. Valdivieso [24] and Hueber [19] reported a higher conversion rate to TURP. Hueber [19] also reported a longer catheterization time in prostate larger than 80ml, conversely Misrai [23] described, for large prostate, shorter catheterization time in PVP than in GreenLEP. Interestingly, Lanchon et al reported a higher rate of re-catheterization and re-hospitalization after PVP compared to open simple prostatectomy. Our results highlight the higher risk to develop early and late complications of large prostate as well as early urge incontinence symptoms, similarly to Hibon et al [25]. In our series early and late storage symptoms/De novo urgency are 22.2% and 4.8% respectively. These data are in line with the results reported in the literature. The groups of Zorn and Misrai [10] reported irritative voiding symptoms of 18.8% at three months. This incidence dropped to 8.46% at one year. In a series of large prostate treated with GreenLaser irritative symptoms are described in 10.2% patients [22]. In agreement with previous series, we confirm no differences in catheterization time. In our series, the PSA drop, used as a proxy of removed tissue, is 51.1% and 64.5% in ≥ 100 versus 44.4% and 51.8% in < 100 group at 6 and 12 months, respectively. The decrease is statistically significant. This reduction is greater in ≥ 100 ($p = 0.013$) and continues over time ($p < 0.001$), but the interaction between prostate volume and follow-up time is not statistically significant ($p = 0.089$), implying that despite the larger amount of tissue removed the magnitude of change is not different between large and small prostate volume: the effectiveness is similar in the two groups. In the literature the cut-off of 50% of PSA reduction is established as the surgical goal to reduce re-treatment risk [28]. Probably the PSA drop recorded in our centers (64.5%) at 12 months might explain our low re-treatment rate (3.5%). Qmax and IPSS improve after surgery, with no difference between the two groups ($p = 0.097$ and $p = 0.207$ respectively), and with improvement over time ($p < 0.001$). At 12 months Qmax increased by 118.3% in < 100 and 162.3% in ≥ 100 . This result might correlate with the major volume of tissue vaporized in large prostate, which is linked to an efficient vaporization and an improvement of urodynamic performances.

Even if Valdivieso et al. reported a 5KJ/cc energy density to achieve 80% of PSA reduction at 24 months in prostate < 100 cc (this target in larger prostate might be time- and fiber-consuming), a 3-4kJ/cc cut-off has been proposed as the minimum threshold to obtain adequate adenoma vaporization [28]. In the ≥ 100 group the mean energy density was 3,3

KJ/cc (IQR 2.3-4.2), less than in <100 group, where it was 4,1 KJ/cc (IQR 2.7-5.4) ($p<0.001$).

The lower energy density in the ≥ 100 group might be explained by the greatest use of aPVP (63%), as already described [15].

There are some limitations in this study: the retrospective design, the involvement of several surgeons with different level of expertise, the heterogeneity between centers to report and manage pre- and post-operative events, and the lack of number of fibers used per procedure. Another confounding factor might be the multi-center nature of this study involving different surgeons with variable surgical experience. Although all these aspects might represent limitations, from our perspective they strengthen the general perception that laser is a safe and reliable procedure which can be adopted also by young surgeons [29-30].

CONCLUSIONS

In the midterm follow-up, Greenlight PVP using the XPS-180W is safe and effective in treating patients with prostate volumes ≥ 100 cc compared to prostate volumes < 100 cc. Even if early and late complications are more frequent in large prostate, the improvement over time in terms of Qmax and IPSS are greater than in small prostate. This study confirms the flexibility and reliability of Greenlight Laser technique. Nevertheless a longer follow up period is necessary to better clarify the re-treatment rate and effectiveness of Greenlight in large prostates.

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DISCLOSURES

Conflict of interest: PD, LR, CD, GF and LC do surgical tutorship for AMS and received honoraria for their tutorship.

