



Effectiveness and Safety of Tansurethral Thulium Laser Enucleation of the Prostate in the Treatment of BPH: Review

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Review Article

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Abstract

This article is dedicated to assessing the efficacy and safety of using transurethral holmium laser enucleation (ThuLEP) in patients with benign prostatic hyperplasia (BPH). BPH and Symptoms of urinary dysfunction are the most common complaints in adult men over 40 years of age and have a serious impact on their quality of life. The ThuLEP method, being less invasive compared to traditional surgical procedures, plays a crucial role in reducing prostate size and alleviating symptoms. The article analyzes the safety profile and clinical outcomes of the ThuLEP method, including postoperative treatment duration, amount of blood loss, and the necessity for re-treatment. Additionally, the advantages and disadvantages of this method compared to traditional treatments are examined.

Keywords: Prostatic Hyperplasia; BPH; LUTS; Surgical Procedure Thulep

Relevance

Urinary symptoms are the most common complaints among adult men over 40, significantly impacting their quality of life [1-4]. In international literature, urologists frequently use the term LUTS (lower urinary tract symptoms), which somewhat indicates the localization of symptom origin, meaning the symptoms arise from the lower urinary tract without specifying the cause. LUTS are divided into storage, voiding, and post-micturition symptoms [5]. For a better understanding of the clinical picture, the following classification is preferred: storage symptoms, or symptoms of urine accumulation or storage, i.e., symptoms arising from issues with urine storage in the bladder; voiding symptoms, related to urination difficulties; and post-micturition symptoms, which occur after the act of urination. The causes of LUTS can include various urological

and non-urological diseases. Among urological conditions, LUTS is often due to infravesical obstruction (IVO), associated with benign prostatic enlargement (BPE), where histologically, benign prostatic hyperplasia (BPH) is detected [6]. Currently, some of the most debated issues in urology regarding BPH treatment involve assessing the efficacy and safety of conservative versus surgical treatment. The aim of our study was to analyze the literature data concerning LUTS associated with benign prostatic hyperplasia and its surgical removal via thulium laser enucleation (ThuLEP).

Material

We performed a meta-analysis of data from the PubMed, EMBASE, Web of Science, and Cochrane Library databases up to December 2023.



Results

Literature suggests that lower urinary tract symptoms (LUTS) have multiple causes. In addition to prostate issues, bladder dysfunctions may also play a role in the development of LUTS [7]. These dysfunctions can be triggered by factors such as obesity, Parkinson's disease, multiple sclerosis, stroke, central nervous system injuries, neurogenic voiding issues, metabolic syndrome [8], chronic kidney disease (CKD), and heart failure [9], with prostate enlargement being only one of the contributing factors [2,6,7]. Benign prostatic hyperplasia (BPH) is one of the most common diseases in elderly men and represents a specific morphostructural condition of the prostate gland characterized by hyperplasia of stromal and epithelial cells. According to the American Urological Association (AUA), BPH is a histological diagnosis indicating the proliferation of smooth muscle and epithelial cells in the transition zone of the prostate. "The transition zone comprises about 5% of the entire prostate and surrounds the proximal part of the urethra. This zone is characterized by continuous growth throughout a man's life" [10]. Although BPH is not life-threatening, the clinical manifestations of the disease, such as lower urinary tract symptoms (LUTS), reduce men's quality of life [7]. This condition is considered progressive. Risk factors for disease progression include age, prostate-specific antigen (PSA), and prostate volume. The only reliable factors associated with the development of BPH are age and hormonal status. The critical role of the testes in the development of BPH was recognized over a century ago. These risk factors for BPH development, such as age, cannot be eliminated, and hormonal status could be altered but is not advisable due to potential undesirable complications.

According to various researchers, LUTS strongly correlate with older age [1,2]. Therefore, the costs associated with the occurrence of LUTS are expected to increase in line with demographic changes [2,11] in specific countries. Most elderly men exhibit at least one LUTS [2]. These symptoms are generally mild and do not cause significant concern [4,12,13]. LUTS typically progress dynamically. In some patients, they persist and worsen over time, while in others, their severity may decrease [2]. Patients require surgical treatment for LUTS/BPH when they experience insufficient relief or residual urine remains in the bladder after urination despite conservative (diet and behavioral therapy) and pharmacological treatment. Today, surgical treatment methods are classified based on their approach: resection, enucleation, vaporization of adenomatous tissue, alternative ablation techniques, and non-ablative techniques. In this article, we examine the radical surgical method of treating BPH-thulium laser enucleation of the prostate (ThuLEP), performed transurethrally. The thulium laser has a wavelength ranging from 1940 nm (fiber laser) to 2013 nm (YAG laser) in continuous mode, with a terminal type

of emission [14]. Existing enucleation techniques include ThuVEP (vapoenucleation, excision technique) and ThuLEP (blunt enucleation).

