Original article

Treatment outcomes of benign prostate hyperplasia by thulium vapoenucleation of the prostate in aging men


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ABSTRACT

Purpose: To analyze the outcomes of thulium vapoenucleation of the prostate (ThuVEP) in the management of benign prostatic hyperplasia. The outcomes of this increasingly popular procedure are yet to be confirmed in patients with various prostate sizes and health status.

Materials and methods: Three hundred and three patients who underwent ThuVEP were included and stratified in subgroups according to prostate size and age. We analyzed patient demographics, preoperative disease-related parameters, and perioperative and follow-up results. Correlation of prostate size and operation time were also assessed.

Results: Baseline mean prostate volume was 61.0 mL (range 19.3–226 mL), mean urinary peak flow rate (Qmax) was 8.6 mL/second (range 1.4–23.25 mL/second), mean postvoid residual volume was 126.2 mL (range 0–649 mL) and mean International Prostate Symptom Score was 25.1 (range 8–35). The mean operation time was 84.0 minutes and 88.6 minutes for total and prostate volume >80 mL, respectively. After laser surgery, there were mean reductions of 5.3 ng/mL, 7.5 ng/mL, 3.7 ng/mL, and 3.5 ng/mL (38.0%, 49.7%, 30.3%, and 36.5% change from baseline) in prostate-specific antigen level among the four groups. As for postvoid residual volume, there was a significant reduction in volume in the total, prostate volume >80 mL and prostate volume <80 mL (−73.9 mL, −70.8 mL, and −67 mL, respectively) but not in the elderly group (−31.4 mL, p = 0.068). Similarly, Qmax improved significantly in all (6.7 mL/second, 5.9 mL/second, and 6.0 mL/second, respectively) except the elderly group (2.3 mL/second, p = 0.103). The operation time was highly correlated with the prostate size.

Conclusion: This study indicates that ThuVEP is an effective treatment option for benign prostatic obstruction in patients with different prostate size and age. The technique allows an efficient surgical course with operation time highly correlated with prostate size.

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1. Introduction

Conventional transurethral resection of the prostate (TURP) has been the standard treatment to alleviate bladder outlet obstruction caused by benign prostate hyperplasia (BPH) for several decades because of its established long-term efficacy. However, the short-term postsurgical morbidity usually imposes a significant burden and stress on this group of elderly patients.1 Laser prostatectomy has been used in the treatment of symptomatic BPH for nearly two decades. Promising results by using a range of lasers with different wavelengths, absorption rate, power capacities, and mode of action have been published. All of them demonstrated similar postoperative outcomes to TURP, with fewer complications and less blood loss. Although there are similarities between laser wavelengths and surgical approaches, different tissue interaction makes it necessary for surgeons to be aware of the existing variations to safely use the laser to achieve the desired outcomes. In principle, laser beams with low tissue absorption coefficient penetrate deeper, whereas a high absorption coefficient offers shallow penetration.

Among all the emerging laser techniques, the introduction of thulium vapoenucleation of the prostate (ThuVEP) has gained high
acceptance and become another alternative therapeutic option. Thulium is a metal that serves as the medium to emit a laser with a wavelength of 2013 nm, allowing it to match with the 1920 nm water absorption peak in tissue. Its high absorption coefficient results in shallow penetration of <0.4 mm that offers more precise incision ability to minimize deep tissue and nerve damage. With less heat release than other lasers, it has the advantage of rapid vaporization and coagulation. On top of these advances, enucleation makes rapid removal of the vast majority of the adenomas possible with minimal regrowth expected. Additionally, enucleation can reserve incised tissue for pathological testing.

After the introduction of various endoscopic laser techniques in our center since early 2000, Lee et al. published the results of 245 patients receiving thulium laser, and the functional outcomes were excellent with a low rate of postoperative complications. Currently, an increasing number of patients with different health background and disease status have been accumulated. We revisited the patient data and stratified them into subgroups for further in-depth analysis of the outcome of this technique in the alleviation of BPH symptoms, to generate an updated reference and evidence-based information for the evolving techniques.

2. Materials and methods

Between August 2006 and April 2015, data were collected and analyzed from all patients who underwent ThuVEP in a single center in Taiwan. The chart numbers of patients who underwent ThuVEP were retrospectively extracted from the institute medical records by linking the International Classification of Diseases (ICD) codes with the procedure codes. The associated clinical, laboratory, disease status and perioperative information of each chart number were then reviewed manually. Patients who had baseline data missing or confirmed diagnosis of cancer were subsequently excluded.