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Figure Legends

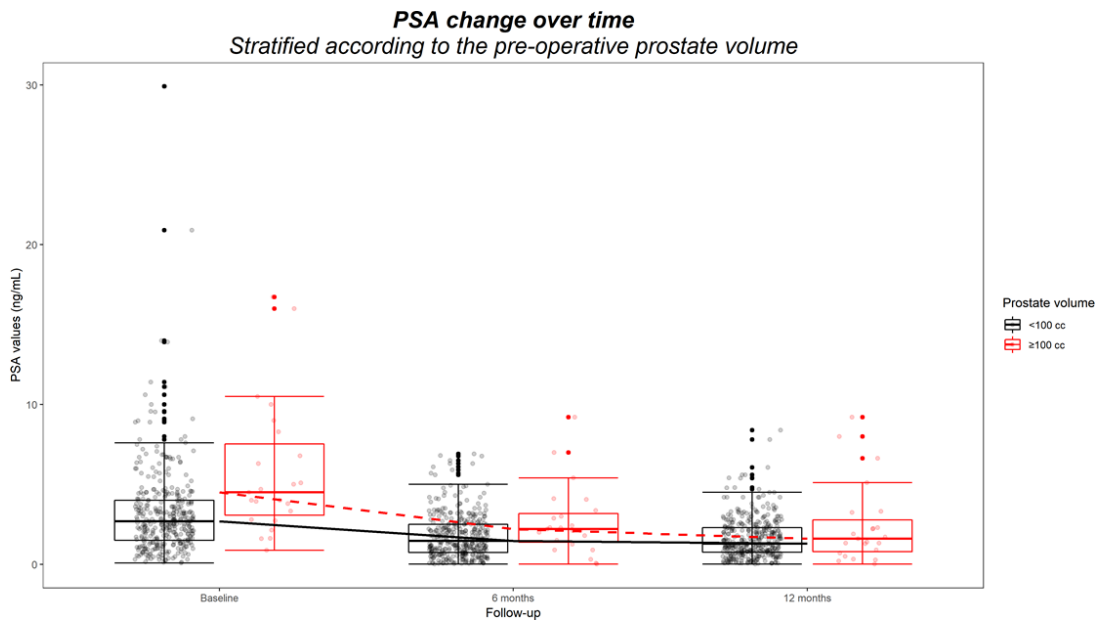


Fig. 1 – Box-whiskers graphs of baseline, 6 month and 12 months of PSA in large and small prostate groups. Box-whiskers plots show the 25th and 75th percentile range (box) with 95% confidence intervals (whiskers) and median values (transverse lines in the box).

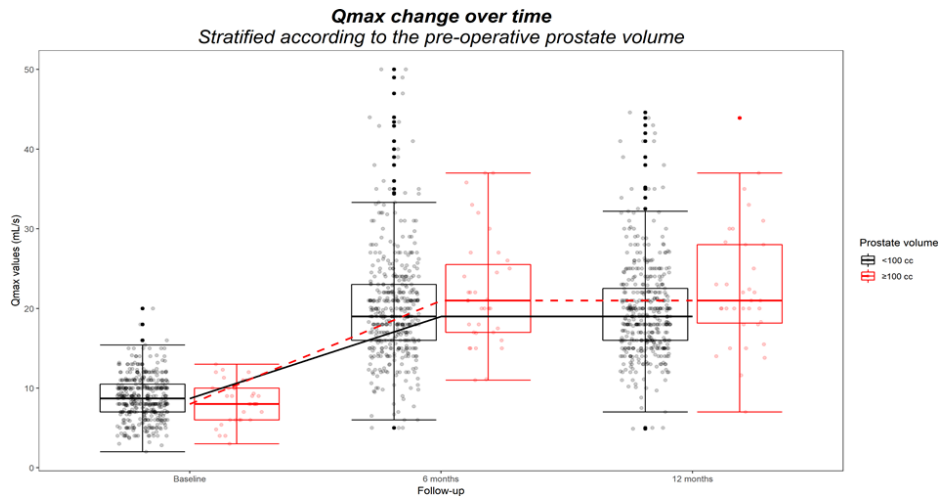


Fig. 2 – Box-whiskers graphs of baseline, 6 month and 12 months of Qmax in large and small prostate groups. Box-whiskers plots show the 25th and 75th percentile range (box) with 95% confidence intervals (whiskers) and median values (transverse lines in the box).

