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Reference

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80-W GreenLight Laser Vaporization versus Transurethral Resection of the Prostate for Treatment of Benign Prostatic Obstruction: 5-year Outcomes of a Single-center Prospective Randomized Trial

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Abstract

Objectives: To assess long term functional and safety follow-up data after 80-W GreenLight photoselective vaporization (GL PV) of the prostate and transurethral resection of the prostate (TURP).

Materials and Methods: Prospective randomized trial at a single tertiary referral center (Geneva, Switzerland). Patients were recruited in the outpatient clinic if they met the criteria for surgical treatment of BPO. At baseline, 238 patients were treated either with the 80-W GL PV or monopolar TURP. After 5 years, data was available
from 105 patients: 44 GL PV patients and 61 TURP patients. The primary outcome measure was the International Prostate Symptom Score (IPSS). Secondary outcome measures included maximum urinary flow rate (Qmax), post-voidal residual (PVR) and re-operation rate. Statistical analyses were performed using Stata 14 (StataCorp).

**Results:** After 5 years of follow-up, mean improvements in IPSS, PVR and Qmax were similar in both groups. The re-treatment rate was 14.3% in the GL PV group vs. 11.9% in the TURP group ($p = 0.9$).

**Conclusion:** Non-inferiority of the GL PV to TURP was confirmed in all functional and safety outcomes at 5 year follow-up. GL-PV could be a safe surgical alternative for patients suffering from BPO.

**INTRODUCTION**

More than 210 million men worldwide (1) suffer from benign prostatic hyperplasia (BPH). BPH can eventually lead to benign prostatic obstruction (BPO) (2), a major cause of lower urinary tract symptoms (LUTS) such as interrupted and weak urinary stream, nocturia, urgency and leaking, as well as sexual dysfunction in some men (3). Medical therapy is usually the first-line treatment (4). The efficacy of drugs such as alpha-blockers and 5-alpha reductase inhibitors is, however, limited. Thus more invasive treatment options have to be considered as the disease progresses.
Transurethral resection of the prostate (TURP) remains the standard treatment of moderate to severe LUTS related to BPH (5). It is an effective technique that results in objective and subjective improvement in symptoms, such as increased peak urinary flow and a decrease in the International Prostate Symptom Score (IPSS) (6). However, TURP is an invasive procedure with a cumulative short-term morbidity of around 11%; moreover, surgical revision is necessary in as many as 6% of cases (7). Bleeding requiring transfusion, TUR syndrome, and genitourinary infections pose serious threats, especially to elderly and frail patients (8).

The potassium tyanil phosphate (KTP) laser was first introduced as a treatment for BPO symptoms by Watson in 1995 (9). Starting with a power of 80W, the GreenLight laser first evolved in 2006 into a 120W system (GL-HPS), and the XPS 180W technique (GL-XPS) introduced in 2011. The increase in power and the further development of laser fibers enabled more efficient ablation of prostate tissue (10).

Debulking of the prostatic tissue is achieved by selective, consistent tissue vaporization. The KTP 532 nm light beam is selectively absorbed by oxyhemoglobin, promoting coagulation and disintegration. Since its introduction, the technique has proved to be safe and effective after short- and medium-term follow-up (11) (12). Moreover, there is evidence that anticoagulant medication does not have to be suspended for surgery, since photoselective vaporization of the prostate is virtually bloodless, which makes it an excellent procedure for high risk patients (13). However, long-term outcomes are still lacking and appropriate studies are needed.
This study outlines the outcomes of green light prostate vaporization (GL PV) versus those of standard TURP based on a 5-year follow-up in a prospective, randomized trial. Interim results of this study have been published elsewhere (14) (15).
MATERIALS AND METHODS

The trial was conducted at a single tertiary referral center in Geneva, Switzerland, between March 2007 and December 2011. Approval from the local ethics committee was obtained (registration number: CER 05-087). Patients with bothersome LUTS were recruited in the outpatient clinic and considered for randomization if they met the criteria for surgical treatment of benign prostatic obstruction. All potential study participants were thoroughly informed about the study and written informed consent was obtained. The IPSS score had to be ≥12 and the prostate size between 20–60 ml. Supplementary Table 1 shows the inclusion and exclusion criteria.

The study was an open-label, prospective, randomized, controlled, non-inferiority trial comparing the outcomes of TURP and 80-Watt GL PV of the prostate. A Consort flow chart is provided in Figure 1, illustrating the study design, randomization, treatment modalities, and the follow-up schedule.

