Efficacy and Safety of 120-W Thulium:Yttrium-Aluminum-Garnet Vapoenucleation of Prostates Compared with Holmium Laser Enucleation of Prostates for Benign Prostatic Hyperplasia

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Abstract

Background: This study compared the efficacy and safety between 120-W thulium:yttrium-aluminum-garnet (Tm:YAG) vapoenucleation of prostates (ThuVEP) and holmium laser enucleation of prostates (HoLEP) for patients with lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH).

Methods: A retrospective analysis of 88 consecutive patients with symptomatic BPH was carried out, who underwent either 120-W ThuVEP or HoLEP nonrandomly. Patient demographics and peri-operative and 12-month follow-up data were analyzed with the International Prostate Symptom Score (IPSS), quality of life (QoL) score, maximum flow rate (Qmax), postvoid residual urine volume (PVR), and rates of peri-operative and late complications.

Results: The patients in each group showed no significant difference in preoperative parameters. Compared with the HoLEP group, patients in the 120-W ThuVEP group required significantly shorter time for laser enucleation (58.3 ± 12.8 min vs. 70.5 ± 22.3 min, \( P = 0.003 \)), and resulted in a significant superiority in laser efficiency (resected prostate weight/laser enucleation time) for 120-W Tm:YAG laser compared to holmium:YAG laser (0.69 ± 0.18 vs. 0.61 ± 0.19, \( P = 0.048 \)). During 1, 6, and 12 months of follow-ups, the procedures did not demonstrate a significant difference in IPSS, QoL score, Qmax, or PVR (\( P > 0.05 \)). Mean peri-operative decrease of hemoglobin in the HoLEP group was similar to the ThuVEP group (17.1 ± 12.0 g/L vs. 15.2 ± 10.1 g/L, \( P = 0.415 \)). Early and late incidences of complications were low and did not differ significantly between the two groups of 120-W ThuVEP and HoLEP patients (\( P > 0.05 \)).

Conclusions: 120-W ThuVEP and HoLEP are potent, safe and efficient modalities of minimally invasive surgeries for patients with LUTS due to BPH. Compared with HoLEP, 120-W ThuVEP offers advantages of reduction of laser enucleation time and improvement of laser efficiency.

Key words: Benign Prostatic Hyperplasia; Holmium Lasers; Laser Surgery; Prostatectomy; Thulium; Transurethral

INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most frequent diseases in aging males and is also the major etiology of lower urinary tract symptoms (LUTS) with a negative impact on quality of life (QoL). For decades, transurethral resection of prostates (TURP) has been considered as the most established surgical treatment for LUTS secondary to BPH at most urological practices. While the status of TURP as “gold standard” has not been threatened, especially in most developing countries, there are still concerns regarding peri-operative morbidity such as severe bleeding, risk of fluid volume absorption, and prolonged recovery.

There have been many proposed alternative surgeries to TURP for BPH. An ideal treatment is the one that removes a significant amount of prostatic adenoma efficiently and has minimal peri-operative morbidity while providing equivalent and durable patient outcomes. The holmium:yttrium-aluminum-garnet (Ho:YAG) laser was the initial energy source used for the procedure of enucleating prostatic adenoma from the capsule. By the time of this study, the holmium laser enucleation of the prostate (HoLEP) has been investigated in multiple randomized trials and proved to be an alternative to size independent endourological treatments for LUTS due to BPH. [5,6]
In recent years, thulium:YAG (Tm:YAG) laser prostatectomy has been introduced into the treatment of BPH at four technical approaches as following: Tm:YAG vaporization, Tm:YAG vaporesection, Tm:YAG enucleation and Tm:YAG laser vapoenucleation of the prostate (ThuVEP). Among those approaches, ThuVEP has been rigorously analyzed and represents a minimally invasive, size independent, and efficacious laser prostatectomy with promising long-term outcomes and low complication rates.[8–10] Both HoLEP and ThuVEP appear to be likely candidates for a new standard for the surgical treatments of BPH replacing the traditional TURP. However, few studies have compared these two vaporizing enucleation technologies. Therefore, through this study, we were committed to evaluate the efficiency, safety, and clinical effects of ThuVEP compared with HoLEP.

