HoLEP: the new gold standard for surgical treatment of benign prostatic hyperplasia

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Introduction: *Transurethral resection of the prostate (TURP) was considered the "gold standard" surgical treatment for medication-refractory benign prostatic hyperplasia (BPH) for decades. With the desire to reduce hospital stay, complications, and cost, less invasive procedures gained usage in the 1990's. With the advent of a soft tissue morcellator, holmium laser enucleation of the prostate (HoLEP) was introduced as an efficacious alternative to TURP and due to its advantageous side effect profile compared to TURP, has grown in popularity ever since. HoLEP has become a size-independent guideline endorsed procedure of choice for the surgical treatment of BPH.*

Materials and methods: *We provide a review on the evolution of HoLEP as a gold standard compared to the historical reference procedures for BPH, and provide a review of emerging laser technologies.*

Results: *A growing body of literature has shown HoLEP to be a safe and efficient procedure for the treatment of BPH for all prostate sizes. Long term studies have proven the durability of HoLEP, as a first line surgical therapy for BPH.*

Conclusions: *HoLEP is a proven modality for the surgical treatment of BPH. It can be performed on patients with high risk for postoperative bleeding, or after previous prostate reducing procedures. HoLEP is the only procedure that is AUA guideline-endorsed for all prostate sizes for the surgical treatment of BPH. Given these considerations, HoLEP has become the new gold-standard for the surgical treatment of BPH.*

Key Words: benign prostatic hyperplasia, HoLEP, TURP

Introduction

Benign prostatic hyperplasia (BPH) is the most common benign lesion affecting men in the United States, affecting 3 in 4 men by the 7th decade of life.[1] BPH becomes clinically significant when it results in lower urinary tract symptoms (LUTS), and affects between 50%-75% of men older than 50 years, and 80% of men older than 70 years.[2] While watchful waiting and medical treatment may be suitable for managing mild symptoms, surgical treatment remains the cornerstone of treatment in the disease for moderate and severe symptoms.[3] Historically, the gold standard surgical treatment for BPH consisted of open prostatectomy (OP), until the introduction of the transurethral resection of the prostate (TURP). TURP was shown to be an effective alternative to OP for prostates between 30 mL and 80 mL.[4] One clinical concern regarding TURP is the well-known risk of TUR-syndrome syndrome, which can lead to fatal morbidity and has a prevalence of 1.1% of all TURPs.[5] TURP also has a significant postoperative bleeding risk, especially for anticoagulated patients, and has limited utility for large prostates > 80 mL.[6] With the continuous aging of the general population and the increased prevalence

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of BPH and LUTS with age, less invasive treatments have become increasingly desirable.[7] In the 1990's with advancements in laser technology, Holmium:YAG was introduced in the application of BPH treatment, first for ablation and soon after for complete enucleation. With the development of morcellation devices, the procedure matured to what we call today holmium laser enucleation of the prostate (HoLEP).[8]

What is a gold standard?

A gold standard is the criteria by which scientific evidence (such as a procedure) is evaluated. This standard, necessarily, changes over time, as new treatments are developed and more evidence becomes available. In defining the gold standard surgical treatment for BPH, many factors should be considered. First, prostate sizes and shapes vary significantly and may or may not have a prominent median lobe or intravesical component, thus a treatment considered the gold standard should be efficacious in treating a wide range of prostate sizes and shapes. Morbidity risk should also be considered. Surgical intervention for BPH is often done on an elective, quality of life basis; as such, treatments should demonstrate acceptably low rates of adverse quality of life impacts from treatment. Additionally, and perhaps most importantly, functional outcome should be demonstrated via both objectively measured data and subjectively from patient reported symptomatic relief and improvement in quality of life. It should be taken into account the risk for/need for additional interventions or therapy in the planning of any surgical treatment for BPH. Lastly, cost must be considered, and the resultant economic burden on the healthcare system and on the patient himself.

