

# Prostatic Diseases and Male Voiding Dysfunction

## Prospective Assessment of the Sexual Function After Greenlight Endoscopic Enucleation and Greenlight 180W XPS Photoselective Vaporization of the Prostate



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<b>OBJECTIVE</b>	To evaluate the impact of Greenlight 180W photoselective vaporization of the prostate (PVP) and endoscopic enucleation of the prostate (GreenLEP) on ejaculatory and erectile functions.
<b>MATERIALS AND METHODS</b>	Between January 2014 and September 2016, 440 men with low urinary tract symptoms or complications related to benign prostate obstruction with prostate >80 g and sexually active, underwent a PVP or GreenLEP performed by experienced surgeons at a single institution. Patients were matched in a 1:1 fashion according to preoperative transrectal ultrasonography prostatic volume and cardiovascular risk factors (smoking, diabetes, and hypertension).
<b>RESULTS</b>	One hundred patients in each group were included. Mean prostatic volume were 110 g (95%CI: 101-118) and 107 g (95%CI: 99-115) in the GreenLEP and PVP groups, respectively ( $P = .68$ ). Mean total energy delivered in the PVP group was 4.42 kJ/g (4.2-4.6). Surgical retreatment was required in 9 patients (10.1%) in the PVP group and none in the GreenLEP group (log rank test: $P = .002$ ). Mean prostate specific antigen level and International Prostate Symptom Score score were significantly lower in the GreenLEP group than in the PVP group at 3, 12, and 24 months ( $P < .001$ ). Preserved antegrade ejaculation was reported in 24 patients (26.9%) in the PVP group vs 1 patient (1.2%) in the GreenLEP group at 12 months ( $P < .001$ ). In multivariate analysis, age, history of coronary artery disease, and surgical treatment with PVP were independent factors of IIEF-5 decline.
<b>CONCLUSION</b>	Despite a poor rate of preserved antegrade ejaculation, GreenLEP was associated with better erectile function outcomes possibly due to greater improvement of low urinary tract symptoms. UROLOGY 131: 184–189, 2019. © 2019 Elsevier Inc.

Sexual dysfunction is commonly encountered in men with low urinary tract symptoms (LUTS).<sup>1</sup> Probably underestimated, sexual activity was reported in 83% of men over 50 years old. LUTS due to benign prostate obstruction (BPO) increases from 50% of men aged 50 to 80% of men over 70 years old. Many men with medical therapy require a surgical approach at some point due to prostatic volume (PV) progression and nature

of the disease.<sup>2</sup> According to European Association of Urology and American Urology Association guidelines, holmium laser enucleation of the prostate (HoLEP) may be the preferred minimally invasive surgical treatment option for prostates larger than 80 g.<sup>3,4</sup> However, this surgical approach requires experience and relevant endoscopic skills that could explain its relatively slow widespread over the past decade.<sup>5</sup> Other minimally laser techniques have been developed, such as photoselective vaporization of the prostate (PVP) with Greenlight laser 180W,<sup>6</sup> whose safety and efficacy in prostates >80 mL have been reported in expert medical centers.<sup>7,8</sup> Recently, endoscopic enucleation of the prostate with Greenlight laser (GreenLEP) has been described as a possibly better approach than PVP 180W in larger prostates in terms of postoperative prostate specific antigen (PSA) decrease and risk of surgical retreatment.<sup>9,10</sup>

**Conflicts of Interest:** Benoit PEYRONNET and Sébastien VINCENDEAU are consultants for Boston Scientific. Romain Mathieu is an investigator for Boston Scientific. Other authors have nothing to disclose.

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The effects of PVP 180W and GreenLEP on sexual function have never been assessed so far. Sexual impact of transurethral resection of the prostate is controversial.<sup>11</sup> Regarding HoLEP, recent studies described a stable sexual function after surgery, despite high prevalence of ejaculatory dysfunction.<sup>12</sup> A maintained sexual function after PVP 80W and 120W was also reported using the International Index of Erectile Function (IIEF-5).<sup>13</sup>

The aim of this study was to assess the sexual impact (ie, impact on ejaculatory and erectile functions (EFs)) of PVP Greenlight 180W and GreenLEP.