The first information on the introduction of thulium vapoenucleation and its outcomes was published in 2008 [15]. According to the authors, the reason for the development and implementation of this technology was the ability to remove adenomatous nodules quickly and effectively, even when they are large [16]. It should be noted that the essence of the vapoenucleation (ThuVEP) method is the use of continuous laser radiation on tissues, leading to extensive vaporization and separation of tissues through laser exposure. Unlike ThuVEP, in ThuLEP, the surgeon performs laser enucleation of hyperplastic prostate tissue primarily by a blunt dissection method through the urethra, similar to traditional adenectomy. Many surgeons performing ThuLEP use Herrmann T.R.'s technique [17]. In this method, after making an incision in the apical part down to the surgical capsule, the prostate is separated by a blunt dissection using the resectoscope beak and the laser fiber tip, unlike the ThuVEP method. At the end of the operation, both in ThuVEP and ThuLEP, the adenomatous tissue is displaced into the bladder cavity, where it undergoes morcellation (cutting into small pieces) and removal. Researchers state that "using the thulium laser allows adjusting the enucleation layer at practically any stage of the operation, which enables maintaining a uniform layer of tissue throughout the gland, while the holmium laser typically does not allow easy movement between layers due to its greater penetration depth" [18]. Enucleation using the ThuLEP method allows for significant improvement in functional outcomes, comparable to the results of transurethral resection and holmium laser enucleation.

In 2011, a study was published where the authors, analyzing various methods of surgical treatment for BPH, concluded that bipolar plasma kinetic enucleation and holmium laser enucleation are technically similar for performing the operation. These enucleation techniques outperform standard monopolar resection [19]. The authors attribute the superiority of these methods to the fact that enucleation techniques allow reaching the surgical capsule and completely removing hyperplastic tissue, minimizing the risk of recurrence. As we know, during transurethral resection of the prostate, the surgical capsule is often not reached due to the risk of perforation. The authors of this study believe that enucleation techniques are challenging to master and should not be performed without adequate experience. In 2016, Herrmann T.R. published a study suggesting that enucleation, regardless of the method, leads to significant postoperative improvement compared to other techniques, such as photoselective vaporization, transurethral resection, and open adenectomy, concluding that enucleation is a

new standard for prostate hyperplasia treatment. However, depending on the energy used to remove hyperplastic tissues, there will be specific differences in the functional outcomes of the interventions [20].

Thus, in 2018, the EAU guidelines on LUTS/BPH treatment introduced the abbreviation EEP (endoscopic enucleation of the prostate) for the first time, encompassing all enucleation techniques [21]. These findings were obtained by comparing the efficacy of bipolar and holmium enucleation with open surgery, showing that the new methods were equally effective but superior in terms of IPSS (International Prostate Symptom Score), Qmax (maximum urine flow rate), catheterization and hospitalization duration, and complication rates compared to open surgery [22-26]. Consequently, EEP was recognized as a treatment for prostate hyperplasia on par with open surgery for prostate volumes over 80 cm³ [21].

The literature mainly features prospective series of observations on ThuVEP, indicating improvement in IPSS scores, QL (quality of life), and PVR (post-void residual volume) [27-30]. Comparative studies on ThuVEP have demonstrated good intraoperative safety [31]. Similar findings were obtained in patient cohorts with larger prostate volumes [27] and patients taking anticoagulants or with coagulopathies [28, 29]. In a cohort study, complications of ThuVEP included urinary tract infection (in 2 patients), urethral stricture and bladder neck sclerosis, with one patient undergoing re-treatment due to disease recurrence [32]. The complication rate after ThuVEP was 31%, with 6.6% of cases having complications greater than grade 2 on the Clavien scale [33]. In a case-control study on ThuVEP with a 48-month follow-up, a stable improvement in urinary parameters was observed, with 2.4% of patients requiring reoperation [29]. Two studies evaluated the impact of ThuVEP on male sexual function. Although erectile function remained unchanged, a large number of patients developed retrograde ejaculation after the surgery [33,34].