Comparison of historical standards

Open prostatectomy (OP)

This procedure, although the most invasive, has a high rate of symptomatic improvement and a low rate of treatment failure; however, it also carries considerable risk of surgical complications and cost.[9-11] The advantages of OP are its durability, efficiency (volume of the resected adenoma and resultant decrease in serum PSA), and the ability to detect incidental prostate cancer. Some of the disadvantages of OP are the relatively high risk of transfusion (reported at 7.5%), prolonged postoperative catheterization, hospitalization, and continence recovery. Further, it involves a lower abdominal incision and the subsequent recovery time.[11] Lin et al[12] conducted a systematic review and metanalysis of nine randomized control trials including 758 patients comparing TURP with OP. Functional outcomes including maximum urinary flow rate, postvoid residual volume, PSA and IPSS scores were similar between the two groups. Operative time favored OP, while blood loss, catheter period, irrigation length and hospital stay favored transurethral enucleation. As for robotic "simple" prostatectomy – the considerations are similar, but the robotic procedure had less blood loss along with a high cost of disposables, similar to reported data for other robotic associated procedures.[13]

TURP

Historically, it took almost a century for the surgical paradigm to shift from OP to TURP. The eventual change was not dictated by better clinical outcomes, but rather based on convenience to the surgeon and the patient, therapeutic burden and economic considerations.[14] TURP has been shown to be an efficient and safe procedure, but has its limitations for patients at increased bleeding risk and in those with large prostates. Because of these limitations, other minimally invasive procedures were introduced in the early 1990's with the purpose to transition the procedure from the operating room to the office, which would reduce cost, free up hospital beds, and allow for the management of high risk surgical patients not candidates for more invasive procedures. A large systematic review and meta-analysis covering 26 randomized controlled trials and 3,283 patients provided analysis of the efficacy and safety of TURP with transurethral enucleation of the prostate.[15] TURP had a shorter operative time, and functional outcome were similar at 6 months follow up; however, at 12 months postoperatively, IPSS and Qmax were significantly higher in the enucleation group, indicating a more complete treatment. Safety profiles and hospital stay also favored transurethral enucleation. These data support the claim that HoLEP should be considered the "gold standard" for smaller prostates.

HoLEP technique

At our institution, HoLEP is performed using a continuous flow 26Fr resectoscope with a laser-bridge and a 550-micron end-fire laser fiber, with laser settings of 50Hz/2J for resection and 30Hz/2J for hemostasis and apical dissection (both settings are set to wide/long pulse). The high-power holmium laser generator (120W, Lumenis, Yokne'am, Israel) uses two pedals and enables alternation between the two laser settings.

Enucleation is performed using the 2-lobe, 3-lobe, or en-bloc techniques, depending on the specific anatomy of the patient. After the urethral mucosa is incised, the plane between the adenoma and the surgical capsule is identified and developed using blunt dissection. The laser is used to assist tissue release and hemostasis. All efforts are made to preserve the bladder neck and avoid using high energy in proximity to the external sphincter. After enucleation, tissue morcellation is performed using a soft-tissue morcellator introduced through an offset nephroscope, followed by insertion of a 24Fr 3-way catheter with postoperative continuous bladder irrigation. The catheter is usually removed the morning after surgery and the patient is discharged after a successful voiding trial on postoperative day 1.

What does HoLEP bring to the table?

HoLEP is considered the endoscopic equivalent to OP as it follows the plane between the adenoma and the surgical capsule similar to the surgeon's finger during OP, which can explain the excellent volume of tissue removal using this modality.[16] In a study comparing results of HoLEP for prostates smaller than 75 mL, between 75 mL and 125 mL, and larger than 125 mL – there was no difference in the need for blood transfusion or incontinence rates between the groups, providing strong evidence of the size-independent efficacious application of HoLEP.[17] In a large retrospective study of 1,065 patients who underwent HoLEP, de-novo incontinence rates were very low at 1.4%, periop complications rate was 2.3%, and an improvement by almost 23 mL/sec in Qmax after 12 months was observed.[18]