Baseline clinical and laboratory characteristics included patients’ age, prostate-specific antigen (PSA) level, prostate size as measured by transurethral ultrasound (TRUS), urinary peak flow rate (Qmax), postvoid residual urine volume (PVR), and International Prostate Symptom Score (IPSS) were collected.

The ThuVEP procedures were performed by a single experienced urology surgeon. Using 2-μm continuous wave emitting end-firing fibers, the procedure was carried out as described previously. After the resectoscope was placed in the urethra at the distal resection border close to the prostatic apex, careful mechanical incisions from the bladder neck were carried out at 5 o’clock and 7 o’clock directions toward the verumontanum. A third incision was then made from the bladder neck to the level of verumontanum in the 12 o’clock direction, and the separated median lobe was enucleated. By moving clockwise for the right lateral lobe and counterclockwise for the left lateral lobe, the two lateral lobes were similarly enucleated along the capsule. The enucleated tissues were flipped toward the bladder. The adenomas were morcellated with a mechanical tissue morcellator and removed from the bladder for routine pathological examination. Residual apical tissue was vaporized as needed using the vaporizing mode. At the end of the procedures, a urethral catheter was routinely inserted into the bladder and irrigation started with normal saline until hematuria subsided. Patients were discharged after confirming that bleeding had subsided and voiding pattern returned to normal after removal of the catheter.

Perioperative parameters including operation time, and postoperative PSA, Qmax, PVR, and IPSS were collected accordingly. The records within 3 months after surgery and the latest record were used for outcome analysis. However, the postoperative TRUS and IPSS data for most patients were missing as these were not mandatory measurements in normal practice.

The data are presented as mean ± standard deviation, range, absolute change, and percentage change from baseline. All analyses were performed with a commercial statistical calculator. Two-sided p < 0.05 was regarded as statistically significant. Analysis of variance was used to compare subgroup data sets. One sample t test was used for pre- and postoperative comparison. A correlation coefficient was calculated to check the correlation between TRUS volume and operation time.

3. Results

From the overall cohort of 309 patient records, 303 records of patients with symptomatic BPH who underwent ThuVEP were retrieved after excluding six cases with confirmed diagnosis of prostate cancer. Among them, 121 patients had a prostate size >80 mL as measured by TRUS. Thiry-eight patients (12.5%) were aged >80 years at the time of surgery.

The baseline characteristics of all study patients and subgroups are shown in Table 1. The mean age (70.1 y) and mean prostate size (61.0 mL) of our study cohort were similar to those reported in previous studies, but the Qmax, PVR, and IPSS varied widely among different study groups.

Between the TRUS >80 mL and TRUS <80 mL subgroups, there was a significant difference in PSA level (10.8 vs. 8.0 ng/mL, p = 0.031) but no significant difference in Qmax, PVR or IPSS at baseline between the groups. Patients with larger prostate size did not seem to have more serious obstructive symptoms and greater urine retention than patients with smaller prostate.

As for the elderly subgroup (>80 y), all the baseline parameters, including PSA level, Qmax, PVR, and IPSS did not differ significantly with the overall patient population.

The perioperative and follow-up data are depicted in Table 2. Among the four groups, the operation time was significantly longer in the TRUS >80 mL group compared to the TRUS <80 mL group (88.6 min vs. 80.9 min, p = 0.018).

The decrease in PSA level from baseline in all four groups (Total, TRUS >80 mL, TRUS <80 mL and age >80 y) was significant

| Table 1 | Baseline characteristics, stratified by prostate size and age. |
|---|---|---|---|---|---|
| Characteristics | Total | TRUS >80 mL | TRUS <80 mL | Age >80 y |
| Patient, n (%) | 303 (100.0) | 121 (39.9) | 182 (60.1) | 38 (12.5) |
| Age (y), mean (SD) | 70.1 (7.9) | 70.5 (7.9) | 69.8 (7.9) | 82.8 (2.4)** |
| PSA (ng/mL) | 9.1 (12.2) | 10.8 (13.9) | 8.0 (8.6)* | 8.4 (6.1) |
| Mean (SD) | 0.34–106.53 | 0.34–106.53 | 0.58–95.5 | 1.1–29.4 |
| Qmax (mL/s) | 61.0 (28.8) | 106.4 (28.2) | 51.8 (15.1)** | 67.2 (27.8) |
| Mean (SD) | 19.3–226 | 80.9–226 | 19.3–79.7 | 26.4–123.5 |
| Range | 8.6 (4.3) | 8.5 (4.4) | 8.6 (4.3) | 8.6 (4.3) |
| Mean (SD) | 126.2 (131.6) | 119.8 (117.0) | 130.0 (140.0) | 123.8 (134.4) |
| Range | 0–649 | 0–506 | 0–649 | 5–540 |
| PVR (mL) | 25.1 (4.7) | 24.9 (5.2) | 25.1 (4.7) | 24.9 (5.0) |
| Mean (SD) | 8–35 | 8–34 | 10–35 | 17–34 |

