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Invited Review

Current evidence of ThuLEP for BPH: A review of literature

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ABSTRACT

Endoscopic enucleation of the prostate (EEP) techniques for the treatment of benign prostatic hyperplasia (BPH) have become increasingly popular among urologists over the past 23 years. Despite the energy source employed, the aim of all these procedures is to endoscopically remove the prostatic lobes by enucleating them from the prostate surgical capsule. The reasons for which EEP has gained popularity among urologists are the reduction in complications and hospital stay compared to endoscopic gold standard Transurethral Resection of the Prostate (TURP), but especially the possibility to treat large prostates, allowing to abandon open simple prostatectomy (OP) and to avoid the burden related to open surgery. Holmium laser enucleation of the prostate (HoLEP) sets the basic principles of all EEP techniques in 1998 and has become the treatment of reference for BPH. Since then, various lasers have been developed and applied to prostatic enucleation. The thulium laser has a slightly shorter wavelength compared to the holmium laser and a continuous wave output, which increase vaporization and reduce penetration depth. These features make it ideal for prostatic enucleation. A vapoenucleating technique called Thulium Laser Vapoenucleation of the Prostate was presented in 2009, followed by a blunt enucleating technique called Thulium Laser Enucleation of the Prostate in 2010. These techniques have become alternatives to HoLEP and TURP; however, the amount of literature and randomized controlled trials available are inferior compared to HoLEP. The aim of this review is to outline, describe, and discuss current evidence on thulium enucleating techniques.

Keywords: Lasers; prostatectomy; prostatic hyperplasia; thulium; transurethral resection of prostate.

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Introduction

For decades, the surgical treatment for benign prostatic hyperplasia (BPH) was carried out by either transurethral resection of the prostate (TURP) for prostates between 30 and 80 mL or open simple prostatectomy (OP) for prostates larger than 80 mL. However, the introduction of lasers for BPH in the late "90 s" revolutionized treatment. Lasers interact with human tissues, thanks to the presence of substances called chromophores that absorb electromagnetic radiations. When a chromophore is hit by a laser excitation of its molecules occurs, the electromagnetic energy is converted into heat. If the tissue is heated beyond the boiling point, it vaporizes, but if the temperature increases below the boiling point, denaturation of proteins occurs, causing coagulation and necrosis. Thanks to the presence of chromophores such as water and hemoglobin inside the prostate, lasers can be used to cut, vaporize, or coagulate the prostatic tissue.[1]

The holmium:YAG (yttrium–aluminum–garnet) laser was the first to be applied for the treatment of BPH; it has a pulsed wave output, a 2,100 nm wavelength (which is highly absorbed by water), and a penetration depth of 0.4 mm in the prostatic tissue. It was initially used to perform Holmium Laser Resection and Ablation of the prostate[2,3]; however, the procedures were time consuming and limited to the treatment of small prostates. To overcome these drawbacks and thanks to the

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introduction of the tissue morcellator, a new innovative technique called Holmium Laser Enucleation of the Prostate (HoLEP) was presented.[4] The procedure consists in a blunt enucleation of the prostatic lobes at the level of the capsular surface, which are morcellated inside the bladder at the end of the procedure.

HoLEP has proved to achieve equivalent clinical and functional outcomes to TURP and OP, but with reduced morbidity, catheterization time, and hospital stay.[5–7] The use of saline solution as medium avoids the risk of transurethral resection syndrome, allowing to treat prostates of virtually all sizes; therefore, HoLEP has become the gold standard treatment for large prostates (>80 mL) and an alternative to TURP for small- and medium-size prostates (30-80 mL).[8]

Advances in laser technologies brought to the development of the thulium:YAG laser, which has a continuous wave output and a 2,010 nm wavelength. Absorption coefficient in water at this wavelength is slightly higher compared to the holmium laser, resulting in better vaporization and reduced penetration depth (0.2 mm).[1]

The thulium laser was initially used to perform Thulium Laser Vaporization and Vapo-Resection of the Prostate.[9] However, prolonged operative time for the treatment of large prostates soon led to attempt enucleation.

