



# Anatomical endoscopic enucleation of the prostate for bladder outlet obstruction: a narrative review

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Anatomical endoscopic enucleation of the prostate (AEEP) differs from other endoscopic modalities for bladder outlet obstruction (BOO) because it extracts the whole benign prostatic hyperplasia component. AEEP has been launched for almost 40 years as a first-line treatment method for BOO regardless of prostate size according to several guidelines. However, it remains underperformed worldwide. In this review article, we elaborate on the advantages and disadvantages of AEEP compared to other surgical modalities for BOO to investigate its efficacy and safety as a gold standard surgical management option for males with BOO.

**Keywords:** Endoscopy; Health care outcome assessment; Prostatic hyperplasia

## Introduction

Benign prostatic hyperplasia (BPH) is the most common benign disease in men, which influence more than 50% of male over the age of 60 years. About 30% of patients with lower urinary tract symptoms (LUTS) due to BPH require management, and about 20% are refractory to clinical management and therefore perform operative management [1]. Recent technological advancements purpose to sustain excellent functional results while diminishing the complications related to the surgical management of BPH. Anatomical endoscopic enucleation of the prostate (AEEP) was initially introduced by Hiraoka [2] and has been determined to be an excellent approach for the surgical management of LUTS due to BPH.

AEEP differs from other endoscopic modalities for bladder outlet obstruction (BOO) as it extracts the whole BPH component of the prostate. Multiple energy sources can be employed to do AEEP such as high-power (100 W or more), low-power holmium (70 W

or less), diode, greenlight, and thulium lasers, and monopolar and bipolar diathermy (Table 1). AEEP apparently exhibits the same safety profile as the excellent endoscopic non-enucleating procedure (ENE) and the same long-term functional results as simple prostatectomy (SP). It can also be safely done in patients using anticoagulants [3,4]. AEEP has been performed for almost 40 years as a first-line treatment modality for BOO regardless of prostate size according to both the American Urological Association and the European Association of Urology guidelines [5,6]. In this review article, we elaborate on the advantages and disadvantages of AEEP compared to other surgical procedures for BOO to investigate its efficacy and safety as a gold standard surgical management modality for males with BOO.

## Advantages of anatomical endoscopic enucleation of the prostate

Endoscopic surgery is usually more favorable than SP for BPH

Received: September 29, 2021 • Revised: October 15, 2021 • Accepted: October 18, 2021

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**Table 1.** A variety of energy sources for anatomical endoscopic enucleation of the prostate

Energy source	Abbreviation
Holmium laser enucleation of the prostate	HoLEP
Thulium laser enucleation of the prostate	ThuLEP
Diode laser enucleation of the prostate	DiLEP
Greenlight laser enucleation of the prostate	GreenLEP
Plasmakinetic enucleation of the prostate	PKEP
Plasma kinetic enucleo-resection of the prostate	PKERP
Photovaporization and enucleation of the prostate	PVEP
Bipolar transurethral enucleation of the prostate	BTUEP
Monopolar transurethral enucleo-resection of the prostate	MTUERP

with a prostate volume of > 80 mL due to its minimally invasive nature [6]. In the last two decades, AEEP for BPH has been advanced and has steadily become a popular modality as an alternative to SP [7]. Holmium laser enucleation (HoLEP) was the first laser method used in BPH endoscopic surgery [8]. After the launch of the holmium laser, diode and thulium lasers were also developed to be used for AEEP [9,10]. Subsequently, AEEP with bipolar energy has arisen as an alternative surgical procedure that can reduce medical costs compared to those incurred for laser AEEP [11]. Both laser and bipolar AEEP are expected to enhance safety outcomes due to better coagulation and fewer transurethral resection syndrome complications.