## MATERIALS AND METHODS

### Study Design

Between January 2014 and September 2016, the data of 440 consecutive men with LUTS or complications related to BPO who underwent a PVP or GreenLEP at our institution were prospectively collected. Surgical indications were based on guidelines of the European Association of Urology.<sup>4</sup> Patients with prostate volume <80 g on preoperative transrectal ultrasonography were excluded as well as patients with a postoperative follow-up <12 months, preoperative IIEF-5 score <5 (not sexually active), a history of neurologic disorder or pelvic radiotherapy, untreated urinary tract infection, history of previous urethral surgery, prostate cancer (PSA >4ng/mL and positive prostate biopsy or suspect digital-rectal examination), and procedures performed by low experienced surgeons (<100 procedures).

### Interventions

Patients with antiplatelet therapy were operated under aspirin only (ie, clopidogrel was always stopped during the perioperative period). Oral anticoagulation was bridged to low molecular weight heparin throughout the perioperative period in patients with high risk of thrombotic event and stopped in the others. PVP was performed with Greenlight 180-W XPS (Boston Scientific System; Inc. ) and the MoXy laser fiber. Surgical technique was based on optimization of laser energy delivered to the prostatic tissue. After the completion of 2 channels at 5 and 7 o'clock with an energy setting of 80 W, median lobe was first vaporized. Then, lateral lobes were removed using an energy setting of 80-140 W towards the surgical capsule. The surgical objective was a widely open prostate cavity based with concomitant transrectal ultrasonography of the prostate during our initial experience.<sup>14</sup>

GreenLEP was performed as previously described by Gomez-Sancha's using the HPS-120W fiber and 532 nm 180W generator.<sup>9</sup> After a circumferential incision at the verumontanum, the adenoma at the apex was removed from the external sphincter. Then, the "en-bloc" enucleation was performed through a blunt dissection between the adenoma and the capsule with the tip of the scope from the apex to the bladder neck. Once removed, "en-bloc" adenoma was placed into the bladder and morcellated using Wolf morcellator and Wolf Pyrana endoscop (Richard Wolf GmbH, Knittlingen, Germany). At last, retrieved tissue were weighted and examined histologically.

### Outcomes

The patients' characteristics, perioperative parameters, and complications were prospectively collected. Postoperative complications were defined as any medical or surgical adverse event

within the first 30 days following surgery using the Clavien-Dindo's classification modified according to the Greenlight Users Group (GUGL).<sup>15</sup> Sexual parameters involved antegrade ejaculation status (persistent or not) and International Index of Erectile Function-5 (IIEF-5 score). Patients were evaluated at the third month after surgery and annually thereafter. Functional outcomes using questionnaires (IIEF-5 score, International Prostate Symptom Score [IPSS] score, quality of life from IPSS scores, and International Continence Society (ICS) male SF score), uroflowmetry and PSA were collected. Postvoid residual was assessed using suprapubic ultrasonography. Retreatment was defined as any LUTS related to BPO that required medical or surgical treatment.

The primary outcome was the change in EF (subjectively defined as any postoperative decline of IIEF-5  $\geq 5$  points).<sup>16</sup> The secondary outcomes were changes in voiding parameters ( $\Delta$  Nocturia, maximum flow rate (Qmax), postvoid residual urine volume,  $\Delta$  IPSS score, Quality of Life question 8 from IPSS, ICS male SF score and urinary incontinence questions from the ICS male SF score).

### Statistical Analysis

Patients were matched in a 1:1 fashion according to the following variables: preoperative transrectal ultrasonography PV and cardiovascular risk factors (any of the following: smoking, diabetes, and hypertension). Continuous variables were reported as mean and standard deviation. Comparisons of continuous and categorical variables were performed using the Mann-Whitney *U* test and chi-square (or Fisher's exact test, as appropriate), respectively. Logistic regression analysis was used to assess predictive factors of  $\Delta$  IIEF-5  $\geq -5$ . Spearman's rho assessed the correlation between continuous variables. Long term retreatment rate free survival estimates were generated using Kaplan-Meier method; Log-rank was applied for pairwise comparison of survival. McNemar test assessed the paired variations of IIEF-5 in each group. All *P* values were 2-sided and statistical significance was defined as a *P*  $\leq .05$ . The statistical analysis was performed with JMP v.12.0 software (SAS Institute Inc, Cary, NC).

## RESULTS

### Patient Characteristics

The patient characteristics are summarized in [Table 1](#). Regarding American Society of Anesthesiology score, hypertension, smoking status, and history of diabetes, GreenLEP and PVP groups were comparable (*P* = .28, *P* = .90, *P* = .79, and *P* = .59, respectively). The mean age was 68 years (95%CI: 66-70) and 33/200 (17.7%) of patients were catheter-dependent before surgery.