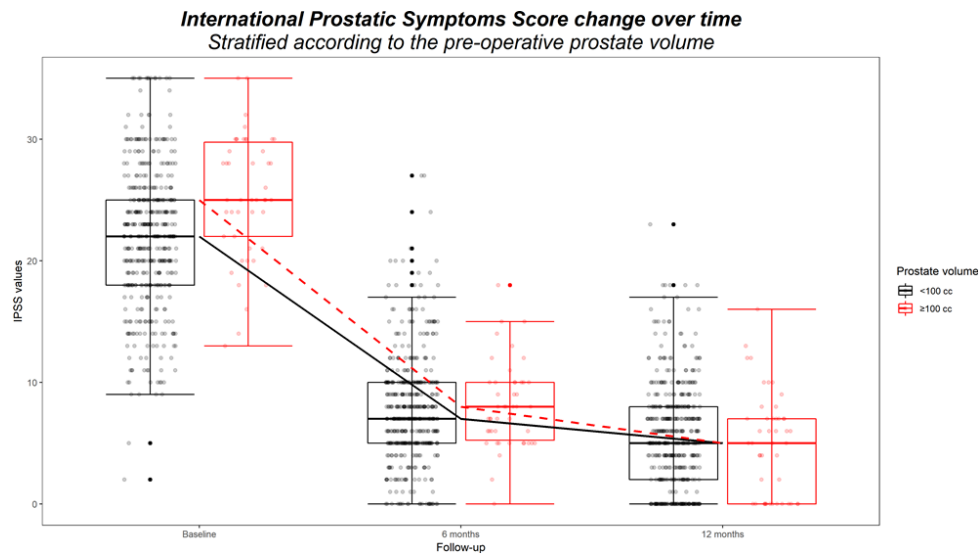


Fig. 3 – Box-whiskers graphs of baseline, 6 month and 12 months of IPSS in large and small prostate groups. Box-whiskers plots show the 25th and 75th percentile range (box) with 95% confidence intervals (whiskers) and median values (transverse lines in the box).

Table 1 – Patients’s pre-operative and intra-operative characteristics stratified according to prostate volume.

Variable	Overall (n=1031)	Prostate volume <100cc (n=916)	Prostate volume ≥100cc (n=115)	<i>p-value</i>
Age (years)	69.0 (64.0-76.0)	69.0 (63.0-76.0)	69.0 (65.0-76.0)	0.259 ^b
Prostate volume (TRUS) (mL)	60.0 (45.0-75.0)	55.0 (43.0-70.0)	112.0 (100.0-130.0)	<0.001 ^b
BPH/LUTS therapy				0.029 ^a
None	164 (15.9)	140 (15.3)	24 (20.9)	
Alpha-blockers	460 (44.6)	405 (44.2)	55 (47.8)	
5-ARI	56 (5.4)	50 (5.5)	6 (5.2)	
Combination	285 (27.7)	255 (27.8)	30 (26.1)	
Unknown	66 (6.4)	66 (7.2)	0 (0)	
Antiplatelet/anticoagulant therapy				0.079 ^a
None	578 (56.1)	510 (55.7)	68 (59.1)	
Antiplatelet	314 (30.5)	286 (31.2)	28 (24.3)	
Anticoagulant	91 (8.8)	75 (8.2)	16 (13.9)	
Unknown	48 (4.7)	45 (4.9)	3 (2.6)	
Indwelling catheter history (unknown=81)	168 (16.3)	137 (15)	31 (27)	<0.001 ^a
ASA score				0.004 ^a
1-2	473 (45.9)	431 (47.1)	42 (36.5)	
3-4	232 (22.5)	211 (23)	21 (18.3)	
Unknown	326 (31.6)	274 (29.9)	52 (45.2)	
Surgical technique				0.079 ^a
Anatomic PVP	481 (46.7)	418 (45.6)	63 (54.8)	