In 2009, Bach et al.[10] presented a vapoenucleating technique called Thulium Laser Vapoenucleation of the Prostate (ThuVEP), whereas in 2010, Herrmann et al.[11] presented a blunt, mechanical enucleating technique called Thulium Laser Enucleation of the Prostate (ThuLEP). Recently, a novel thulium laser with a 1,940 nm wavelength, the thulium fiber laser (TFL), was applied to prostatic enucleation. The 1,940 nm wavelength matches the absorption peak in water, potentially halving the penetration depth of the thulium:YAG laser.[12] Moreover, it can work in a continuous or pulsed mode.

Main Points

- Endoscopic enucleation of the prostate (EEP) techniques have revolutionized the treatment of benign prostatic hyperplasia (BPH), allowing to abandon open simple prostatectomy.
- Thulium enucleation of the prostate is one of the most investigated treatments for BPH.
- Thulium enucleation has proved to be as effective as other gold standard procedures on short and mid-term.
- Studies with long-term follow-up are needed to complete the evaluation of thulium enucleation.

ThuVEP and ThuLEP are currently considered alternatives to TURP and HoLEP by EAU Guidelines; however, strength rating is weaker, due to the lack of randomized controlled trials with long-term follow-up. The aim of this review is to explore current evidence on thulium enucleation focusing on available techniques and comparison with other techniques of reference.

Methods

A PubMed title search between the years 2000 and 2021, including the terms "ThuLEP" or "ThuVEP" or "thulium," was performed, producing 626 articles. This search was followed by a title search including the terms "enucleation" or "vapoenucleation" and "prostate," producing 705 results. The two searches were added with an "or" producing 1,234 articles. Title and abstract of the articles were screened. Only articles dealing with prostatic enucleation using a Tm:YAG laser or TFL were considered. Articles with no abstract, or in non-English language, Case Reports, Comments, Editorials, and Letters to the Editor were excluded. One hundred papers that were deemed relevant to this review were selected and fully read. Two articles were excluded after reading them because the technique did not resemble enucleation. Ninety-eight articles were finally considered.

Thulium Enucleating Techniques

Despite the different energy source, ThuVEP and ThuLEP resemble HoLEP with respect to equipment, sequence, and direction of the enucleation.

Equipment

- A 26F continuous-flow resectoscope with an operative channel for the laser fiber.
- A camera system.
- A Tm:YAG laser generator.
- A front-firing laser fiber.
- A mechanical morcellator.
- A suction pump.

Surgical Procedure

ThuVEP and ThuLEP both start by performing an inverted-U-shaped incision above the veru montanum. Subsequently, two incisions are performed at 5 and 7 o'clock from the bladder neck to the previous U-shaped incision, separating the median lobe from the lateral lobes. All the incisions are deepened to the level of the capsular surface. At this point, the median lobe is lifted with the tip of the resectoscope above the veru montanum and enucleated following the surgical capsule toward the bladder neck. The lateral lobes are then enucleated one after the other following the capsular surface from the prostatic apex to the bladder neck, with a semicircumferential movement of the resectoscope. At the end of the enucleation, after performing hemostasis, the prostatic lobes are removed by morcellating them inside the bladder.[10,11]

Thulium Fiber Laser Enucleation of the Prostate (ThuFLEP) is performed in the same manner; however, a TFL generator is used, which has the advantage of being smaller compared to the thulium:YAG generator.[12]

The difference between ThuVEP and ThuLEP lies in the different use of the laser while enucleating the prostatic lobes. During ThuVEP, the laser is fired in a continuous manner to carve the adenomatous tissue from the capsule, whereas during ThuLEP, the pressure is applied to the adenoma with the tip of the resectoscope to “peel” it from the capsule, and the laser is only used as an aid to cut the tissue fibers connecting the two structures and coagulate bleeding blood vessels. These two ways of using the laser are often both employed within the same procedure, according to prostatic features and surgeon’s preference.[13] For instance, during ThuFLEP, enucleation is performed by using the laser for about 70% of the procedure and 30% by bluntly enucleating the adenoma.[12] Due to the overlapping between these techniques, ThuVEP, ThuLEP, and ThuFLEP can be considered as one and referred to as Thulium Enucleation of the Prostate (ThuEP) techniques.