### Perioperative Outcomes

The intraoperative data and postoperative results are shown in [supplementary table 1](#). Mean preoperative prostate volume was 110 g (95%CI: 101-118) and 107 g (95%CI: 99-115) in the GreenLEP and PVP groups, respectively (*P* = .68). Mean total energy delivered in the PVP group was 4.42 kJ/g (4.2-4.6). Mean enucleation and morcellation times were 54 minutes (95%CI: 40-60) and 14 minutes (11-17), accounting for 63% and 16% of total operative time, respectively. Mean prostate tissue enucleated was 75.1  $\pm$  38.7 g according to final pathology. Total operative time was significantly longer in the GreenLEP group compared to the PVP group (*P* = .03). Irrigation, catheter, and hospitalization times were comparable in both groups (*P* = .79,

**Table 1.** Patients characteristics

	GreenLEP <i>n</i> = 100	PVP <i>n</i> = 100	<i>P</i> Value
Age (y)	68 (66-69)	68 (67-70)	.216
ASA score			
1	41 (41.4)	26 (31.3)	.279
2	55 (55.6)	52 (62.6)	
3	3 (3.0)	5 (6.1)	
Hypertension	54 (54.0)	51 (53.1)	.902
Smoking	16 (16.0)	14 (14.6)	.783
Diabetes	14 (14.0)	11 (11.5)	.593
Preoperative indwelling catheter	16 (16.2)	17 (19.5)	.547
Alpha-blockers	70 (70.7)	55 (63.2)	.278
5-ARI	32 (32.3)	27 (32.1)	.979
Warfarin	1 (1.0)	3 (3.4)	.253
Aspirin	28 (28.3)	20 (25.8)	.410

5-ARI, 5alpha reductase inhibitor; ASA score, American Society of Anesthesiology; GreenLEP, Greenlight enucleation of the prostate; PVP, photoselective vaporization of the prostate. *n* (%). Data are mean (95%CI). *P* value: Mann-Whitney or chi-square test.

*P* = .32, and *P* = .11, respectively). About 98.9% of patients in GreenLEP group recovered spontaneous voiding after surgery vs 88.5% in the PVP group (*P* = .002). The rates of postoperative complications were comparable in the 2 groups (*P* = .93).

### Urinary and Anatomic Outcomes

Regarding baseline IPSS score, nocturia and Qmax, no statistically differences were observed between the 2 groups (*P* = .33, *P* = .29, and *P* = .27, respectively). All urinary outcomes favored the GreenLEP group (supplementary table 2). IPSS score was

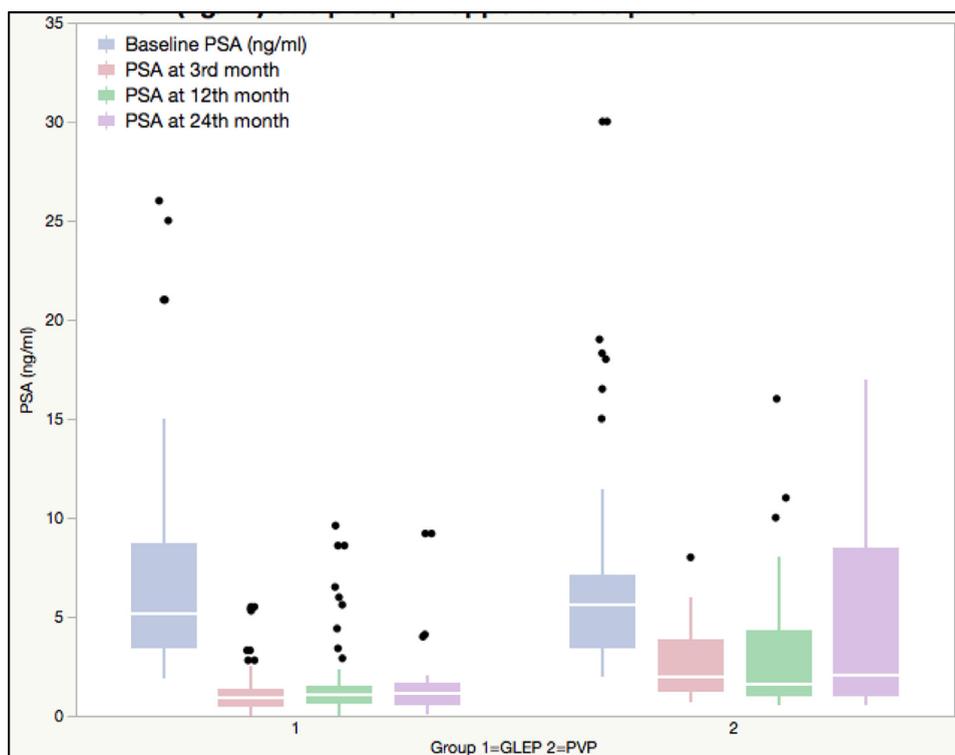
significantly lower in the GreenLEP group than in the PVP group at 3, 12, and 24 months postoperatively (*P* < .001). The postoperative IPSS-QoL evolution favored the GreenLEP group as well (*P* = .003, *P* = .007, and *P* < .001 at 3, 12, and 24 months respectively). Compared to the GreenLEP group, nocturia evolution postoperatively in the PVP group was poorer with a mean variation of  $0.5 \pm 1.5$ ,  $0.8 \pm 1.6$ , and  $0.9 \pm 0.2$  at 3, 12, and 24 months, respectively (*P* < .05). The Qmax was significantly greater in GreenLEP group at each time point (*P* < .001, *P* = .003, and *P* = .003).