The primary outcome measure was the International Prostate Symptom Score (IPSS). Secondary outcome measures included maximum urinary flow rate (Qmax), post-voidal residual (PVR), length of stay (LOS), and re-operation rates at 5-year follow-up.
Randomization and statistical analysis

Randomization was performed in a 1:1 ratio, using a computer-based random sequence generator. A sample size of 2 x 124 patients was calculated as necessary to show equivalence using the IPSS as the primary endpoint and a non-inferiority margin of three points (16). This sample size corresponds to a power of 80% power with a two-sided alpha of 0.05 between experimental and control group to accept the null hypothesis of no difference with an assumed 10% loss to follow-up. To avoid false-positive analyses, we introduced a correction for multiple comparisons. All statistical analyses were performed using Stata 14 (StataCorp).

Surgical procedures

Surgeons were either staff urologists or experienced registrars-in-training who performed the interventions under the supervision of a staff urologist. This reflected the every-day hospital situation and avoided expert bias. Nine surgeons were involved in the TURP group and 8 surgeons in the GL PV cohort. The surgical technique for GL PV was performed in a standardized fashion according to previously described recommendations (17).
TURP was performed using a 26-Fr Storz resectoscope with a cutting power of 150 W and a coagulation power of 60 W with a standard tungsten monopolar wire loop (Karl Storz Endoskopie; Anklin AG, Binnigen, Switzerland). An electrolyte-free mannitol-sorbitol solution (Purisole®) was used, and surgery was performed under spinal or general anesthesia according to the anesthetist’s and patient’s preference.

GL PV was performed using an 80-W KTP laser generator equipped for energy application with a StarPulse quasi-continuous wave laser (Laserscope) through a 21- or 23-Fr continuous flow cystoscope (Olympus or Storz respectively). The 532 nm laser beam was delivered by a side-firing glass fiber with a 70° angle. Starting from the prostate floor at the bladder neck, the median and lateral lobes were sequentially vaporized progressing distally and laterally, the final result resembling a TURP cavity. After the procedure, a 20 or 22 Fr three-way transurethral catheter with continuous irrigation was inserted.
RESULTS

Study population

Over 4.5 years, 269 patients were recruited and enrolled into the trial. Due to technical breakdown of the GL PV laser, 16 patients initially randomized to the GL PV group could not be treated and therefore dropped-out from the study. This left two groups with a slight number asymmetry in favor of the TURP population. Seventy-seven patients terminated their follow-up earlier because of prostate cancer diagnosis (14 patients), surgical retreatment (31 patients), and death (32 patients). This left 161 patients available for final evaluation, of whom 56 (35%) were lost to follow-up (Supplementary Table 2). After 5 years, final follow-up data was available for 105 patients, 44 treated with GL PV and 61 with TURP, meaning that 65% of the patients considered were available for final evaluation.

Baseline characteristics were similar in both groups and are illustrated in Table 1. In terms of our primary outcome measure, IPSS was 20.3 (SD ± 7) in the GL PV group and 20.4 (SD ± 7.5) in the TURP group (p= 0.8). Qmax was 8.9 ml/s (SD ± 4.1) in the GL PV group and 8.5 ml/s (SD ± 4.6) in the TURP group (p= 0.4).
5-year outcomes

Perioperative and short-term functional outcomes have been reported elsewhere (15).

At 5 years, the outcome for both procedures was similar and there were no statistically significant differences between the groups for the primary outcome functional parameters (Table 2). The five-year postoperative mean improvement in IPSS was 11.2 (SD ± 7.6) in the GL PV group and 13.1 (SD ± 9.1) in the TURP group, and was not statistically different between the two groups ($p=0.3$). This was reflected in the QoL score, the post-void residual and the Qmax. The course of the IPSS and Qmax over time are illustrated in Figure 2.

16 patients (14.3%) in the GL PV group and 15 (11.9%) in the TURP group underwent reoperation ($p = 0.9$). Reasons for reoperation are given in Supplementary Table 3. Re-intervention due to prostate tissue regrowth was performed in 10 patients after GL PV and 6 patients after TURP. 6 patients in the GL PV group and 9 in the TURP group developed bladder neck sclerosis and urethral strictures. Prostate cancer was incidentally detected in 12 of the 126 patients (9.5%) treated with TURP. 5 of these patients subsequently underwent radical prostatectomy and 7 patients were assigned to a watchful-waiting strategy, considering age and general condition. In a 5-year follow-up prostate cancer was diagnosed in 2 patients who initially underwent GL PV. One of these patients underwent selective ultrasound ablation of the prostate and the other patient was treated with a radical prostatectomy.
DISCUSSION

To our knowledge, this trial is the first comparison of long-term follow-up data following treatment with an 80-W GL PV or TURP in a prospective, randomized setting. The results confirm the non-inferiority of the 80-W GL PV for all major functional outcomes compared to TURP after 5 years. Both techniques proved to be safe, with re-treatment rates of 14.3% in the GL PV group and 11.9% in the TURP group.