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Standard PVP	550 (53.3)	498 (54.4)	52 (45.2)	
Operative time (min)	60.0 (40.0-75.0)	55.0 (40.0-70.0)	75.0 (60.0-94.8)	<0.001 ^b
Lasing time (min)	26.0 (19.0-36.0)	24.9 (18.0-33.9)	41.7 (34.0-52.0)	<0.001 ^b
Energy used (kJ)	221.0 (145.0-334.0)	205.0 (137.4-302.0)	390.0 (308.5-501.0)	<0.001 ^b
Energy used (kJ)/prostate volume (mL)	3.9 (2.7-5.2)	4.1 (2.7-5.4)	3.3 (2.3-4.2)	<0.001 ^b
Catheterization time (days)	1 (1-2)	1 (1-2)	1 (1-2)	0.769 ^b
Post-operative stay (days)	2 (1-2)	2 (1-2)	2 (1-2.2)	0.126 ^b

^a Chi-squared test, ^b Mann-Whitney U test prostate volume ≤ 100 vs. ≥ 100 cc. Table values are n(%) or median (IQR). PVP: photoselective vaporization of the prostate, TRUS: transrectal ultrasonography, PSA: prostate-specific antigen, IPSS: International Prostate Symptoms Score, 5-ARI: 5-alpha reductase inhibitors.

Table 2 – Main outcomes after photoselective vaporization of the prostate stratified according to prostate volume.

Variable	Overall (n=1031)	Prostate volume <100cc (n=916)	Prostate volume ≥100cc (n=115)	<i>p-value</i>
Follow-up duration (Months)	17.0 (12.0- 25.3)	16.0 (12.0-24.0)	25.0 (16.5- 35.0)	<i><0.001^b</i>
Acute urine retention	84 (8.1)	78 (8.5)	6 (5.2)	<i>0.299^a</i>
Overall early complications	385 (37.3)	327 (35.7)	58 (50.4)	<i>0.003^a</i>
Early urge/incontinence symptoms	315 (30.6)	268 (29.3)	47 (40.9)	<i>0.015^a</i>
Clavien-Dindo classification of early complication*				<i>0.065^a</i>
I	341 (88.6)	287 (87.8)	54 (93.1)	
II	31 (8.1)	30 (9.2)	1 (1.7)	
IIIa	3 (0.8)	3 (0.9)	0 (0)	
IIIb	3 (0.8)	3 (0.9)	0 (0)	
IVa	7 (1.8)	4 (1.2)	3 (5.2)	
Overall late complications	142 (13.8)	117 (12.8)	25 (21.7)	<i>0.001^a</i>
Patient global impression of improvement				<i>0.012^a</i>
1	510 (49.5)	447 (48.8)	63 (54.8)	
2	302 (29.3)	272 (29.7)	30 (26.1)	
3	70 (6.8)	68 (7.4)	2 (1.7)	
4	24 (2.3)	22 (2.4)	2 (1.7)	
5	8 (0.8)	8 (0.9)	0 (0)	
6	4 (0.4)	3 (0.3)	1 (0.9)	
7	1 (0.1)	0 (0)	1 (0.9)	

* Percentage refers only to the group of patients who experienced early complications. a Chi-squared test, b Mann-Whitney U test prostate volume <100 vs. ≥100 cc. Table values are n(%) or median (IQR).

Table 3 – Early and late complications stratified according to prostate volume.