*Significant difference in PSA, p = 0.031 between TRUS >80 mL versus TRUS <80 mL group.
**Significant difference in Qmax, p < 0.001 between TRUS >80 mL versus TRUS <80 mL group; significant difference in age, p < 0.001 between age >80 years versus total.
IPSS = International Prostate Symptom Score; PSA = prostate-specific antigen; PVR = postvoid residual volume; Qmax = urinary peak flow rate; SD = standard deviation; TRUS = transrectal ultrasound.

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(−5.3 ng/mL, −7.5 ng/mL, −3.7 ng/mL and −3.5 ng/mL, respectively; all p < 0.001). Further subgroup analysis of the changes between the TRUS >80 mL and TRUS <80 mL groups did not reveal any significant difference in the magnitude of change.

The improvement in Qmax in the three groups (Total, TRUS >80 mL and TRUS <80 mL) also showed significant differences (6.7 mL/s, 5.9 mL/s, and 6.0 mL/s, respectively; all p < 0.001). However, the increase in mean Q max in the elderly group (age >80 y) of 2.3 mL/second did not reach statistical significance from baseline (p = 0.103).

Similarly, the reduction in PVR volume in the three groups (Total, TRUS >80 mL and TRUS <80 mL) also showed significant differences (−73.9 mL, −70.8, and −67.0 mL, respectively; all p < 0.001). However, the decrease in PVR in the elderly group (age >80 y) was lower (−31.4 mL), with no significant difference from baseline (p = 0.068).

In general, there was no major clinical meaningful differences in these study reports regarding effectiveness.

The thulium:yttrium–aluminum–garnet laser has four application modes: vaporization, vaporesection, ThuVEP, or enucleation. The availability of higher energy output satisfies the different needs during the course of removal of the adenomas, thus improving the efficiency of the procedure. In the last few years, holmium laser enucleation has the greatest number of well-controlled study results for prostatectomy among different lasers and was proposed as the new gold standard in 2013.11 Unlike pulsed holmium laser, thulium laser is a continuous wave laser that produces faster cuts during prostatectomy. Thulium laser fiber equipped with 150 W 2 μm thulium:yttrium–aluminum–garnet can perform vaporization and resection or enucleation modes in prostatectomy. Not surprisingly, from our study results, a promising functional outcome improvement was seen across all the patient subgroups. Theoretically, a larger volume of prostate tissue should have been removed in the large prostate group, as reflected in the greater reduction in PSA level in the TRUS >80 mL group (−7.5 ng/mL vs. −3.7 ng/mL versus the TRUS <80 mL group). However, this did not

### Table 2

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total</th>
<th>TRUS &gt;80 mL</th>
<th>TRUS &lt;80 mL</th>
<th>Age &gt;80 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation time (min)</td>
<td>84.0 (31.3)</td>
<td>88.6 (27.9)</td>
<td>80.9 (27.3)*</td>
<td>84.7 (32.3)</td>
</tr>
<tr>
<td>PSA (ng/mL)</td>
<td>4.4 (4.5)</td>
<td>4.3 (4.8)</td>
<td>4.5 (4.2)</td>
<td>4.4 (4.5)</td>
</tr>
<tr>
<td>Qmax (mL/s)</td>
<td>−5.3 (−38.1)**</td>
<td>−7.5 (−49.7)**</td>
<td>−3.7 (−30.3)**</td>
<td>−3.5 (−36.5)**</td>
</tr>
<tr>
<td>PVR (mL)</td>
<td>14.2 (7.9)</td>
<td>14.0 (7.2)</td>
<td>14.3 (7.8)</td>
<td>11.2 (5.3)</td>
</tr>
<tr>
<td>Change (%)</td>
<td>6.7 (110.3)**</td>
<td>5.9 (114.7)**</td>
<td>6.0 (99.4)**</td>
<td>2.3 (67.7)*</td>
</tr>
<tr>
<td>Change (%)</td>
<td>58.4 (51.7)</td>
<td>56.7 (50.9)</td>
<td>53.6 (52.1)</td>
<td>82.6 (60.7)</td>
</tr>
<tr>
<td>Change (%)</td>
<td>−73.9 (−19)**</td>
<td>−70.8 (−26)**</td>
<td>−67.0 (−27.3)**</td>
<td>−31.4 (180.6)**</td>
</tr>
</tbody>
</table>

*Significant difference, p < 0.018, between TRUS >80 mL versus <80 mL.
**Significant difference, p < 0.001, change from baseline.
*p No significant difference, p < 0.103 change from baseline.
**p No significant difference, p = 0.068 change from baseline.