Over the past 10 years, a substantial diversification has been observed in pharmacological and surgical treatment options for bladder outlet obstruction (BOO) (18) (19). In 1990, TURP accounted for 97% of operations performed to relieve BOO in the USA (20). Twenty years later, only around 48% of surgeries to relieve BOO are performed by conventional TURP (21). Therapeutic alternatives include a variety of techniques such as transurethral microwave thermotherapy (TUMT), transurethral needle ablation of the prostate (TUNA), prostatic stents, minimally invasive simple prostatectomies, prostatic urethral lifts, and prostatic artery embolization (22).

The ongoing search for less invasive techniques is mainly a result of the significant complication rate with TURP(8). Accordingly, laser-based prostate obstruction relief has been propagated to minimize the risk of bleeding complications, such as TUR syndrome. Risk reduction is even more important, considering the shift towards a more elderly and frail patient population frequently bearing coronary stents or suffering from atrial fibrillation, coronary artery disease, valvular heart diseases, or deep venous thrombosis. These conditions are mainly managed by the use of oral
anticoagulant or antithrombotic agents. In a recent review, nearly 40 percent of adults in the USA were take aspirin for its antiaggregation properties.(23)

The advantages of laser-based prostate surgery are reflected in its increasing use in everyday clinical practice. The rate of laser-managed BPO has increased from 6% in 2000 to 45% in 2011(21). Since its introduction in 1995, the KTP laser today accounts for around 23% of BPO surgeries in France(24).

In terms of functional outcomes, GL PV was effective in the short- and medium-term in two randomized controlled trials (11). Hai et al. and Ruszat et al. reported sustained medium- and long-term functional outcomes of the 80-W KTP laser with a re-treatment rate of around 9% after 2.5 years follow-up and 15% after 5 years (25) (26). These results, however, were based on case series and not findings collected in a randomized, controlled setting. It has to be emphasized that so far no other operative technique has stood the test of time as well as TURP. In this respect, our long-term data provide further evidence to support the broad application of GL PV.

Large, non-randomized studies have reported a more favorable safety profile for KTP laser than TURP (27) regarding major complications. A slightly higher re-operation rate after KTP laser than after TURP has been reported in the literature. The difference between the two techniques in this respect was not statistically significant in our analysis. This was reflected in similar rates of bladder neck sclerosis and urethral strictures. The re-operation rates in this study are comparable to data published in long-term cohort-studies. It can, however, not be excluded, that the
proportion of patients which had to undergo re-do surgery might be a bit higher, considering the 56 patients, that were lost to-follow-up.

Long-term safety and reintervention rates with high power laser systems (i.e. 120-W and 180-W) have yet to be demonstrated (12).

Prostate cancer was detected incidentally in almost 10% of our TURP patients. However, only half of these patients qualified for active treatment. Diagnosis of prostate cancer might indeed be delayed in the GL PV group, which has to be taken into account especially in younger patients. The clinical relevance of the delay in elderly patients is questionable.

Limitations of this study include the attrition of patients within the 5 year follow-up period. However, actual loss to follow-up concerned only 56 patients. A substantial proportion of patients could not be considered for final evaluation regarding functional outcomes because of subsequent prostate cancer diagnosis, surgical retreatment, mental impairment, death and other factors but data regarding the whereabouts of these patients could still be obtained. Slightly higher PSA values were observed in the TURP group at baseline, possibly accounting for higher volume glands. This was not the case, however, as TRUS prostate volumes were similar in both groups. PSA was not measured at the 5-year follow-up in our patients, and this might have enabled us to quantify the prostatic tissue-regrowth rate over time. Sexual function was not assessed within the study and more information regarding erectile and ejaculatory function would have been valuable.
These shortcomings are counterbalanced by our provision of long-term comparative follow-up data based on a population of a hundred patients prospectively randomized.