ThuEP Variations in Technique

Variations to the classical 3-lobe technique have been presented with the idea of improving enucleation speed and efficacy. Wolters et al.[14] performed a 2-lobe enucleation by enucleating the left lobe first, followed by the enucleation of the median and right lobe in one piece, whereas Dellabella and Castellani[15] performed the enucleation of the median lobe first, followed by the enucleation of the lateral lobes (joined anteriorly) in one piece. Kim et al.[16] presented a 1-lobe (or en-bloc) enucleation using the thulium laser. During this procedure, the entire transitional zone is enucleated in one piece. After performing the initial U-shaped incision above the veru montanum, a circular incision is performed at the prostatic apex to mark the distal limit of the enucleation, and the entire adenoma is enucleated in a circumferential manner proceeding cranially toward the bladder neck. Saredi et al.[17] presented a variation of the en-bloc technique: after performing the apical circumferential incision, an anterograde incision is made from the bladder neck to the prostatic apex at 5 o’clock. This incision is used to identify the capsular plane, which is followed circumferentially each side of the incision until the whole adenoma is enucleated. The idea of en-bloc enucleation is to be as anatomical as possible and avoid mismatching enucleation planes by following the same plane throughout the procedure. Nevertheless, none of the above-mentioned procedures has shown clear superiority over another. The goal is to enucleate the adenoma at the level of the capsular surface, and 1-lobe, 2-lobe, or 3-lobe enucleation should be performed according to surgeon’s preference and comfort.

To try and improve speed and simplify classical ThuLEP, Bozzini et al.[18] presented a technique called 7U-ThuLEP: classical ThuLEP is broken down to seven consecutive steps, which all start with U-shaped incisions. Novel surgeons can, therefore, learn ThuLEP progressively with a structured program, by learning each step before moving onto the next one.

One of the main downsides of BPH surgery is ejaculatory dysfunction in the form of anejaculation, retrograde ejaculation, reduction in ejaculate volume, or painful ejaculation. According to studies on ejaculation physiology, a fundamental role in the progression of semen is played by the musculus ejaculatorius, a longitudinal strain of muscle fibers that originate from around the ejaculatory ducts and extend caudally in the urethral crest inserting below the urethral sphincter. To preserve these muscular structures, Bozzini et al.[19] presented an Ejaculation-Sparing ThuLEP (ES-ThuLEP): 1.5 cm of tissue above the veru montanum and two hills of tissue each side of the veru montanum were spared while performing a 3-lobe ThuLEP. Seventy-seven percent of the patients treated with ES-ThuLEP maintained their ejaculation, and micturition improvement was comparable to standard ThuLEP at 6-month follow-up. Despite promising results, further studies are needed to confirm ejaculation-sparing rates and micturition improvement on a long-term basis.

ThuEP Learning Curve

Identifying and following, the correct plane during prostatic enucleation can be challenging, especially for inexperienced urologists. Cutting through the adenoma, instead of along the surgical capsule, can cause loss of orientation and bleeding, increasing the length of the procedure. Previous studies showed that 20-60 cases are necessary to complete the learning curve for HoLEP,[20,21] and many urologists have abandoned the technique due to excessive operative time and technical difficulties.[22]

Netsch et al.[23] evaluated the ThuVEP learning curve of three different surgeons: a resident (surgeon A), a ThuVEP-naïve—an experienced endourologist (surgeon B), and a ThuVEP expert (surgeon C). Surgeons A and B familiarized with

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ThuVEP by watching videos of the procedure and by assisting surgeon C during 10 ThuVEPs prior to the study. Thirty-two procedures were then performed by each surgeon. None of the surgeons required for the mentor to take over or conversion to TURP. According to the authors, ThuVEP was performed by the ThuVEP-naïve surgeons with reasonable efficiency after 8-16 procedures with respect to operation efficiency (resected weight/operative time), enucleation efficiency (resected weight/enucleation time), and morcellation efficiency (resected weight/morcellation time). However, the ThuVEP-naïve surgeons had participated in 10 procedures prior to the study, which should be considered in the learning process.