**METHODS**

From August 2012 to June 2013, 88 symptomatic BPH patients were retrospectively enrolled in the study, who underwent transurethral laser prostatectomy and met our inclusion criteria. Among these patients, 46 accepted HoLEP group, and 42 accepted 120-W ThuVEP group. Before the surgery, detailed urological examinations, including a digital rectal examination (DRE), transrectal ultrasound, assessment of the International Prostate Symptom Score (IPSS), and QoL score, were carried out. Postvoid residual urine (PVR) and urinary peak flow rate (Qmax) were reviewed. Workup included urine analysis, blood tests (including hemoglobin), and the measurement of serum prostate-specific antigen (PSA), which was carried out before DRE and instrumentation. In patients with abnormal PSA values or suspect DREs, a 12-core needle biopsy of the prostate was carried out. Oral anti-coagulation and platelet inhibition was terminated prior to the surgery and bridged with low molecular weight heparin, it was indicated by the patient. The study inclusion criteria included the followings:

- Maximum urinary flow rate (Qmax) was <15 ml per second
- IPSS was >7 points
- All patients were previously treated with conservative medical therapy using α-blockers and/or 5α-reductase inhibitors, which did not result in significant improvement in LUTS
- Excluded criteria in this study were: Patients with severe pulmonary disease or heart disease, bladder calculus, urodynamically diagnosed neurogenic bladder dysfunction, prostate cancer, previous prostate or urethral surgery.

In all cases, the operations were performed by two experienced surgeons. Spinal anesthesia was applied in the most patients except those who failed spinal anesthesia, in which case general anesthesia was used. As for equipment, it was selected as following: For HoLEP, the energy source was an 100-W Ho:YAG laser (Versapulse®, Lumenis Inc., Santa Clara, CA, USA), delivered through a 550-nm end-firing fiber (SlimLineTM 550, Lumenis Inc.). For ThuVEP, the energy source was the 120-W 2-μm continuous-wave Tm:YAG laser (RevoLix®, LISA Laser Products, Katlenburg, Germany), delivered through a 550-nm optical core bare-ended, re-usable laser fiber (RigiFib®, LISA Laser Products). Both groups proceeded with a 26F continuous-flow laser resectoscope with a video system in combination with a mechanical tissue morcellator (Piranha® TUR-Set, Richard Wolf, Knittlingen, Germany). All interventions were carried out using normal saline as irrigation fluid.

The HoLEP procedure was performed as “three-lobes technique.”[11] In brief, after marking of the distal resection border close to the apex of the prostate, a Turner-Warwick-like incision was made at the 5 and 7 o’clock positions down to the surgical capsule. The median lobe was first enucleated in a retrograde manner. And then the lateral lobes were respectively enucleated by dissecting the prostatic adenoma from the peripheral zone at the layer of the surgical capsule. Enucleated tissue was positioned into the bladder and morcellated through a 26F nephroscope. The HoLEP procedure was performed at a laser setting of 2 J and 50 Hz for enucleation, and 0.5 J and 40 Hz defocused laser for hemostasis when bleeding vessels were encountered. The 120-W ThuVEP technique was similar to the three-lobes technique for HoLEP.[9] After finishing the above procedures, a three-way Foley catheter (20F or 22F) was placed into the bladder, and continuous irrigation is provided overnight.

After the surgery, hemoglobin levels were measured within 1 day. Operation time, laser enucleation time, morcellation time, resected prostatic weight, hemoglobin decrease, and peri-operative complications were recorded. Catheterization time and hospitalization duration were noted. Follow-up was assessed at 1, 6, and 12 months after surgery. Postoperative assessments during the follow-ups consisted of IPSS, QoL score and Qmax at the 1, 6 and 12 months; PVR volume and late complications at the 12 months.