Variable	Overall (n=1031)	Prostate volume <100cc (n=916)	Prostate volume ≥100cc (n=115)
Early complications			
Fever < 38 °C	18 (1.7)	14 (1.5)	4 (3.5)
Fever > 38 °C	39 (3.8)	38 (4.1)	1 (0.9)
Burning urination	136 (13.2)	112 (12.2)	24 (20.9)
Frequency	61 (5.9)	56 (6.1)	5 (4.3)
De novo urge	105 (10.2)	89 (9.7)	16 (13.9)
De novo urge incontinence	63 (6.1)	53 (5.8)	10 (8.7)
Stress incontinence	44 (4.3)	41 (4.5)	3 (2.6)
Capsule perforation	8 (0.8)	8 (0.9)	0 (0.0)
Haematuria	28 (2.7)	26 (2.8)	2 (1.7)
Urinary tract infection	19 (1.8)	18 (2)	1 (0.9)
Blood transfusion	6 (0.6)	6 (0.7)	0 (0.0)
Minor cardiovascular event	5 (0.5)	7 (0.8)	5 (4.3)
MACE	7 (0.7)	4 (0.4)	3 (2.6)
Late complications			
Urethral stenosis	22 (2.1)	19 (2.1)	3 (2.6)
Bladder neck contracture	24 (2.3)	24 (2.6)	0 (0.0)
Prostatic fossa sclerosis	10 (1.0)	8 (0.9)	2 (1.7)
Stress incontinence	34 (3.3)	27 (2.9)	7 (6.1)
Re-intervention	25 (2.4)	21 (2.3)	4 (3.5)
TURP	11 (1.0)	7 (0.8)	4 (3.5)
Bladder neck incision	8 (0.8)	8 (0.9)	0 (0.0)
Urethrotomy	6 (0.6)	6 (0.7)	0 (0.0)
Storage symptoms/De novo urgency	50 (4.8)	42 (4.6)	8 (7.0)

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Table 4 – Multivariable logistic regression models predicting acute urinary retention, overall early and late complications rates in patients with prostate volume <100 cc vs. ≥100 cc (reference: prostate volume <100 cc). All the models were adjusted for age, baseline PSA, BPH\LUTS therapy, antiplatelet\anticoagulant therapy, surgery type and history of catheter indwelling prior surgery.

	Univariable		Multivariable	
	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value
Acute urinary retention	0.5 (0.2-1.3)	<i>0.170</i>	0.5 (0.2-1.4)	<i>0.217</i>
Overall early complications	1.6 (1.1-2.4)	<i>0.017</i>	1.8 (1.2-2.9)	<i>0.009</i>
Overall late complications	1.8 (1.1-2.9)	<i>0.023</i>	2.2 (1.3-3.9)	<i>0.004</i>

Table 5 - Median values (interquartile range) of PSA (ng/mL), Qmax (mL/s), IPSS stratified according to the prostate volume with the p-values derived from ranked based model for differences between the prostate volume, follow-up time points and interaction prostate volume and follow-up time.

	Prostate volume <100cc			Prostate volume ≥100 cc			<i>p-value</i>		
	Baseline	6 months	12 months	Baseline	6 months	12 months	<i>Prostate volume</i>	<i>time</i>	<i>interaction</i>
PSA (ng/mL)	2.7 (1.5-4.0)	1.5 (0.7-2.5)	1.3 (0.7-2.3)	4.5 (3.1-7.5)	2.2 (1.4-3.2)	1.6 (0.8-2.8)	0.013	<0.001	0.089
Qmax (mL/s)	8.7 (7.0-10.5)	19.0 (16.0-23.0)	19.0 (16.0-22.5)	8.0 (6.0-10.0)	21.0 (17.0-25.5)	21.0 (18.2-28.0)	0.097	<0.001	0.022
IPSS	22.0 (18.0-25.0)	7.0 (5.0-10.0)	5.0 (2.0-8.0)	25.0 (22.0-30.0)	8.0 (5.3-10.0)	5.5 (0.5-7.0)	0.207	<0.001	0.013

VHP= Very High Power

KTP= Potassium Titanyl Phosphate

HPS= high-performance system

LBO= Lithium Triborate

PVP= photoselective vaporisation of the prostate

BPO= Benign Prostatic Obstruction

IPSS= International Prostate Symptom Score

XPS= Xcelerated Performance System

EAU= European Association of Urology

LUTS= lower urinary tract symptoms

LE= level of evidence

sPVP= standard PVP

aPVP= anatomical PVP

ASA= American Society of Anesthesiology score

TRUS= trans-rectal ultrasound

Qmax= maximum urinary flow

PGI-I= Patient Global Impression of Improvement

IQR= interquartile range

HoLEP= Holmium laser enucleation of the prostate

MACE= Major Acute Cardiovascular Event