Initial PSA levels were similar in the 2 groups (*P* = .64) (supplementary Table 3 and Fig. 1). Mean reductions of PSA levels were 81.3% and 63.2% after 3 months, 73.4% and 54.4% after 12 months, 73.4% and 33.8% after 24 months, in the GreenLEP and PVP groups, respectively (*P* < .001, *P* = .026, and *P* = .004). After a mean follow up of 25.1 and 18.6 months, retreatment rate was needed in 9 patients (10.1%) in the PVP group vs no patient in the GreenLEP group (log rank test: *P* = .002).

### Impact on Sexual Functions

Antegrade ejaculation was reported as being preserved in 24 patients (26.9%) in the PVP group vs 1 patient (1.2%) in the GreenLEP group at 12 months (*P* < .001). Postoperative IIEF-5 evolution was reported in Table 2. At baseline, IIEF-5 scores were comparable in both groups (*P* = .62). In the GreenLEP group, IIEF-5 increased from 1.1 point, 1.3 and 0.7 point at 3, 12, and 24 months postoperatively. In the PVP group, IIEF-5 remained stable after 3 months and decreased significantly after 12 and 24 months (*P* = .031).

An IIEF-5 decline  $\geq 5$  points was observed in 2 and 19 patients in the GreenLEP and PVP groups, respectively (*P* < .001). The mean postoperative change in IIEF-5 favored GreenLEP at each time point, being +1.1 vs -0.6 at 3 months



**Figure 1.** Changes in PSA level (ng/mL) from baseline and at the third, 12th, and 24th month in PVP and GreenLEP groups. (Color version available online.)

**Table 2.** Changes in International Index of Erectile Function-5 (IIEF-5 score) from baseline at the third, 12th, and 24th month of follow-up

	Baseline (n = 186)		3 mo (n = 151)		12 mo (n = 115)		24 mo (n = 89)	
	GLEP	PVP	GLEP	PVP	GLEP	PVP	GLEP	PVP
IIEF-5 score	13.6 ± 6.9	14.1 ± 6.8	15.7 ± 6.2	14.2 ± 6.7	16.3 ± 6.5	13.2 ± 7.1	15.8 ± 5.8	13.2 ± 7.1
P value	—	.619	1.1 ± 2.3	−0.6 ± 3.1	1.3 ± 2.2	−1.1 ± 3.3	0.7 ± 2.1	−1.0 ± 3.3
Δ IIEF-5	—	—	1.1 ± 2.3	−0.6 ± 3.1	1.3 ± 2.2	−1.1 ± 3.3	0.7 ± 2.1	−1.0 ± 3.3
P value	—	—	1.123	<.001	1.3 ± 2.2	<.001	0.7 ± 2.1	.061
								.002

GreenLEP, Greenlight enucleation of the prostate; PVP, photoselective vaporization of the prostate. n (%). Data are mean (95% CI). P value: Mann-Whitney between GLEP and PVP groups.

( $P < .0001$ ); +1.3 vs −1.3 at 12 months ( $P < .0001$ ) and +0.8 vs −1.3 at 24 months ( $P = .008$ ).

In multivariate analysis (adjusted to body mass index, smoking, hypertension and diabetes status,  $\Delta$  Nocturia  $>2$ , and  $\Delta$  IPSS  $<5$ ) age, history of coronary artery disease and surgical treatment with PVP (vs GreenLEP) were independent predictors of IIEF-5 decline over 5 points (Table 3).