Between the groups, baseline characteristics, as well as peri- and post-operative outcome parameters, including IPSS, QoL score, Qmax, and PVR volume, were compared using the Student’s t-test and are presented as the mean ± standard deviation. Postoperative adverse events were evaluated using the two-tailed Chi-square test, and Fisher’s exact tests when appropriate. For repeated measures, two-way analysis of variance was used to compare the pre- and post-operative LUTS parameters within each group, including IPSS, QoL score, Qmax, and PVR volume. Statistical tests were performed with the Statistical Package for Social Sciences, version 13.0 for Windows (SPSS, Chicago, IL, USA). \( P < 0.05 \) indicates a statistical significance.

**RESULTS**

The baseline characteristics between the two groups were comparable regarding the patient’s age, the prostate...
adenoma volume, PSA levels, IPSS, QoL score, Qmax, and PVR [Table 1]. All the procedures in both the HoLEP and ThuVEP groups were successfully completed. The peri-operative data are listed in Table 2. Although the operation time in the ThuVEP group (90.6 ± 17.8 min) was shorter than the HoLEP group (98.2 ± 26.0 min), no statistical significance was found in the difference (P = 0.109). Despite the overall operation time, the time on laser enucleation by ThuVEP was shorter than the holmium laser significantly (58.3 ± 12.8 min vs. 70.5 ± 22.3 min, P = 0.003). Moreover, results showed a significant superiority in laser efficiency for the 120-W Tm:YAG laser compared to the Ho:YAG laser (0.69 ± 0.18 vs. 0.61 ± 0.19, P = 0.048). The results did not show a significant difference between the two groups in mean values of resected prostate weight, enucleation ratio, morcellation time, or morcellation efficiency.

Mean peri-operative decrease of hemoglobin in the HoLEP group was similar to the ThuVEP group (17.1 ± 12.0 g/L vs. 15.2 ± 10.1 g/L, P = 0.415). Three in the HoLEP group and two in the ThuVEP group showed decreased hemoglobin concentration of more than 40 g/L. During the procedures, 2.4% of cases (1/42) found capsular perforation in the ThuVEP group, comparable with 2.2% (1/46) in the HoLEP group (P = 0.948). The results also demonstrated similar rates of blood transfusion in the HoLEP group (2/46, 4.3%) and in the ThuVEP group (1/42, 2.4%) (P = 0.612). Both groups required similar mean time for catheterization and hospital stay as listed in Table 2. In the table, there were three patients in the HoLEP and ThuVEP groups respectively, using prolonged postoperative catheterization because of continuous gross hematuria. Peri-operative symptomatic urinary tract infection occurred in five patients, consisting of two in the HoLEP group and three in the ThuVEP group, which did not show a significant difference between the two groups (4.3% vs. 7.1%, P = 0.917). No findings of other early complications were reported including transurethral resection syndrome, clot retention, hemorrhage requiring cystoscopy for coagulation, ureteric orifice injury, bladder injury during morcellation, or incomplete morcellation. No patient was lost during the 12-month follow-up except one patient who accepted two reoperations at the 1.5 and 5 months after HoLEP respectively because of bladder neck contracture. Both the HoLEP and the ThuVEP groups were comparable on IPSS, QoL score, Qmax, and PVR volume at the 1, 6 and 12 months follow-up [Table 3]. These parameters were significantly improved at every follow-up point in each group compared with the baseline values (P = 0.000). Complications within 12 months were reported. At the 1 month follow-up, five patients complained urge incontinence (5/46, 10.9%) and two had slight stress incontinence (2/46, 4.3%) in the HoLEP group. There is no significant difference in the ThuVEP group, either for urge incontinence (2/42, 4.8%, P = 0.507) or for slight stress incontinence (1/42, 2.4%, P = 0.612). All 10 patients’ continence recovered within 6 months. No patients had