Saredi et al.[24] assessed the possibility for experienced endourologists to perform ThuLEP with a self-teaching program. ThuLEP was performed by two laser-naïve, experienced endourologists after training on a simulator for 2 weeks. Forty-eight cases were performed by surgeon A and 52 by surgeon B. According to the authors, 30 cases were sufficient for an experienced endourologist to complete the learning curve. However, no parameters to measure competency were reported, and no stratification by consecutive groups of patients was used.

Enikeev et al.[25] compared the learning curve for HoLEP, ThuFLEP, and monopolar enucleation of the prostate (MEP). Ninety patients were randomly assigned to either HoLEP, ThuFLEP, or MEP (30 patients per group). The procedures were performed by three experienced urologists with no previous endoscopic enucleation of the prostate (EEP) experience. The patients in each group were stratified into three consecutive groups of 10 patients each. All three surgeons watched a mentor performing five procedures prior to the study and received assistance, if needed, during the first 10 procedures. Enucleation efficiency progressively improved throughout the study. The authors concluded that 30 cases were sufficient to perform EEP proficiently using a mentored teaching program.

ThuEP appears to be quicker to learn compared to HoLEP, both for the inexperienced and experienced surgeons. Nevertheless, there is a lack of high-quality studies and no consensus on the parameters to be used for correct assessment of surgeons' proficiency. Further studies assessing enucleation and morcellation efficiency, operative time, resected tissue, and complications, also stratifying results by consecutive groups of patients are needed. A mentor-based approach with a structured training program is to be preferred when teaching any EEP, especially to the inexperienced surgeon, to acquire the basic skills of endoscopic surgery, familiarize with the instruments, tactical feedback, and orientation.[26]

ThuEP vs TURP and Plasmakinetic Resection of the Prostate (PKRP)

In 2012, Swiniarski et al.[27] published the first Randomized controlled trial (RCT) with 3-month follow-up comparing ThuLEP (54 patients) and TURP (52 patients). ThuLEP was performed according to the "mushroom technique" (the prostatic lobes were left attached to the bladder neck at the end of the enucleation and removed by resecting the tissue instead of morcellating it).[28] International Prostate Symptom Score (IPSS), Quality of Life score (QoLs), maximum flow rate (Q_{max}), and postvoid residue (PVR) improved significantly after both procedures with no significant differences between the two. Hemoglobin drop after ThuLEP was almost half as much than after TURP (0.95 vs 1.81 g dL^{-1}, $P < .0001$); however, operative time was longer (102.2 vs 74.5 minutes, $P < .0001$) and resected tissue weight lower (24.8 vs 34.8 g, $P = .0005$) with ThuLEP. Catheterization time, Prostatic Specific Antigen (PSA) drop, and complications were comparable.

Wang et al.[29] retrospectively compared ThuVEP (63 patients) and TURP (59 patients), focusing on sexual functions. International Index of Erectile Function (IIEF) scores showed no significant postoperative changes with respect to intercourse satisfaction, sexual desire, and overall satisfaction. Mild but not significant improvement was seen with regard to erectile function (EF), and a positive linear correlation was found between EF and IPSS, QoLs, and Q_{max}. Nevertheless, more than half of the patients in each group experienced retrograde ejaculation, which resulted to be an independent predictor for deterioration in the orgasmic function.

In 2015, Chang et al.[30] published an RCT with 1-year follow-up comparing ThuVEP (29 patients) and TURP (30 patients). Significant improvement in micturition and LUTS was achieved with both procedures. Resected tissue weight was lower in the ThuVEP group (37.4 vs 21.3 g, $P = .024$); nevertheless, residual prostate volume was comparable. Catheterization time (1.8 vs 2.3 days) and hospital stay (3.0 vs 3.4 days) were significantly shorter after ThuVEP. Hemoglobin drop was similar; however, 26.7% of the patients in the TURP group required blood transfusions compared to 13.8% in the ThuVEP group. No major complications were reported after both procedures.