## Functional outcomes

### 1. Detrusor pressure at maximum flow rate (PdetQmax): better relief of bladder outlet obstruction

In the first randomized clinical trial (RCT) of HoLEP vs. transurethral resection of the prostate (TURP), greater release of BOO was observed after HoLEP compared to after TURP with mean PdetQmax improving from 76.2 to 20.8 cmH<sub>2</sub>O vs. 70 to 40.7 cmH<sub>2</sub>O, respectively. This is particularly relevant for patients with impaired detrusor function and those with refractory urinary retention [12].

### 2. International prostate symptom score, maximum urinary flow rate, post-void residual volume and quality of life: at least equivalent, if not better improvements

Level 1a demonstration recommends that AEEP furnishes at least equivalent, but possibly greater enhancements, in international prostate symptom score (IPSS), maximum urinary flow rates (Qmax), and post-void residual volumes (PVR) compared to those provided by vaporization and resection procedures [13].

A meta-analysis of data from several RCTs described that of the following techniques: bipolar TURP, HoLEP, and greenlight laser photoselective vaporization of the prostate (PVP), only HoLEP provides a greater level of enhancements in IPSS, Qmax, and PVR when compared to that provided by monopolar TURP [14]. Another meta-analysis comparing AEEP to ENE presents significant precedence for AEEP in terms of IPSS, Qmax, and PVR; however, the clinical significance of these findings remains questionable as they are limited: IPSS superiority of 0.29 to 1.44 points, Qmax superiority of 0.26 to 1.87 mL/sec, and PVR superiority of -3.69 to -14.98 mL. There were no clinically significant differences between ENE and AEEP in terms of advancement in quality of life (QoL) scores [3].

## Perioperative outcomes

### 1. Less bleeding, shorter catheter time, and hospital stay

While TURP procedure meets blood vessels with every swipe, AEEP merely meets blood vessels on the inner aspect of the peripheral zone (PZ), and perforates between transitional zone and PZ. RCTs and meta-analyses constantly present less bleeding, shorter catheter times and consequently shorter hospital stays for AEEP when compared to those for TURP [13]. A recent meta-analysis presented a lesser reduction in serum hemoglobin (-0.54 mg/dL,  $p < 0.005$ ), fewer blood transfusions (odds ratio, 0.83;  $p < 0.005$ ), shorter catheter times (-0.58 days,  $p < 0.05$ ), and shorter hospital stays (-0.91 days,  $p < 0.005$ ) after AEEP compared to those after resection procedures [3].

### 2. Superior catheter-free rates for males with urinary retention and high effectiveness in males with impaired detrusor contractility

One of the most outstanding dominance of AEEP is its particularly high catheter-free rate in patient with urinary retention even in the condition of decreased or absent detrusor contractility. Elzayat et al. [15] showed that 98.3% of males with non-neurogenic repeated urinary retention became catheter-free state after HoLEP. A retrospective comparison of 72 patients who underwent HoLEP vs. 31 patients who underwent PVP for refractory urinary retention was presented. The catheter-free rates at a median follow-up period of 6 months were 74% for PVP patients and 99% for HoLEP patients despite 41.9% of PVP patients and 37.5% of HoLEP patients showing proof of decreased detrusor contractility [16].

In a prospective study, Mitchell et al. [17] performed HoLEP to males with nonneurogenic bladder hypocontractility or acontractility. About 35.7% of those with hypocontractility had catheter-free state.

ter-dependent urinary retention as did all those with acontractility. At a median follow-up period of 24.7 months, all patients who had preoperative urinary retention and hypocontractility were catheter-free, and 94.7% of patients who had urinary retention and acontractility were voiding without the requirement for a catheter. Interestingly, 78.9% of patients with acontractile bladders showed significant improvement of detrusor contractility postoperatively [17]. In a retrospective study comparing results of HoLEP to those of TURP in patients with detrusor underactivity, 57% of TURP patients needed  $\alpha$ -blocker medications and 28% required anticholinergics postoperatively. These demands were lower for HoLEP at 12% and 17%, respectively [18].