In addition to the functional outcomes and safety profile of the procedure, it is important to look at the patient's perspective on the procedure. Abdul-Muhsin et al[19] conducted a prospective study using a third-party administered survey among patients who underwent surgical treatment for BPH – HoLEP, TURP, photoselective vaporization of the prostate (PVP), transurethral incision of the prostate (TUIP), OP, and HoLAP, aiming to assess subjective quality of life impact among patients post-procedure. Mean IPSS score was lowest for HoLEP, and responses involving quality of life impact and lack of regret significantly favored HoLEP versus all other treatment modalities. HoLEP was also shown to be durable. Elmansy et al[20] conducted a retrospective study looking at the durability of HoLEP among 949 patients with a mean follow up time of 62 months, with 89 patients that had been followed up on for 10 years or more. Total re-operation rate was 0.7%. At 10 years of follow up, IPSS was 3.6, Qmax was 27 mL/sec, and PSA reduction was stable at 84%, which implicates the large amount of tissue that is removed, and demonstrates the complete treatment of the bladder outlet obstruction that this modality offers. HoLEP was also shown to be effective for very large prostates. In a retrospective study of 88 patients with prostates over 200 mL, only 10 patients (11.4%) required a conversion to an OP or required a cystotomy for tissue extraction. Enucleation time was 78 minutes and morcellation time was 49.7 minutes. Only 3 patients (3.9%) needed continence surgery 1 year out of the HoLEP.[21]

Recently, papers have been published about the feasibility of removal of the catheter the same day of HoLEP. Agarwal et al conducted a retrospective analysis of 30 patients undergoing HoLEP with same-day catheter removal. Mean prostate size was 81 mL. In order to facilitate same-day catheter removal, a laryngeal mask was used for ventilation (instead of endotracheal tube), no neuromuscular paralysis was used, opiate use was reduced, and early ambulation before catheter removal was encouraged. Same-day voiding trial was done after a mean of 4.9 hours, and was successful in 90% of patients.[22] Another study by Comat et al looked at not only same-day catheter removal, but also same-day discharge.[23] Among 90 patients, same-day discharge was successful in approximately 80% of patients, with the remaining 20% requiring continuous bladder irrigation at least overnight. In an attempt to stratify which of the patients were eligible for same-day discharge, Abdul-Muhsin et al conducted a prospective trial of 47 patients with prostates smaller than 200 mL.[24] Per-protocol, continuous bladder irrigation was performed for 2 hours post-surgery, then stopped for 2 hours. Urine color was documented and graded according to a hematuria grading scale. For discharge, hematuria grade 4 or less had to be present. Using this method, 59.5% of patients were able to be discharged the same-day of surgery. Twenty-four same-day discharged patients were compared to 19 patients that could not be discharged the same day. Four hr. urine color (hematuria grade) was found to be associated with same-day discharge.

Guidelines

AUA guidelines on management of BPH was published in 2018, and was amended in 2019, and 2020.[6] HoLEP was recommended as a size-independent option for surgical management of BPH. For larger prostates, open, lap, or robotic assisted prostatectomy is recommended, depending on the expertise of the surgeon. For high-bleeding patients, HoLEP, PVP or ThuLEP should be considered. In a sub-stratification of recommendations according to prostate size, the only surgical procedure that is represented across the spectrum of sizes, is HoLEP. This makes HoLEP the standard across multiple prostate sizes and other variables that we can compare other treatments to. In the EAU guidelines on BPH management released on 2021, OP is considered effective but invasive with less favorable safety profile compared to HoLEP. Compared to TURP, HoLEP demonstrated longer operative times, but a favorable perioperative safety profile compared to TURP. According to the EAU guidelines, if laser enucleation is not available, OP should be offered.[3] Similar to the AUA guidelines, we see HoLEP across the spectrum of the disease.

Emerging techniques

The science behind MOSES and MOSES 2.0

MOSES laser technology (Lumenis, Yokne'am, Israel) was launched in 2017 to reduce stone retropulsion and increase the efficiency in treatment of stones. This technology uses pulse modulation to maximize the photothermal effect that breaks down the stone, while minimizing the photomechanical effect that pushes the stone away. The first part of the pulse modulation (initiation sequence) creates an air bubble. The second pulse modulation (target sequence) passes through that bubble and pushes the energy towards the target and not back to the fiber. In this way, less energy is lost and energy transmission is optimized per working distance from stone, and well as soft tissue.[25,26] MOSES 2.0 was optimized for soft tissue and specifically for BPH, by maximizing the photomechanical effect without increasing the photothermal charring effect. In a study comparing HoLEP using non-MOSES laser with MOSES 2.0, enucleation time was reduced by 43% in the MOSES 2.0 group, hemostasis time was decreased by 50%, and fiber degradation was decreased by 79%.[27] All of these advantages of MOSES 2.0 laser may help facilitate HoLEP for larger prostates by allowing for shorter operative times, allow expanded usage of HoLEP in anti-coagulated patients due to better hemostasis, and subsequently facilitate same-day discharge.