In 2016, Bozzini et al.[31] compared ThuLEP (102 patients) and PKRP (106 patients). ThuLEP determined reduced hemoglobin drop (0.45 vs 2.83 g dL^{-1}, $P = .005$), catheterization time (1.3 vs 4.8 days, $P = .011$), and hospital stay (1.7 vs 5.2 days, $P = .016$), whereas no differences were found regarding operative time, resected tissue weight, and micturition improvement.

In 2020, Shoji et al.[32] published another RCT comparing ThuLEP (performed according to the "mushroom technique") and PKRP (70 patients per group). Similar to Bozzini et al.,[31] hemoglobin drop, catheterization time, and hospital stay were significantly lower after ThuLEP, whereas resected tissue volume, PSA drop, and operative time were significantly higher. IPSS, QoLs, Overactive Bladder Symptom Score (OABSS), Q_{max}, and PVR significantly improved in both groups. OABSS transiently deteriorated in 30% of the patients after ThuLEP; in these patients, irradiation time and total delivered energy were higher, indicating that increased exposure to the laser and higher energy could worsen postoperative irritative symptoms. EF was significantly impaired in both groups at 1-month follow-up. However, the IIEF score returned to preoperative levels at 3-month follow-up in the ThuLEP group and showed slight improvement at 12-month follow-up, whereas it did not return to baseline levels in the PKRP group. Total delivered energy and laser irradiation time were significantly higher in patients who presented postoperative ED.

Hou et al.[33] also compared ThuLEP (135 patients) and PKRP (141 patients). Similar to Shoji et al.,[32] operative time was longer with ThuLEP, whereas no significant differences were found in hospital stay and removed tissue. ThuLEP resulted in greater reduction in the IPSS voiding domain and QoLs at 2-week follow-up, but no significant differences were found at 6-month follow-up. ThuLEP proved to be superior in terms of postoperative pain, reported by the patients on a numeric rating scale. A significantly higher percentage of patients in the PKRP group required additional injections of narcotics after surgery (20.6% vs 5.2%) and increased use of oral analgesics for more than 1 week after surgery (12.2% vs 4.4%).

In 2018, Enikeev et al.[12] retrospectively compared ThuFLEP (211 patients) and TURP (258 patients) focusing on EF. No significant differences in IIEF-5 scores were found compared to baseline at 6-month follow-up. However, the IIEF-5 score slightly improved after ThuFLEP, whereas it slightly decreased after TURP.

Enikeev et al.[34] published another study comparing the two techniques focusing on perioperative parameters and micturition improvement in prostates <80 cc. Operative time was significantly higher in the ThuFLEP group (46.6 vs 39.9 minutes). However, catheterization time (1.4 vs 2.4 days), hemoglobin drop (1.01 vs 1.8 g dL^{-1}), serum sodium decrease (1.1 vs 4.1 mmol L^{-1}), and hospital stay (3.4 vs 4.7 days) were significantly lower after ThuFLEP. PSA drop (80 vs 72%) and prostate volume decrease (81.0% vs 71.5%) were significantly higher in the ThuFLEP group. Again, no differences were found in micturition improvement at 12-month follow-up.

According to the above-mentioned studies, ThuEP has proved to be as effective as TURP and PKRP in improving patients' micturition and LUTS. ThuEP is longer to perform, due to the additional time required for morcellation, but offers the advantage of reduced catheterization time, hospital stay, and hemoglobin decrease, as also highlighted by systematic reviews and meta-analyses.[6,35] Few studies showed that resected tissue weight was inferior after ThuEP; nevertheless, postoperative assessment of prostatic volume and PSA drop showed that an equivalent amount of tissue was removed. The reduced resected tissue weight can be attributed to the quote of vaporized tissue that is lost for final weighing when using the thulium laser. Despite this quote of vaporized tissue, Carmignani et al.[36] showed that histological features of tissue specimens from ThuVEP are preserved, and that the detection rate of incidental prostatic adenocarcinoma was comparable to TURP. ThuEP, TURP, and PKRP do not seem to significantly impair EF; however, two studies suggested that ThuEP could lead to mild improvement, possibly due to the reduced thermal damage of the laser compared to TURP. Interestingly, one study showed that ThuLEP caused less postoperative pain. Future studies evaluating this parameter are certainly welcome. Complication rates between these procedures are similar with very few major complications requiring reintervention. The main issue with the above-mentioned studies is the short follow-up, not exceeding 1 year. Future studies with long-term follow-up (≥36 months) are needed to confirm durability of results with ThuEP.