PSA = prostate-specific antigen; PVR = postvoid residual volume; Qmax = urinary peak flow rate; SD = standard deviation; TRUS = transrectal ultrasound.

4. Discussion

Ever since the first successful results reported by Bach et al6 in 54 patients receiving thulium vaporesection (ThuVaRP) in 2007, a series of studies were published by the same German group, providing information of intermediate-term follow-up,4 using different energy units and different size of prostates.3–10 In general, there was no major clinical meaningful differences in these study reports regarding effectiveness.

Figure 1. Prostate size versus operation time.
seem to exert a different impact on the magnitude of change in Qmax and PVR. No significant difference was observed between the two groups. It seems that the evaluation of postoperative functional improvement may be unavoidably confounded by the subjective patient-reported outcomes.

Important concerns for TURP are intraoperative bleeding and the need for blood transfusion. Laser techniques greatly alleviate these concerns, Shao et al.\(^\text{15}\) and Zhang et al.\(^\text{12}\) have reported less blood loss by thulium than holmium laser enucleation of the prostate.

The risk of blood loss is higher in selected patients on anticoagulants and antiplatelet agents. Anticoagulant users who received TURP were associated with significantly longer hospitalization and higher rate of bladder clots, blood transfusions, prolonged hematuria, and thromboembolic events, even after anticoagulants had been discontinued at the time of surgery.\(^\text{14}\) In this regard, Netsch et al.\(^\text{15}\) demonstrated that ThuVEP could be a safe and efficacious alternative for the treatment of symptomatic BPH in patients in whom continuous oral anticoagulants are recommended.

In our patient cohort, aside from the previous report of relatively low rate of intraoperative complications by our colleagues,\(^\text{7}\) our elderly subgroup confirmed the safety of this laser technique through the normal operation length and uneventful perioperative results. Although the procedures were demonstrated to be safe in elderly people, the postoperative improvement in urination function tends to be less significant in this group, which may have been due to other coexisting health problems in the aging process.

TURP is more difficult in patients with a large prostatic adenoma. Large prostates >80 mL may need two stages of resection. Intra-vasation of hypotonic fluid and risk of Transurethral resection (TUR) syndrome is high in large prostates. Our results have been encouraging with a short mean procedure time of 84 minutes in the overall patient cohort and 88.6 minutes in patients with a large prostate, which is comparable with Bach et al.\(^\text{10}\) who reported a mean operation time of 72 minutes in the general patient pool and 100.3 minutes in a group of patients with prostate size >80 mL by using ThuVEP. Further stratification of our patient cohort according to prostate size showed that the larger the prostate, the longer the operation time required. This might help to provide information regarding the expected operation time based on the size of the prostate when this laser technique is chosen.

Generally speaking, TURP is a difficult procedure to master and requires a significant learning curve. Thulium has a shorter learning curve, and ThuVEP can be performed by surgeons with reasonable operating experience only after 8–16 procedures.\(^\text{16}\)

By using GreenLight laser (532 nm wavelength) with tissue penetration of 0.8 mm, photoselective vaporization of prostate has been limited to small to medium size prostate at the initial stage and requires a gradual learning curve, starting from vaporization, partial enucleation, and progression to entire adenoma enucleation. Removal of a large prostate was only attempted after a refined technique of GreenLight photoselective en bloc enucleation was proposed.\(^\text{17}\)

The data from our study are consistent with most of the recent reported results that demonstrate a significant improvement in urinary flow and reduced postvoid urinary retention following ThuVEP. In addition, patients with removal of a large prostate demonstrated similar functional improvement as those with smaller prostates.

It should be noted that the retrospective nature of our study lowered the level of evidence-based medicine. Despite this limitation, our data reinforce the current existing knowledge and add to what is already known about thulium lasers.

Conflict of interest

The authors have no financial or other conflicts of interest related to the content discussed in this manuscript.

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