Holmium laser enucleation of the prostate (HoLEP): a review and update

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Introduction: *Lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) is one of the most common diseases affecting the aging man, with almost 80% of men greater than 70 affected. Historically, transurethral resection of the prostate (TURP) has been considered the historical gold standard in the treatment of LUTS due to BPH for many years, contemporary literature indicates that holmium laser enucleation of the prostate (HoLEP) has replaced TURP and open simple prostatectomy as the size independent surgical gold standard for BPH treatment.*

Materials and methods: *In this review, we discuss the current techniques utilized, outcomes and safety, as well as the long term durability of results. Adverse events associated with the HoLEP procedure, both enucleation and morcellation, are covered as well.*

Results: *HoLEP has a robust body of literature supporting the technique, which demonstrates its ability to surpass other surgical BPH procedures, including TURP and open simple prostatectomy. Additionally, there is long term durability of both subjective and objective outcomes greater than 10 years associated with this procedure. One randomized trial showed specific postoperative outcome measures that were superior to TURP at 7 years of follow up, including Qmax (4.36 mL/s improvement), erectile function (2.39 points improvement on the IIEF erectile function section), and weight of prostate removed (15.7 grams greater), while other studies have shown greater reduction in postoperative PSA, lower detrusor pressure at Qmax, and more.*

Conclusions: *Overall, HoLEP has proven to be an extremely durable and effective treatment for patients suffering from LUTS due to BPH. Both the Europeans and AUA guidelines on the surgical treatment of BPH recommend HoLEP as a size-independent treatment option for those men with moderate to severe symptoms. HoLEP is an excellent option for many patients who may not be good candidates for other procedures based on prostate size, age, or bleeding risk.*

Key Words: HoLEP, BPH, LUTS

Introduction

Benign prostatic hyperplasia (BPH) is a common condition affecting many men over the age of 50, with almost 80% of men greater than 70 affected.[1] BPH is caused by unregulated proliferation within the prostate, which can cause physical obstruction of the prostatic urethra and result in anatomic bladder outlet obstruction (BOO).[2] Historically, transurethral resection of the prostate (TURP) has been the gold standard to which all endoscopic procedures for BPH are compared.[3] This technique, although efficacious, has typically been reserved for smaller prostates and is associated with poor hemostasis and increased morbidity compared to newer methods.[4] This morbidity is associated with many complications which can arise from this procedure, such as transurethral resection syndrome which can lead to significant electrolyte abnormalities, prolonged postoperative catheterization, high retreatment rates, and prolonged hospital stay. These shortcomings of TURP have prompted the rise of newer modalities to treat BPH, such as holmium laser enucleation of the prostate (HoLEP).[5] In addition to TURP, open simple prostatectomy (OP) has historically been used to treat BPH, particularly for the treatment of patients with prostate size greater than 100 g. Contemporary literature comparing OP to HoLEP shows significantly less blood loss, shorter hospital stays, and less catheterization time in the HoLEP patients.[6]

The Holmium:Yttrium Aluminum Garnet laser (Holmium), with a wavelength of 2140 nm, was one of

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the earliest lasers to be successfully adopted for soft-tissue use within the lower urinary tract, specifically for BPH.[5] During HoLEP the complete adenoma is enucleated from the surgical capsule and displaced into the bladder before removal with an endoscopic device (transurethral soft-tissue morcellator). The HoLEP technique takes advantage of the distinct anatomical planes to remove the entire prostatic transition zone, thus removing more tissue than TURP and leading to a lower retreatment rate.[7] By removing the entire transition zone of the prostate, HoLEP is the endoscopic equivalent of an OP. HoLEP has proven to be more efficacious than TURP with improved outcomes such as; improved hemostasis, better short term urinary parameter improvements, fewer immediate complications, shorter catheter times and shorter hospital stays.[4,8] The American Urological Association (AUA) guidelines on the surgical treatment of BPH states that laser enucleation, with either holmium or thulium, is the only minimally invasive treatment options for BPH that is size independent.[9] This review will discuss the technique, outcomes, and safety of the HoLEP procedure.

Technique

The classical HoLEP technique has been described previously.[10] It is performed using a high-power holmium laser (100 or 120Watt platform, Lumenis, Yokneam, Israel) and an end-firing 550-micron laser fiber with energy settings of 2.0 J and frequency settings of 40-50 Hz. Many of the newer systems now offer two separate foot pedals, one for the enucleation settings and the other for hemostasis settings. Usually, hemostasis settings are set to 1.5 J and 30 Hz with a wide pulse but can vary depending on the surgeon's preference. Power requirements also differ amongst different platforms, with the 100W laser requiring 30 amp service, while the 120W laser requires 50 amp service.

HoLEP, in brief, is accomplished using a 26 French continuous flow endoscope with a laser bridge while morcellation requires an off-set nephroscope. The laser fiber is delivered through a laser catheter to help stabilize the laser fiber while at the end of the catheter there is a locking mechanism to keep the laser fiber at a fixed length during the procedure. The outflow port is placed to gravity, and the inflow port is wide open connected to 3 L of normal saline due to the large fluid requirements needed during the procedure. This set up may differ depending on which equipment is used, with Storz and Wolf having the three most commonly used products, and each having a slightly different variation for setup.