ThuEP vs OP

Various studies have shown the feasibility and efficacy of ThuEP in the treatment of large prostates.[37–41] One study by Becker et al.[39,42] showed that outcomes were sustained at 4-year follow-up with only 1/90 patients requiring retreatment and 3/90 patients requiring treatment for urethral stricture or bladder neck contraction. Nevertheless, very few studies comparing ThuEP and OP were found in our research.

In 2018, Nestler et al.[40,43] performed a matched-pair analysis comparing ThuVEP, OP, and robot-assisted simple prostatectomy (RASP) for prostates larger than 80 cc (35 patients per group). Operative time was significantly shorter with ThuVEP compared to OP and RASP (83 vs 130 vs 182 minutes). Hemoglobin drop was significantly lower with ThuVEP compared to OP and RASP (1.2 vs 3 vs 1.5 g dL^{-1}), whereas the difference between ThuVEP and RASP was not significant. Similarly, the transfusion rate was significantly lower after ThuVEP than after OP (0% vs 34.4%), but no significant differences were found between ThuVEP and RASP. Catheterization time (2 vs

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7 vs 5 days) and hospital stay (2 vs 8 vs 5 days) were significantly shorter with ThuVEP compared to OP and RASP. Early continence based on postoperative pad use 24 hours after catheter removal was significantly higher after ThuVEP and RASP compared to OP. Complications were higher in the OP group, mostly due to bleeding. Only one case of bleeding requires surgical revision occurred in the ThuVEP group.

Enikeev et al.[41,44] performed a retrospective comparison between OP (40 patients) and ThuFLEP (90 patients). Mean operative time, resected tissue weight, and resection speed were similar. However, catheterization time (6.4 vs 1.4 days), hospital stay (9.0 ± 2.4 vs 3.3 ± 0.6 days) and hemoglobin drop after surgery (2.8 vs 1.0 g dL^{-1}) were significantly lower after ThuFLEP. No blood transfusions were required in the ThuFLEP group compared to two patients (5%) in the OP group. At 6-month follow-up, IPSS, QoLs, Q_{max}, and PVR significantly improved in both groups with no significant differences between the two. PSA levels were also comparable.

In the above-mentioned studies, ThuEP achieved equivalent micturition improvement compared to OP, allowing to reduce blood loss, transfusion rate, and overall complications. Moreover, postoperative catheterization time and hospital stay were significantly shorter with ThuEP. Future studies comparing the two procedures are welcome; however, due to its morbidity, OP has already been abandoned by many urologists in favor of enucleation, making comparisons between the two procedures more and more rare.

ThuEP vs HoLEP

In 2012, Zhang et al.[42,45] published the first RCT comparing ThuLEP (71 patients) and HoLEP (62 patients) performed according to the "mushroom technique." ThuLEP required longer operative time (72.4 vs 61.5 minutes, $P = .034$) but determined lower blood loss (130.1 vs 166.6 mL, $P = .45$). However, hemoglobin drop, catheterization time, serum sodium decrease, postoperative PSA, and complications were comparable. No blood transfusions were needed in either group. IPSS, QoLs, Q_{max}, and PVR significantly improved at 18-month follow-up with no significant differences between the two procedures.