### Table 1: Baseline characteristics of patients in HoLEP and ThuVEP groups

| Characteristic          | All patients | HoLEP group | ThuVEP group | P     |
|-------------------------|--------------|-------------|--------------|-------|
| Patients (n)            | 88           | 46          | 42           | 0.948 |
| Age (year)              | 71.2 ± 4.8 (59-79) | 70.3 ± 5.3 (59-78) | 72.1 ± 4.1 (61-79) | 0.075 |
| Prostate volume (ml)    | 55.5 ± 12.7 (35-95) | 56.1 ± 13.6 (35-95) | 54.7 ± 11.7 (35-80) | 0.609 |
| PSA (ng/ml)             | 2.81 ± 1.66 (0.71-8.73) | 3.03 ± 1.19 (0.71-8.73) | 2.56 ± 1.19 (1.05-5.69) | 0.189 |
| IPSS                    | 27.0 ± 5.7 (13-35) | 27.4 ± 5.4 (15-35) | 26.7 ± 6.0 (13-35) | 0.570 |
| QoL score              | 4.9 ± 1.0 (3-6) | 4.7 ± 1.1 (3-6) | 5.0 ± 0.9 (3-6) | 0.107 |
| Qmax (ml/s)             | 6.0 ± 2.5 (2-13) | 5.7 ± 2.6 (2-13) | 6.2 ± 2.4 (3-10) | 0.373 |
| PVR (ml)               | 128.1 ± 95.7 (30-420) | 136.4 ± 90.9 (40-350) | 119.0 ± 110.9 (30-420) | 0.398 |

Results are shown as the mean ± SD (range). SD: Standard deviation; HoLEP: Holmium laser enucleation of prostates; ThuVEP: Thulium:yttrium-aluminum-garnet vapoenucleation of prostates; PSA: Prostate-specific antigen; IPSS: International Prostate Symptom Score; QoL: Quality of life; PVR: Postvoid residual.

### Table 2: Peri-operative outcomes between HoLEP and ThuVEP groups

| Parameters                                      | HoLEP group (n = 46) | ThuVEP group (n = 42) | P     |
|------------------------------------------------|----------------------|-----------------------|-------|
| Operation time (min)                           | 98.2 ± 26.0 (70-180) | 90.6 ± 17.8 (60-130) | 0.109 |
| Laser time (min)                               | 70.5 ± 22.3 (40-140) | 58.3 ± 12.8 (30-80)  | 0.003 |
| Morcellation time (min)                        | 27.4 ± 6.1 (20-45)   | 29.8 ± 9.1 (20-55)   | 0.152 |
| Resected weight (g)                            | 41.6 ± 13.3 (18-76)  | 39.6 ± 10.3 (18-61)  | 0.444 |
| Enucleation ratio (g/ml) (resected weight/prostate volume) | 0.73 ± 0.08 (0.47-0.84) | 0.72 ± 0.08 (0.43-0.88) | 0.588 |
| Laser efficiency (g/min) (resected weight/laser time) | 0.61 ± 0.19 (0.30-1.18) | 0.69 ± 0.18 (0.43-1.20) | 0.048 |
| Morcellation efficiency (g/min) (resected weight/morcellation time) | 1.55 ± 0.48 (0.60-3.04) | 1.40 ± 0.43 (0.70-2.44) | 0.118 |
| Hemoglobin decrease (g/L)                      | 17.1 ± 12.0 (8-65)   | 15.2 ± 10.1 (7-55)   | 0.415 |
| Catheterization time (d)                       | 2.9 ± 1.0 (2-6)      | 2.7 ± 1.2 (2-7)      | 0.668 |
| Hospital stay (d)                              | 3.8 ± 1.0 (3-7)      | 3.7 ± 1.0 (3-8)      | 0.422 |

Results are shown as the mean ± SD (range). HoLEP: Holmium laser enucleation of prostates; ThuVEP: Thulium:yttrium-aluminum-garnet vapoenucleation of prostates; SD: Standard deviation.
persistent irritative urinary symptoms or incontinence, urethral stricture requiring reoperation, or sub-urothelial stenosis.

**Discussion**

For many years, TURP was referred as the “gold standard” surgical therapy for patients with BPH. Recently while major drawbacks of contemporary TURP remain, such as intraoperative and perioperative complications, many new endoscopic technologies have been introduced to treat BPH.[4] In fact, there is great competition among the various modalities of endoscopic treatment for BPH in a race for minimal invasiveness, decreasing surgical morbidity, and long-term efficacy. From our point of view, laser-based transurethral prostatectomy has been proven as a safe and effective therapy for patients with BPH. Recently while major drawbacks of contemporary TURP remain, such as intraoperative and perioperative complications, many new endoscopic technologies have been introduced to treat BPH.[4] In fact, there is great competition among the various modalities of endoscopic treatment for BPH in a race for minimal invasiveness, decreasing surgical morbidity, and long-term efficacy. From our point of view, laser-based transurethral prostatectomy has been proven as a safe and effective therapy for patients with BPH.