### 3. Highly safe and effective for males with large prostates and independent of prostate volume

One of the most widely approved advantages of AEEP is its efficacy and safety in patients with large prostates [13]. A meta-analysis of three RCTs comparing HoLEP and SP reported similar enhancements in IPSS, QoL, Q<sub>max</sub>, and PVR at both 12 and 24 months. HoLEP was related to less blood loss, fewer blood transfusions, shorter catheter time, and shorter hospital stay. The influence on potency and continence were similar in both groups, but postoperative complications were less often after HoLEP. No reoperations were needed for the regrowth of BPH in both groups [19,20].

Kuntz et al. [21] showed that about four hundred patients performing HoLEP were stratified into three groups according to preoperative prostate volume (< 40, 40–79, and  $\geq$  80 mL). The association between the reduction in serum hemoglobin level and prostate volume was very puny ( $r = 0.229$ ). There were no clinically significant differences seen in terms of blood loss or blood transfusions among the groups. The median catheter time and hospital stay were similar among the groups. At the 1-month follow-up period, there were no clinically significant differences seen in Q<sub>max</sub> or PVR scores. In a Korean retrospective study, a total of 502 HoLEP patients were stratified into three groups based on the preoperative prostate volume; group A (< 100 mL), group B (100–200 mL), and group C (> 200 mL). Catheter time and hospital stay were longer, and transient postoperative urinary incontinence was more common in group C. However, there were no clinically significant differences observed in terms of blood transfusion rate, urinary tract infection, recurrence, reoperation, clot retention, de novo urethral stricture, and bladder neck contracture. And IPSS with QoL, Q<sub>max</sub>, and PVR scores were not significantly different at the 6-month follow-up [22].

## Other advantages of anatomical endoscopic enucleation of the prostate

### 1. High durability of anatomical endoscopic enucleation of the prostate

AEEP is the most durable surgical procedure for BOO. The longest follow-up period currently obtainable in peer-reviewed literature is over 10 years after HoLEP. Mean IPSS and QoL scores were 3.6 and 0.7, respectively, with mean Q<sub>max</sub> at 26.9 mL/sec. Additionally, the reoperation rate due to regrowth of prostate was 0.7%. In another RCT comparing HoLEP and TURP with a mean follow-up period of 7.6 years, none of the patients in the HoLEP group needed reoperation compared to 18% in the TURP group [23,24].

### 2. Efficacy and safety in elderly patients

Piao et al. [25] divided HoLEP patients into four groups according to age at operation (group A, 50–59 years; group B, 60–69 years; group C, 70–79 years; and group D,  $\geq$  80 years). Despite patients aged  $\geq$  80 years taking significantly higher American Society of Anesthesiologists grades and rates of anticoagulation usage, greater enucleation weights, longer surgery times, and the incidence of adverse events were similar among the groups. The duration of hospital stay was longer for patients in group D compared to the other groups. There were no clinically significant differences observed across groups for IPSS, Q<sub>max</sub>, and PVR scores at 6 months.

## Limitations of anatomical endoscopic enucleation of the prostate

Why has AEEP not yet been accepted as the gold standard surgical modality of BPH despite having the aforementioned advantages and being introduced for almost 40 years [26]? A gold standard procedure must be safe, efficient, reproducible, and cost-effective compared to the current best choice of management. AEEP has not attained this status due to several issues, and therefore, it still remains seriously underused [27].

### 1. Multiple energy sources and technique

AEEP can be performed using various equipment and energies. Some of them apply retrograde blunt dissection during the operation along the prostate capsule plane whereas others apply the energy source to dissect. Specimen removal can also be performed in multiple methods, with the mushroom technique or with various morcellators [26]. The absence of superiority in these options over another and the lack of standardization makes it difficult to launch an enucleation program and choose among the multiple surgical

techniques and energy sources. Each has a unique technical aspect and needs specific surgical techniques that may not inevitable be transposable.