In 2015, Hong et al.[43,46] performed a retrospective analysis of 88 patients who underwent either HoLEP or ThuVEP. Unlike the study by Zhang et al.,[42,45] enucleation time was shorter with ThuVEP (58.3 vs 70.5 minutes, $P = .003$) and enucleation efficiency higher (0.69 vs 0.61 g min^{-1}, $P = .048$), whereas operation time, morcellation time, resected tissue weight, morcellation efficiency, hemoglobin decrease, catheterization time, and hospital stay were similar. Both procedures resulted in significant micturition improvement at 12-month follow-up, and no significant differences in complications or blood transfusions were found.

In 2017, Netsch et al.[44,47] performed a RCT comparing ThuVEP (48 patients) and HoLEP (46 patients) with 4-week follow-up. Similar to the study by Hong et al.,[43,46] enucleation time was shorter (27.03 vs 40 minutes, $P \leq .004$) and enucleation efficiency higher (1.87 vs 1.19 g min^{-1}, $P \leq .005$) with ThuVEP. No significant differences were found between the two procedures with respect to other intraoperative parameters, hemoglobin decrease, catheterization time, and postoperative stay. Acute urinary retention (AUR) after catheter removal was significantly higher in the HoLEP group (15.2% vs 2.1%) and so was overall complication rate (12.5% vs 33.3%). Micturition improved significantly in both groups; however, QoLs was significantly lower after ThuVEP. The results of the 6-month follow-up were published in 2018.[38,39] Both procedures determined a significant reduction in PSA levels and prostatic volume compared to baseline. LUTS and micturition showed further improvement in both arms with no significant differences in QoLs.

In 2018, Pirola et al.[45,48] performed a matched-pair analysis between two groups of 117 patients each who underwent either HoLEP or ThuLEP. Operative time was shorter with ThuLEP (90 vs 82.25 minutes, $P = .0003$), due to reduced enucleation time (75.5 vs 70.5 minutes, $P = .0011$). Morcellation time, hemoglobin drop, catherization time, and hospital stay were comparable. Both resulted in equivalent tissue removal, but PSA drop resulted to be higher after HoLEP (−52.83% vs −47.85%, $P = .013$) at 12-month follow-up. No significant differences in complications were reported. Micturition and LUTS improved significantly compared to baseline, with no differences between the two procedures.

Similar results were reported in an RCT by Zhang et al.[37,38] who compared ThuLEP and HoLEP for the treatment of prostates larger than 80 cc. However, in this study, a higher number of patients in the HoLEP group presented CD grade 1 complications (22.4% vs 6.9%, $P = .033$), mainly due to a higher number of patients with transitory urinary incontinence. Only two patients (3.4%) per group presented CD 3a complications (urethral stricture and bladder neck contraction) requiring reintervention.

In 2020, Bozzini et al.[46,49] performed an RCT comparing HoLEP (121 patients) and ThuLEP (115 patients). No differences were found with respect to operative time, catheterization time, enucleated tissue weight, and hospital stay. Hemoglobin decrease resulted to be significantly lower after ThuLEP (2.77 vs 0.45 g dL^{-1}) and so was the need for blood transfusions (6.6% vs 1.7%). No significant differences in micturition improvement and PSA were seen at 3 and 12-month follow-up. Similar to the study by Zhang et al.,[37,38] HoLEP resulted in a significantly higher percentage of patients with stress incontinence (7.4% vs 1.7%) and AUR after catheter removal (10.7% vs 6.1%).

Recently, Kaya et al.[41] compared HoLEP (121 patients) and ThuLEP (104 patients) in the treatment of prostates larger than 100 cc. Both procedures significantly improved IPSS, QoL, Q_{max}, and PVR with no significant differences between the two, maintaining a low complication rate. However, ThuLEP was superior in terms of total operative time, laser efficiency, enucleation time, and enucleation efficiency.[41] Compared to Bozzini et al.,[49] no significant differences were found in terms of postoperative stress incontinence or AUR.