Classic laser enucleation technique involves the release of the three lobes (one median and 2 lateral) into the bladder. First step in enucleation is incising the urethral mucosa from bladder neck to the verumontanum and identifying the surgical capsule at the 5 and 7 o'clock positions. These incisions are carried distally to the level of the verumontanum, and widened while staying on the surgical capsule, thus isolating the median lobe. Next, the 5 o'clock and 7 o'clock incisions are joined proximal to the verumontanum. The median lobe is then dissected off the capsule in a retrograde fashion. The beak of the endoscope is used to mechanically push the tissue off the capsule, as the laser is used to develop the plane. The median lobe is separated from the capsule in a distal to proximal direction proceeding toward the bladder neck. The median lobe is then pushed up into the bladder, and the final prostatic attachments are released from the bladder neck allowing the median lobe to float into the bladder. The same approach is utilized for the lateral lobes, which are enucleated one at a time. Lateral lobe enucleation is accomplished with an additional incision of the urethral mucosa at the 12 o'clock position from bladder neck to verumontanum. This 12 o'clock incision is carried down to the surgical capsule and the adenoma is separated off the capsule using both the beak of the endoscope and the pulsed holmium laser. The 12 o'clock incision is widened, and thus separating the two lateral lobes anteriorly. The left lateral lobe is enucleated by connecting incisions from the 12 o'clock to 5 o'clock position and pushing the lobe in a retrograde fashion and placing it in the bladder. The right lateral lobe is enucleated by connecting incisions from the 12 o'clock to the 7 o'clock position and pushing the lobe in a retrograde fashion and placing the enucleated lobe into the bladder. Just prior to retrograde enucleation of the lateral lobes, a small bridge of urethral mucosa remains anteriorly and is taken down precisely with the laser to prevent damage to the external sphincter. This step is important in separating the urethral sphincter anteriorly from prostatic adenoma. Prior to tissue removal, hemostasis must be completed to optimize visibility during morcellation. The three lobes removed off the capsule, free floating in bladder, are retrieved using an endoscopic soft tissue morcellator. The morcellator has rigid hollow blades and requires an off-set nephroscope that has a straight working channel for placement of the morcellator blades. The blades of the morcellator can either oscillate or reciprocate depending on the type of morcellator. The morcellator sucks the morcellated tissue through the hollow blades into a retrieval device. During

morcellation, it is important to have the bladder full to ensure there is optimal visibility and to limit damage to the bladder mucosa.

To optimize visibility during enucleation and eventually morcellation, hemostasis is fully accomplished by defocusing the laser fiber tip away from the bleeding tissue, blanching of tissue is observed, during the incision and enucleation process. It is important to note that hemostasis is occurring during the enucleation portion of the procedure due to the unique properties of the holmium laser that coagulates as it cuts tissue. The relatively short wavelength of the holmium laser allows for significant absorption by water within the tissue that leads to rapid vaporization of the tissue and thus minimizes the depth of penetration to tissue at 0.4 mm, while still allowing for effective coagulation up to 3 mm. There is also an added benefit of only cutting across vessels once with pulsed laser energy of the holmium laser, rather than multiple cuts required with other more ablative lasers. With this excellent hemostasis seen with the endoscopic use of the holmium laser, this procedure is able to be utilized on anticoagulated patients, due to the low risk of bleeding secondary to the effective hemostasis the laser provides as shown by multiple studies.[11,12] In one large retrospective study of 1,124 HoLEP patients, Sun and colleagues compared the complication rates in patients not on anticoagulation versus single antiplatelet therapy versus dual antiplatelet therapy.[13] Results in this study showed that overall complications rate within 30 days did not differ (dual antiplatelet: 23.2%, single antiplatelet: 24.8%, no antiplatelet: 27.8%), though there is a significantly longer enucleation time in patients who were anticoagulated, likely due to visibility (dual antiplatelet: 56.9 min, single antiplatelet: 44.4 min, no antiplatelet: 38.5 min). In this study, no patients on dual or single antiplatelet therapy require postoperative transfusions, while one patient (0.1%) not on anticoagulation did.

Laser settings have also been studied, with one group performing HoLEP with a low-power system at 39.6W.[14] While this study did show the feasibility of using the holmium laser at these settings, they also reported increased total complication rate at 24.1%, many of which were postoperative bleeding. These results suggest that the higher energy laser is more effective for coagulation, and is beneficial for anticoagulated patients, but that a low-powered HoLEP is safe and feasible as we await directly comparative trials.