Thulium fiber laser

Tm-Fiber laser is a laser with custom wavelengths of 1800 to 2050nm, a frequency that can range to 2000Hz, delivered via relatively small-diameter laser fibers and unique characteristics which make it ideal for soft tissue applications as well as lithotripsy. Compared to Ho:YAG laser, the depth of penetration in tissue is much lower (0.077 mm) but the energy absorption is much higher, which enables the laser to operate at lower energy and achieve the same results.[28-30] The reduction of penetrance length adds precision to tissue cutting without adding carbonization, and makes this laser an ideal candidate for soft tissue applications such as laser enucleation of the prostate. In a prospective trial comparing this modality with TURP, enucleation with thulium laser was shown to have good functional outcomes with a comparatively larger decrease in PSA, suggestive of a more complete removal of the adenoma.[31] Further studies about soft tissue applications and specifically laser enucleation of the prostate are currently being conducted.

Conclusions

HoLEP is a proven modality for the surgical treatment of BPH, with a growing body of evidence in the literature citing its safety, and efficiency in all prostate sizes. HoLEP can be performed on patients with higher bleeding risk, or after previous prostate reducing procedures. According to the recent AUA guidelines, HoLEP is the only procedure that should be offered to patients with all prostate sizes for surgical treatment of BPH. HoLEP is as effective as other procedures like TURP and OP, with fewer complications, shorter catheterization times, and shorter hospital stays. Penetrance of the procedure has been limited due to high initial cost, and a relatively steep learning curve, especially for larger prostates. Recent advancements in laser technology have further increased the efficiency of the procedure. Given all of these considerations, HoLEP has become the procedure of choice, and the gold-standard for the surgical treatment of BPH. ☐

References

1. Wei JT, Calhoun E, Jacobsen SJ. Urologic diseases in America project: benign prostatic hyperplasia. *J Urol* 2005;173(4):1256-1261.
2. Egan KB. The epidemiology of benign prostatic hyperplasia associated with lower urinary tract symptoms: prevalence and incident rates. *Urol Clin North Am* 2016;43(3):289-297.
3. Gravas S, Cornu JN, Gacci M et al. EAU guidelines on management of non-neurogenic male LUTS, 2021 update. Presented at the EAU Annual Congress Milan 2021.