Only the GreenLEP resulted in statistically significant improvement of IIEF-5 at each postoperative assessment compared to baseline ( $P = .002$ ). Using Spearman correlation, we found a significant correlation between  $\Delta$  Nocturia and  $\Delta$  IIEF-5 ( $r = -0.574$   $P < .0001$ ) and between  $\Delta$  IPSS and  $\Delta$  IIEF-5 ( $r = 0.273$   $P = .0006$ ) at 3 months.

## DISCUSSION

The present study is the first prospective evaluation of sexual function after surgical treatment of BPO due to larger prostates. We observed an improvement of EF in the GreenLEP group while the EF worsened over time with recurring LUTS after PVP. PVP (vs GreenLEP) was also a predictor of significant IIEF-5 decrease postoperatively ( $\geq 5$  points) in multivariate analysis. Surgical technique seemed to be an independent factor of the postoperative evolution of EF. Elshal et al reported an improvement of EF compared to the control group with HoLEP in patients with a mean prostate volume of  $132 \pm 54$  g.<sup>12</sup> However, in a subgroup of patients with a normal baseline IIEF-5 score, EF had decreased at the 12th month of follow-up. The same author described in a previous study a decline of EF in 17.2% of HoLEP group vs 29.3% of patients in the PVP group.<sup>16</sup> Univariate analysis had identified baseline IIEF-5 score as an independent factor of EF decline. In our study, 2 patients in the GreenLEP group and 19 in the PVP group had a lowered postoperative EF score ( $P < .001$ ). Interestingly, mean initial IIEF-5 in these patients was  $19.7 \pm 4.8$  vs  $13.1 \pm 6.7$  ( $P < .001$ ). With monopolar or bipolar transurethral resection of the prostate, Akman et al also showed 17.0% of patients with worsening EF after surgery.<sup>17</sup> This finding has also been reported after PVP. Most studies showed a comparable baseline vs postoperative EF.<sup>18</sup> However, Bruyere et al and Kumar et al reported a significant decrease in IIEF-5 score in the subgroup of men with normal baseline EF.<sup>13,19</sup> Underlying assumptions were thermal damage to proximal cavernosal nerves during procedures, and the role of cardiovascular comorbidity such as diabetes.<sup>20</sup> We could easily explain a surgical stress in the early postoperative period in patients with normal initial EF, affecting their sexual life.

EF remains a narrow vision of sexual life.<sup>21</sup> There is multidimensional aspects of the sexuality, desire or libido, orgasm, happiness, ejaculatory function that are not addressed by an erectile score such as the IIEF-5.<sup>22</sup> The present study reported a rate of antegrade ejaculation in 26.9% and 1.2% of patients in PVP and GreenLEP groups, respectively. Conversely the evolution of IIEF-5 score postoperatively favored the GreenLEP group. For urologists, main objective in the management of LUTS

**Table 3.** Univariate and multivariate logistic regression analysis for risk of postoperative IIEF-5 decline  $\geq 5$  points

Independent Variable	Univariate			Multivariate		
	OR	(95% CI)	P Value	OR	(95% CI)	P Value
Age	2.05	(1.11-2.15)	.001	1.22	(1.04-1.43)	.007
Hypertension	4.94	(1.05-23.3)	.04	3.6	(0.9-14)	.074
Coronary artery disease	4.3	(1.03-18.3)	.045	3.6	(1.7-74.4)	.021
Surgical technique						
PVP GLEP = Reference	15.4	(1.9-121.5)	.009	12.3	(1.5-101.9)	.019
$\Delta$ Nocturia $>2$	7.8	(1.9-31.7)	.004	3.4	(0.7-15.2)	.107
$\Delta$ IPSS $<5$	1.85	(0.51-6.75)	.347	—	—	—
Persistent antegrade ejaculation	2.2	(0.2-22.7)	.499	—	—	—

BMI, body mass index; GreenLEP, Greenlight enucleation of the prostate; IPSS, International Prostate Symptom Score; PVP, photoselective vaporization of the prostate.  
*n* (%). Data are mean (95%CI). *P* value: Mann-Whitney between GLEP and PVP groups.

due to larger prostates remains an anatomic treatment of the adenoma to avoid the risk of recurring LUTS due to residual adenoma and a compromise with persistent antegrade ejaculation.<sup>9</sup> Since McVary's works, relationship between LUTS and erectile dysfunction (ED) are now acknowledged by all.<sup>23</sup> Nitric oxide decrease in prostate and penile smooth muscle remains the pharmacological target of PDE5-inhibitors in LUTS and DE medical treatments.<sup>24</sup>

In our cohort, initial prostate volumes were comparable in both groups. Mean energy delivered in PVP group was 4.42 kJ/g. In an international multicenter study, energy delivered over 3 kJ/g provided a PSA reduction over 50%. Higher energy  $>7$  kJ/g seemed to reduce PSA up to 83%. Using high energy density was not associated with higher rate of perioperative complications.<sup>25</sup> The same rate of retreatment was observed all groups. Postoperative PSA reduction is considered as a great surrogate of the PV treated for Greenlight users.