## 2. High costs

Most hospitals have typical bipolar TURP system that would be sufficient for the treatment of BPH. The requirement for laser fibers, high-power laser generators, and morcellators is a hurdle to the widespread achievement of AEEP [28]. It has been demonstrated that HoLEP is related with a 9.6%–24.5% hospital net cost savings as compared to SP due to the shorter hospital stay related with it [26,29]. However, the initial investment for procuring its equipment can be a significant obstacle mainly because the cost of initial hospitalization is at most comparable between TURP and HoLEP [29].

## 3. Steep learning curve

A perception of the learning curve (LC) is crucial for deciding the extent to which surgical experience is needed to offer reproducible results. In AEEP, the LC tends to be sheer and 50 to 60 cases are needed to efficiently do enucleation with effective morcellation [30]. The other limiting factor for the execution of AEEP is the requirement for a mentor during the LC. Under the guidance of a mentor, the LC can be decreased to < 25 cases [31]. The lack of easily reachable mentorship is the other limiting factor in AEEP execution, although some surgeons have overcome AEEP in a self-taught manner. Another limitation for the widespread performance of AEEP is that most residents complete their training period without grasping this surgical technique. Thus, urologists who purpose to start AEEP must experience a fellowship or at least devote money and time in observerships and hands-on courses [26].

## 4. Postoperative outcomes and complications

### 1) Outcomes

TURP and PVP fulfill adequate and durable symptom release in most cases, but they do not always complete the removal of whole adenoma, frequently without reaching the true prostate capsule. This may lead the patient to symptom relapse and adenoma regrowth. In a recent meta-analysis, AEEP showed significantly better IPSS and Q<sub>max</sub> enhancements than ENE. Nevertheless, these differences are questionable because the Q<sub>max</sub> enhancement between groups was 1.0 mL/sec in the short term and 1.77 mL/sec in the long term, respectively. Furthermore, the IPSS score was only 0.86 points lower in the endoscopic enucleation of the prostate group and was merely noted in the mid-term follow-up analysis. There was no clinically significant difference observed in other

functional results and QoL scores regardless of the follow-up duration. While comparing perioperative data between ENE and AEEP, there were clinically significant differences observed that favor AEEP in terms of catheterization time and duration of hospital stay, but with longer operation time [3,26].

### 2) Complications

The complication profile of AEEP differs from that expected with ENE. AEEP is related to less bleeding and lower blood transfusion rate, but a higher incidence of bladder injury [3]. Elevated incontinence rates during the early AEEP LC period can also be assumed [32]. Moreover, transient stress urinary incontinence (SUI) is an adverse event caused by sphincteric stretching due to wider intraurethral movements done to remove adenoma. The incidence of transient SUI has been reported to be as high as 26% at 3 months after AEEP [26]. Urethral stenosis is another complication that may happen due to longer surgical procedures that also often require larger scopes, especially for morcellation. The incidence of this status in AEEP ranges from 1.4% to 3.0% [33,34].

## Conclusion

AEEP is considered an alternative surgical treatment of BPH since it provides the capacity to manage many patients safely and effectively than any other BPH modality. It offers at least equivalent enhancements in Q<sub>max</sub>, PVR, and IPSS scores when compared to those in TURP in patients with prostate volumes of < 100 mL and is more likely to make patients catheter-free even in the condition of impaired detrusor function. However, it is still underperformed globally. The most commonly reported cause is its steep LC. To overcome this problem, a well-structured and focused mentorship program that is more practicable now than ever before because of the increasing accessibility of experienced mentors is suggested. More long-term RCTs may offer an answer to whether AEEP could substitute ENE as the gold standard for surgical management of BPH in the future.

## Notes

### Conflicts of interest

No potential conflict of interest relevant to this article was reported.

### Author contributions

Conceptualization: THK, PHS; Formal analysis, Supervision: THK; Writing-original draft: THK, PHS; Writing-review & editing: PHS.

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