So far no long-term data is available for the 120-W and the 180-W laser systems. Results from ongoing prospective randomized trials will help to contextualize our data and will further guide the application perspectives of laser systems in the treatment of BPH.

**CONCLUSION**

Non-inferiority of the GL PV to TUR-P was confirmed for all major functional and safety outcomes at 5-year follow-up. GL PV appears to be a safe surgical alternative for patients suffering from BPO.
REFERENCES


**Figure Legend**

**Figure 1** Flow chart of the study including randomization, treatment and follow-up of patients. TURP = transurethral resection of the prostate; GL-PV = 80-W GreenLight PV

**Figure 2** Boxplots for International Prostate Symptom Score and $Q_{\text{max}}$. Boxplots depicts median, first and third quartiles, minimum and maximum for GL-PV and TURP. IPSS = International Prostate Symptom Score; $Q_{\text{max}}$ = maximum urinary flow; TURP = transurethral resection of the prostate; GL-PV = 80-W GreenLight PV.
Table 1 - Baseline characteristics of treated patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>GL-PV (n=112)</th>
<th>TURP (n=126)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>68.4 (8.7)</td>
<td>67.6 (8.4)</td>
<td>0.7</td>
</tr>
<tr>
<td>ASA score #</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1=20 (18%)</td>
<td>1=25 (20%)</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>2=72 (65%)</td>
<td>2=84 (67%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3=18 (16%)</td>
<td>3=17 (13%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4=1 (1%)</td>
<td>4=0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPSS</td>
<td>20.3 (7)</td>
<td>20.4 (7.5)</td>
<td>0.8</td>
</tr>
<tr>
<td>QoL</td>
<td>4.2 (1.1)</td>
<td>4.3 (1.4)</td>
<td>0.2</td>
</tr>
<tr>
<td>Qmax, ml/s</td>
<td>8.9(4.1)</td>
<td>8.5(4.6)</td>
<td>0.4</td>
</tr>
<tr>
<td>PVR, ml</td>
<td>91.1 (88.3)</td>
<td>114.5 (136.4)</td>
<td>0.3</td>
</tr>
<tr>
<td>PSA, ng/ml</td>
<td>3.6 (3.1)</td>
<td>4.9(5.3)</td>
<td>0.046</td>
</tr>
<tr>
<td>TRUS prostate volume, ml</td>
<td>36.1(11.5)</td>
<td>37.9(14.3)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

IPSS = International Prostate Symptom Score; Qmax = maximum flow rate; QoL = quality of life; PSA = prostate specific antigen; PVR = postvoid residual; TRUS = transrectal ultrasonography; GL-PV = 80-W GreenLight PV; TURP = transurethral resection of the prostate.

Values shown represent mean (standard deviation) unless otherwise noted.

# For ASA score values shown represent number of patients for each ASA score group (percentage on total arm treatment population)

* The p value reported is for statistical test of difference between groups.
Table 2 - Primary outcomes at each follow-up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Time point</th>
<th>GL-PV</th>
<th>TURP</th>
<th>p value *</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IPSS score</strong></td>
<td>Baseline</td>
<td>n = 112</td>
<td>n = 126</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20.3 (7)</td>
<td>20.4 (7.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 mo</td>
<td>n = 44</td>
<td>n = 61</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.1 (6.7)</td>
<td>6.4 (4.7)</td>
<td></td>
</tr>
<tr>
<td><strong>QoL</strong></td>
<td>Baseline</td>
<td>n = 112</td>
<td>n = 126</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.2 (1.1)</td>
<td>4.3 (1.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 mo</td>
<td>n = 44</td>
<td>n = 61</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.4 (1.4)</td>
<td>1.1 (1.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Q(\text{max}) (ml/s)</strong></td>
<td>Baseline</td>
<td>n = 112</td>
<td>n = 126</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.9 (4.1)</td>
<td>8.5 (4.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 mo</td>
<td>n = 44</td>
<td>n = 61</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17.8 (11.3)</td>
<td>17.8 (9.7)</td>
<td></td>
</tr>
<tr>
<td><strong>PVR (ml)</strong></td>
<td>Baseline</td>
<td>n = 112</td>
<td>n = 126</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>91 (88)</td>
<td>115 (136)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 mo</td>
<td>n = 44</td>
<td>n = 61</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>56 (57)</td>
<td>41 (52)</td>
<td></td>
</tr>
</tbody>
</table>

Values shown represent mean (standard deviation)

* The p value reported is for statistical test of difference between groups
Figure 2.