Actually, there are few studies showing the outcome of GreenLEP. Among them, GreenLEP seemed to have a superiority in term of retreatment rate.<sup>26</sup> In our study, 10% of patients in the PVP group required another medical or surgical treatment of LUTS after a median follow-up of 25.1 months. Using PVP 180W laser, Meskawi et al recently reported in a multicenter study a retreatment rate of 5.4% and 9.3% at 24 and 36 months, respectively.<sup>27</sup> Hueber et al reported this rate from 1.0 to 1.2 at 12 and 24 months of follow-up, respectively, Calves et al, a rate of 4.8% with a mean follow-up of  $57.4 \pm 6.8$  months in smaller prostate volumes.<sup>7,28</sup>

Most of these retreated patients experienced a lower energy delivered to the tissue, a lower postoperative PSA reduction and had a higher prostate volume. Our findings reinforce the existing evidence regarding the poor reliability of PVP in larger prostates with high retreatment rate in the medium to long run.

Our poorer outcomes regarding EF and IIEF-5 in the PVP group could be explained by this rate of retreatment and recurring LUTS. This relationship was underlined with statically correlation between postoperative  $\Delta$  Nocturia,  $\Delta$  IPSS, and  $\Delta$  IIEF-5 ( $P < .0001$  and  $P < .0006$ ,

respectively). This association between LUTS and EF is well depicted in many epidemiologic studies.<sup>1</sup>

Cardiovascular disease (CVD), age, hypertension, and coronary disease, were also reported as predictive factors of worsening EF. ED and cardiovascular disease share common risk factors included diabetes, hypertension, age, obesity, metabolic syndrome hypercholesterolemia, sedentary lifestyle, and depression.<sup>29</sup> They also share the same pathophysiology basis. Despite atherosclerotic burden, subclinical cavernosal inflammation, endothelial dysfunction, and androgen deprivation interactions were clearly advocated. According to the "artery size" hypothesis, the smaller penile arteries suffer earlier than larger coronary arteries.<sup>30</sup> ED is now recognized as an early predictor of coronary artery disease.<sup>29</sup>

The present study has several limitations that should be acknowledged. We evaluated the impact of modern and minimally laser treatments in BPO-related LUTS using PVP 180W and GreenLEP with a minimal EF score (IIEF-5) and ejaculatory status alone. Larger sexual function scores as IIEF-15 score, Danish Prostatic Symptom Score (Dan-PSS-Sex) or Ejaculation domain-male sexual health questionnaire may have provided a more appropriate assessment of sexual function. Moreover, although statistically significant, the clinical significance of the difference in postoperative IIEF-5 evolution between the 2 groups could be called into question. Another possible shortcoming is that follow-up was not comparable in both groups with only 18.6 months in the GreenLEP group. A prospective controlled study could provide a more accurate comparative evaluation of the sexual impact of these 2 surgical procedures. The relatively limited number of events for the primary outcomes (21 patients had a decline of more than 5 points in the IIEF-5) resulted in an underpowered multivariate assessment. Finally, owing to the increasing evidence on the poorer outcomes of PVP in larger glands, the 2 techniques compared herein (PVP and GreenLEP) could be seen as indicated for different patients' population and the clinical relevance of their comparison could therefore be regarded as debatable.

## CONCLUSION

In this first prospective comparison of EF after surgical treatment of BPO due to larger prostates, we found a significant improvement of IIEF-5 postoperatively in the GreenLEP group despite a poor rate of preserved ante-grade ejaculation. Conversely EF slightly declined in the PVP group over time, concomitantly to recurring LUTS. Age, history of CAD, and surgical treatment of BPO with PVP (vs GreenLEP) were independent predictors of significant IIEF-5 decline ( $\geq 5$ ). Further studies are needed to confirm our findings and the potential impact of recurring LUTS after PVP on EF.

## SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.urology.2019.06.020>.

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