The HoLEP is the first technique using an end-firing laser fiber to enter the native anatomical plane between the prostatic lobe and surgical capsule and then to enucleate the prostate adenoma from the capsule. A series of clinical studies have proven the efficacy and safety of HoLEP.[5,6] A recent systematic review and meta-analysis revealed superiority with HoLEP in the improvement of LUTS parameters in both the intermediate and the long-term results with a low rate of morbidity, compared with contemporary mono-polar TURP. However, it also showed HoLEP, including enucleation and morcellation, was associated with longer operation time than TURP.[6] Recently introduced Tm:YAG laser vapoenucleation (ThuVEP) has been reported as a minimally invasive, size-independent treatment modality for BPH with promising intermediate and long-term follow-up outcomes.[8,10,12] ThuVEP has the similar retrograde approach to HoLEP, but very few data had been available for the comparison between these two techniques. In fact, the significant difference between these laser techniques in terms of laser-tissue effects may confuse the evaluation of the roles with different laser methods in the treatment of LUTS due to BPH.[13]

In the present study, 120-W ThuVEP was compared with HoLEP. Not surprisingly, both procedures removed prostatic adenoma with high efficacy and safety, and obtained satisfactory outcomes in relief of LUTS. At the 12-month follow-up, the mean IPSS decreased about 70% and the mean QoL score was improved five-fold in both groups. Compared with the baseline parameters, those patients available for the follow-up showed better durability in PVR improvement and sufficient increases in Qmax in both groups. At assessment points of the follow-up, no significant difference was found in voiding parameters or symptom scores between the ThuVEP and HoLEP groups. It is expected that the amount of tissue removal will result in urodynamic improvement with regards to increased uroflowmetry, obstruction relief, and reduced PVR urine. Following a HoLEP-like approach, ThuVEP has been proved capable of reducing the volume of the prostate more than 80%, which confirmed the adequate removal of the prostate adenoma and corresponded with published series on HoLEP.[8,14]

We did not find any significant superiority in total operation time comparing ThuVEP to HoLEP in this study. However, 120-W Tm:YAG laser system was compared with HoLEP. Zhang et al. reported 120-W Tm:YAG laser system was used instead in Zhang et al.’s study.[15] It has been proved that the more powerful Tm:YAG laser resulted in an increased rate of tissue ablation but without apparently increased risks of complications. In an ex vivo evaluation of Tm:YAG laser treatment for BPH, Bach et al. observed the tissue ablation rate was improved by nearly 70% (from 9.80 g/10 min to 16.41 g/10 min) when the power output increased from 70 W to 120 W.[14] Also, Netsch et al. reported 120-W Tm:YAG laser system enhanced the effectiveness of ThuVEP compared with the 70-W Tm:YAG device, regarding enucleation and overall operation efficiency.[17]
The difference in enucleation efficacy between ThuVEP and HoLEP may be attributed to the physical properties of the laser itself. With a chromophore of targeting water and a wavelength around 2000 nm, Tm:YAG laser can vaporize prostate tissues efficiently in a shallow optical penetration of approximately 0.2 mm.\(^{[18]}\) The continuous mode of radiation emission supports Tm:YAG laser to perform efficient resection and vaporization simultaneously with optimal coagulation and hemostasis effects.\(^{[14]}\) Therefore, due to the excellent ablation capacity, the Tm:YAG laser can vaporize prostate tissue easily upon the surgical capsule in a nearly non-bleeding surgical environment.\(^{[12,19]}\) On the contrary, Ho:YAG laser is emitted in a pulsed mode and uses several kilowatt pulse peak power. During the enucleation, high-energy concentration can be achieved with each short high-power laser pulse, resulting in vigorous expanding and collapsing steam bubbles, which create disruptions of prostatic tissue through the surgical plane between the adenoma and the capsule.\(^{[20]}\) Under a relatively high power Ho:YAG laser, these disruptions may make hemostasis more challenging at the time of enucleating. So the HoLEP operator has to take adequate time to adjust energy density by reducing the radiation energy and pulse rates, or by increasing the distance from the tip of the laser to the target bleeding vessels.\(^{[21]}\)