All the above-mentioned studies showed that HoLEP and ThuEP determine equivalent micturition and quality of life improvement even in patients with large prostates. Catheterization time and hospital stay were also comparable. ThuEP seems to improve enucleation time and efficacy, probably due to the higher ablation capacity of the thulium laser that allows faster enucleation and a rapid correction of the enucleation plane, if lost. Improved vision, thanks to the smooth and clean incisions of the thulium laser, could also be a main factor in improving enucleation efficiency. These results were also reported by recent systematic reviews and meta-analyses.[47,48,50,51] Nevertheless, both procedures required similar overall operative time and resulted in equivalent tissue removal. Only one study demonstrated a longer operative with ThuEP, whereas three studies showed a longer operative time with HoLEP. These differences can be considered negligible in daily practice. Despite many believe in the better hemostatic properties of the thulium laser, only one of the studies reported a significantly higher hemoglobin decrease with ThuLEP. Complication rate was low and comparable between the two procedures and mainly consisted of CD one to two complications, such as bleeding or AUR. Two studies reported a significantly higher rate of early postoperative stress incontinence and AUR after HoLEP. This could be related to increased traction on the external sphincter while performing HoLEP and to the higher thermal damage caused by the deeper penetration of the holmium laser. However, Kaya et al.[41] suggested that these results could be due to the technique, rather than laser features. Studies with long-term follow-up (≥3 years) are needed to compare disease recurrence, late complications, and stability of results between ThuEP and HoLEP.

ThuEP vs Other Procedures

Feng et al.[49,52] performed an RCT comparing ThuLEP (61 patients) and Plasmakinetic Enucleation of the Prostate (PKEP, 66 patients) performed according to the "mushroom technique." PKEP is already recommended by EAU Guidelines for the treatment of large prostates. However, mean prostate size in this study was 69.02 mL in the ThuLEP group and 67.05 in the PKEP group. No differences were found in operation time, resected tissue weight, sodium decrease, and hospital stay. Complication rate was also similar. However, hemoglobin drop (0.80 vs 0.99 g dL^{-1}, $P = .037$) and catheterization time (1.85 vs 2.28 days, $P = .042$) were lower in the ThuLEP group. IPSS, QoLs, Q_{max}, and PVR all improved significantly with no significant differences between the two procedures throughout the 12-month follow-up.

Castellani et al.[50,53] compared ThuVEP (214 patients) and Photoselective Vaporization of the Prostate (PVP, 291 patients). PVP is recommended by EAU guidelines as an alternative to TURP for the treatment of prostates <80 mL. No significant differences were shown between PVP and ThuVEP with respect to operative time (55 vs 55 minutes), catheterization time (2 vs 2 days), and hospital stay (2 vs 3 days). Hemoglobin drop was significantly lower in the PVP group (0.5 vs 0.8 g dL^{-1}). Nevertheless, transfusion rate was similar (2.2% of the patients per group). Both procedures determined significant improvement in IPSS and Q_{max}, but PVP determined a higher decrease at 12-month follow-up. Complication rate was comparable.

According to the above-mentioned studies, ThuEP appears to be equivalent to PKEP and PVP for the treatment of medium-size prostates. All determined effective micturition improvement, maintaining a low complication rate. Despite being statistically significant, differences in hemoglobin drop appear to be clinically irrelevant, considering that no difference was found in transfusion rates. Higher IPSS and Q_{max} reduction after PVP compared to ThuLEP needs to be verified.

Conclusions

ThuEP has been embraced by many urologists for 12 years now. Several studies have proved that it is as safe and effective in improving micturition and quality of life as other gold standard procedures, such as TURP, PKRP, and PVP for the treatment of medium size prostates, and HoLEP, PKEP, and OP for

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the treatment of large prostates. ThuEP offers the advantage of reduced hemoglobin drop, catheterization time, and hospital stay compared to TURP and OP, and a lower complication rate compared to OP. ThuEP might also offer the advantage of faster enucleation, increased enucleation efficiency, and reduced early postoperative stress incontinence and AUR compared to HoLEP. Nevertheless, there is a severe lack of studies with long-term follow-up comparing ThuEP to other treatments of reference. Studies with long-term follow-up are now needed to assess durability of outcomes, retreatment rate, and late complications for ThuEP to be fully recommended by the guidelines.

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