Publications assessing the efficacy of different methods have compared ThuLEP, mono- and bipolar TURP, with no clinically significant differences found in Qmax, IPSS score, and quality of life [35,36]. In a randomized controlled trial (RCT) with a follow-up of 5 years, ThuLEP and bipolar TURP were compared, showing comparable changes in Qmax, IPSS score, quality of life, and post-void residual volume (PVR) [37]. In a meta-analysis [38] comparing ThuLEP and HoLEP (holmium laser enucleation of the prostate), no clinically significant differences were observed in IPSS score, quality of life, and Qmax at 12 months, consistent with RCT results with an 18-month follow-up [39]. Additionally, an RCT demonstrated comparable efficacy between ThuLEP and plasma kinetic enucleation of the prostate with a 12-month follow-up [40].

In another study with an average follow-up of 36.5 months after ThuVEP, Qmax improved from 7.75 ml/sec to 19.1 ml/sec, PVR decreased from 150 ml to 31.9 ml, the IPSS score decreased from 24 to 4.5, quality of life improved from 5 to 1, and PSA level decreased by 86.5% [41]. In a study on the tolerability and safety of the methods, ThuLEP was compared with mono- and bipolar TURP. Enucleation required more operating time, catheterization duration was similar to monopolar TURP, and hospitalization time was shorter than bipolar TURP [35,36]. ThuLEP had a lower blood transfusion rate than monopolar TURP and a lower bladder tamponade rate than bipolar TURP, with no differences in other complications among the three techniques [35,36]. An RCT showed the advantage of ThuLEP over bipolar TURP in terms of the IIEF-5 (International Index of Erectile Function) score at 12 months. In the ThuLEP group, erectile function was significantly impaired one month after treatment compared to the pre-treatment level but returned to baseline after three months. However, in the TURP group, erectile function did not recover [42].

According to a comparative meta-analysis, hemoglobin reduction after the procedure was less pronounced in the ThuLEP group than in the HoLEP group [38]. Transient urinary incontinence was more common after HoLEP. ThuLEP required less operating time [36] and, according to a multicenter study, resulted in less hemoglobin reduction than HoLEP [43]. A meta-analysis comparing ThuLEP and HoLEP showed ThuLEP's advantage in enucleation time with comparable overall surgery time, catheterization, hospitalization, and early complication rates [44,45], consistent with an RCT with an 18-month follow-up, which found no differences in the frequency of urethral strictures and bladder neck sclerosis [39].

An RCT comparing ThuLEP and plasmakinetic enucleation with a 12-month follow-up [40] found no differences in complication rates, but ThuLEP showed advantages in hemoglobin reduction and catheterization duration. In another retrospective comparative study, there were no differences between (super) pulsed and continuous-wave (CW) ThuLEP with regard to intra-operative, peri-operative data and clinical efficacy [46]. Thus, recent literature on BPH enucleation outcomes indicates that enucleation, or "shelling out," is considered the most effective technique for transurethral prostate removal. The thulium laser, with its shallow penetration depth, allows for precise enucleation along the surgical capsule. Both thulium enucleation and vapoenucleation significantly improve functional parameters such as IPSS, Qmax, and reduce post-void residual volume. The short-term efficacy of this method is comparable to mono-TURP, with lower intraoperative complication rates than standard resection. This method involves incisions mainly in the apical zone of the prostate and bladder neck

area. Vessels leading from the periphery to the transition zone are precisely cauterized, leaving the capsule largely intact [47]. However, our analysis also showed that the results obtained by different authors often vary. According to some authors, the outcomes of ThuLEP are comparable to those of TURP for BPH, while others suggest that the new method outperforms TURP in all parameters, and still others claim that the new method only falls short in terms of procedure duration. There is also a limited amount of research on patients who required additional medication postoperatively due to developed erectile dysfunction and/or the presence of LUTS and low quality of life despite the surgical removal of adenomatous tissue. This highlights the need for further study into the safety and efficacy of modern surgical treatments for patients with LUTS caused by BPH.

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