In our series, the mean blood loss was low in both groups, due to the peri-operative hemoglobin decrease and the transfusion rate. The mean blood loss showed no significant difference between HoLEP and ThuVEP groups. Five patients, three by HoLEP and two by ThuVEP, decreased the hemoglobin concentration of more than 40 g/L. The prostate adenoma volume of these patients was all larger than 60 ml. The increased surface area of the prostatic capsule along with more vascular density can influence and achieve hemostasis despite the ablation efficiency of the laser.\(^{[21]}\) It is worth noting that capsular perforation occurred in only one patient with 120-W ThuVEP, and this incidence (2.4%) appears comparable to those reported previously (1.4–3.2%) in series of both 70- and 120-W ThuVEP studies.\(^{[8,10,22]}\) Satisfactory control of unintended collateral tissue damage was achieved and contributed to the shallow penetration depth of the Tm:YAG laser, which produced a coagulation zone in a stable extent even with high-powered laser devices.\(^{[16]}\)

Overall, HoLEP and ThuVEP showed a low incidence rate of late complications at the 12-month follow-up in our study. Bladder neck contracture requiring surgical treatment occurred in 2.2% (1/46) of the patients with HoLEP, which is comparable to the previous series of studies (0.6–3.0%).\(^{[5,6]}\) By contrast, none of the 42 patients in ThuVEP group occurred bladder neck contracture. Previously, the incidences of bladder neck contracture reported after ThuVEP were <2%,\(^{[10,14,22]}\) and even absent in large prostate volume series and in patients on anticoagulant therapy.\(^{[8,21]}\) Besides, transient urge/stress urinary incontinence to a certain degree was present in both groups, and the incidence rates had no significant difference, in which cases the patients recovered within 6 months. Transient stress incontinence is a well-known problem after HoLEP, developing in up to 44% of patients.\(^{[24]}\) In contrast after ThuVEP, previous reports on incidences of urge urinary incontinence ranged from 0.8% to 5.4%\(^{[10,14,22,23]}\) and those on stress incontinence presented in 1.7–11.5%.\(^{[8,10,14,23,25]}\) From the experience with HoLEP, the surgical technique is an important factor contributing to the risk of postoperative incontinence.\(^{[16]}\) In the same way, extra caution should be taken to avoid injury to the sphincter when treating the apical tissue, as well as to the superficial bladder during morcellating.\(^{[14]}\) The continuous vaporizing performance of the Tm:YAG laser offers a potential advantage over HoLEP to obtain an optimal view with less bleeding, which means more uncomplicated correction of the anatomical layer and less coagulation in bladder neck tissues.\(^{[12]}\)

The major limitations of our study lie within the nonrandomized retrospective study design, the possible bias when reporting own complications, and the fact that this series was conducted at a single institution. Moreover, another limitation of this study may be the small sample size, which limited the power of the analysis. A much larger initial trial would have been required to maintain high numbers at a long-term duration of follow-up. However, strength of this work may be summarized as the first direct comparison of efficacy and safety between 120-W ThuVEP and HoLEP, and our data suggested that ThuVEP offers a significant superiority in efficiency of laser enucleation during the procedure.

Both 120-W ThuVEP and HoLEP are safe and efficient and minimally invasive treatment modalities for patients with LUTS due to BPH. Compared with HoLEP, 120-W ThuVEP offers advantages in reducing laser enucleation time and improving laser efficiency. Assessment at the 12-month follow-up showed no difference in urinary parameters and morbidity incidences. However, well-designed randomized trials with extended follow-up and larger sample sizes, may be needed to draw final conclusions about the long-term efficacy of these procedures.

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