4. Cornu JN, Ahyai S, Bachmann A et al. A systematic review and meta-analysis of functional outcomes and complications following transurethral procedures for lower urinary tract symptoms resulting from benign prostatic obstruction: an update. *Eur Urol* 2015;67(6):1066-1096.
5. Rassweiler J, Teber D, Kuntz R, Hofmann R. Complications of transurethral resection of the prostate (TURP)--incidence, management, and prevention. *Eur Urol* 2006;50(5):969-979.
6. Parsons JK, Dahm P, Köhler TS et al. Surgical management of lower urinary tract symptoms attributed to benign prostatic hyperplasia: AUA guideline amendment 2020. *J Urol* 2020;204(4):799-804.
7. Kupelian V, Wei JT, O'Leary MP et al. Prevalence of lower urinary tract symptoms and effect on quality of life in a racially and ethnically diverse random sample: the Boston Area Community Health (BACH) Survey. *Arch Intern Med* 2006;166(21):2381-2387.
8. Fraundorfer MR, Gilling PJ. Holmium:YAG laser enucleation of the prostate combined with mechanical morcellation: preliminary results. *Eur Urol* 1998;33(1):69-72.
9. Salonia A, Suardi N, Naspro R et al. Holmium laser enucleation versus open prostatectomy for benign prostatic hyperplasia: an inpatient cost analysis. *Urology* 2006;68(2):302-306.
10. Naspro R, Suardi N, Salonia A et al. Holmium laser enucleation of the prostate versus open prostatectomy for prostates > 70 g: 24-month follow-up. *Eur Urol* 2006;50(3):563-568.
11. Gratzke C, Schlenker B, Seitz M et al. Complications and early postoperative outcome after open prostatectomy in patients with benign prostatic enlargement: results of a prospective multicenter study. *J Urol* 2007;177(4): 1419-1422.
12. Lin Y, Wu X, Xu A et al. Transurethral enucleation of the prostate versus transvesical open prostatectomy for large benign prostatic hyperplasia: a systematic review and meta-analysis of randomized controlled trials. *World J Urol* 2016;34(9):1207-1219.
13. Sorokin I, Sundaram V, Singla N et al. Robot-assisted versus open simple prostatectomy for benign prostatic hyperplasia in large glands: a propensity score-matched comparison of perioperative and short-term outcomes. *J Endourol* 2017;31(11):1164-1169.
14. Tubaro A. BPH treatment: a paradigm shift. *Eur Urol* 2006; 49(6):939-941.
15. Zhang Y, Yuan P, Ma D et al. Efficacy and safety of enucleation vs. resection of prostate for treatment of benign prostatic hyperplasia: a meta-analysis of randomized controlled trials. *Prostate Cancer Prostatic Dis* 2019;22(4):493-508.
16. Elzayat EA, Elhilali MM. Holmium laser enucleation of the prostate (HoLEP): the endourologic alternative to open prostatectomy. *Eur Urol* 2006;49(1):87-91.
17. Humphreys MR, Miller NL, Handa SE, Terry C, Munch LC, Lingeman JE. Holmium laser enucleation of the prostate--outcomes independent of prostate size? *J Urol* 2008;180(6): 2431-2435.
18. Krambeck AE, Handa SE, Lingeman JE. Experience with more than 1,000 holmium laser prostate enucleations for benign prostatic hyperplasia. *J Urol* 2013;189(1 Suppl):S141-S145.
19. Abdul-Muhsin HM, Tyson MD, Andrews PE et al. Analysis of benign prostatic hyperplasia patients' perspective through a third party-administered survey. *Urology* 2016;88:155-160.
20. Elmansy HM, Kotb A, Elhilali MM. Holmium laser enucleation of the prostate: long-term durability of clinical outcomes and complication rates during 10 years of follow up. *J Urol* 2011;186(5):1972-1976.
21. Zell MA, Abdul-Muhsin H, Navaratnam A et al. Holmium laser enucleation of the prostate for very large benign prostatic hyperplasia (≥ 200 cc). *World J Urol* 2021;39(1):129-134.
22. Agarwal DK, Rivera ME, Nottingham CU, Large T, Krambeck AE. Catheter removal on the same day of holmium laser enucleation of the prostate: outcomes of a pilot study. *Urology* 2020;146:225-229.
23. Comat V, Marquette T, Sutter W et al. Day-case holmium laser enucleation of the prostate: prospective evaluation of 90 consecutive cases. *J Endourol* 2017;31(10):1056-1061.
24. Abdul-Muhsin H, Critchlow W, Navaratnam A et al. Feasibility of holmium laser enucleation of the prostate as a 1-day surgery. *World J Urol* 2020;38(4):1017-1025.
25. Elhilali MM, Badaan S, Ibrahim A, Andonian S. Use of the Moses technology to improve holmium laser lithotripsy outcomes: a preclinical study. *J Endourol* 2017;31(6):598-604.
26. Large T, Nottingham C, Stoughton C, Williams J, Krambeck A. Comparative study of holmium laser enucleation of the prostate with MOSES enabled pulsed laser modulation. *Urology* 2020;136:196-201
27. Nevo A, Faraj KS, Cheney SM et al. Holmium laser enucleation of the prostate using Moses 2.0 vs. non-Moses: a randomised controlled trial. *BJU Int* 2021;127(5):553-559.
28. Kronenberg P, Traxer O. The laser of the future: reality and expectations about the new thulium fiber laser—a systematic review. *Transl Androl Urol* 2019;8(Suppl 4):S398-S417.
29. Enikeev D, Okhunov Z, Rapoport L et al. Novel thulium fiber laser for enucleation of prostate: a retrospective comparison with open simple prostatectomy. *J Endourol* 2019;33(1):16-21.
30. Ventimiglia E, Doiz S, Kovalenko A, Andreeva V, Traxer O. Effect of temporal pulse shape on urinary stone phantom retropulsion rate and ablation efficiency using holmium:YAG and super-pulse thulium fibre lasers. *BJU Int* 2020;126(1):159-167.
31. Enikeev D, Netsch C, Rapoport L et al. Novel thulium fiber laser for endoscopic enucleation of the prostate: A prospective comparison with conventional transurethral resection of the prostate. *Int J Urol* 2019;26(12):1138-1143.