There have been some recent updates to the both the HoLEP technique and equipment utilized. Newer techniques include complete en-bloc enucleation and the more commonly used two lobe enucleation techniques. The two-lobe enucleation technique, the median lobe is undermined at the capsular level and is enucleated with the lateral lobe as one unit.[15] Initial reports on these newer techniques suggest a decrease in both enucleation and total operative time, and easier identification of the surgical capsule.[16,17] Another big change in operative efficiency has come from the improvements in the type of morcellators available. Currently, there are two commercially available morcellators in the USA. VersaCut, by Lumenis, was the first morcellator used for HoLEP. Piranha, by Wolf, is the newer perhaps more advanced morcellator is also available. The VersaCut has reciprocating blades which are controlled by a foot pedal, while the Piranha has oscillating blades which rotate at a selected rate. The suction mechanism is different for each as well, with the Lumenis allowing for continuous suction with or without morcellation, while the Wolf only provides microbursts of suction. Studies have compared the two morcellators.[18,19] Comparisons revealed similar results between the two, though the Piranha had a lower cost of use and higher rates of morcellation with a negligible learning curve. Most HoLEP surgeons' prefer the Piranha to the VersaCut due to the improved ergonomic design, efficient tissue removal properties and its safety profile. Lastly, recent advancement in laser technology in the form of a larger vapor bubble per pulse has initially shown to be useful in dissecting the adenoma off the capsule quicker with better hemostasis. This technology is currently being evaluated at several centers to see if there is a reduction in enucleation time.

Outcomes and safety of HoLEP

HoLEP has been highly scrutinized, with multiple large studies outlining results and complications. To our knowledge, the first randomized control trial comparing HoLEP to bipolar TURP with the inclusion of urodynamic findings was by Tan and colleagues.[20] This study highlighted significant improvements in the HoLEP group, especially that the detrusor pressure at Qmax to void was significantly less than in those who underwent TURP. This is important for patients undergoing the procedure who have compromised bladders. This patient population was followed out for 7 years, which showed that HoLEP is at least equivalent to TURP when comparing long term results, with a lower reoperation rate.[21] The study reported average ± standard deviations for the following results (HoLEP versus TURP): Qmax of 22.09 ± 15.47 versus 17.83 ± 8.61 (TURP) mL/s; AUA symptom score (AUASS) of 8.0 ± 5.2 versus 10.3 ± 7.42; quality of life (QOL) scores of 1.47

± 1.31 versus 1.31 ± 0.85; IIEF-EF (erectile function) of 11.6 ± 7.46 versus 9.21 ± 7.17; ICS male voiding score of 4.2 ± 3.76 versus 3.0 ± 2.41; ICSmale Incontinence Score of 3.07 ± 3.3 versus 1.17 ± 1.4. Although none of these results were significantly different, the paper did show significantly better results for HoLEP in terms of weight of resected prostate tissue in grams (40.4 ± 5.7, 24.7 ± 3.4), postoperative catheter time in hours (17.7 ± 0.7, 44.9 ± 10.1), and overall hospital time in hours (27.6 ± 2.7, 49.9 ± 5.6). Many additional large studies have looked at HoLEP. Krambeck et al analyzed 1,065 patients undergoing HoLEP, which reported both subjective and objective findings.[22] They found that HoLEP effectively reduced AUASS by an average of 15 points at the 12 month postoperative time point, as well as improving Qmax by a mean of 14.3 cc/s at the 12 month time point. Interoperative and postoperative complications were rare, with a report rate of 2.3%. Complications included 3 (0.28%) patients who suffered from postoperative retention, transient stress incontinence in 12.5% of patients at 6 weeks postoperation, permanent incontinence in 15 (1.4%) patients, and urethral strictures in 24 (2.25%) patients. Incidental prostate cancer was identified in 106 patients (10.1%).

These results are independent of age as well.[23] Mmeje et al retrospectively compared HoLEP results across age groups in 311 patients. Patients were stratified into groups 1-4 based on decade of life at time of surgery (50-59, 60-69, 70-79, and 80+). Overall complication rates (20%, 24.4%, 21.6% and 22.1%, in groups 1-4 respectively), severe complications defined as Clavien-Dindo grade 3 or higher (0%, 5.6%, 3.9%, 4.4%), average hospital length of stay (1.18, 1.28, 1.26, 1.68 days) and change in serum hemoglobin levels (1.22, 1.42, 1.57, 1.78 g/dL) were similar across the four groups. At 1 year of follow up, there were no reported differences in continence (100%, 95%, 93%, 88%), average AUA symptom score (6.4, 4.6, 5.2, 7.5), Qmax (24.0, 24.4, 22.4, 16.2 mL/s), or average PVR (16.3, 47.1, 65.5, 46.4 mL) across the groupings. This study shows that both the quality of life and functional improvements seen following the HoLEP procedure are not age limited, and that age does not appear to increase the risk of HoLEP or be a predictor of poor outcome. Considering these data, this procedure has no age limit and is useful for all BPH patients. This is in contrast to TURP, which has been previously shown to have an increasing incidence of blood transfusions and other morbidity associated with increasing age.[24] Another study looking at TURP in elderly patients, above the age of 80, found that significant complications occurred in 13.2% of the cohort studied, which is much higher than the 4.4% of severe complications seen in the same age group of this study.

In addition to objective subjective significant improvements associated with this procedure, it is also important to note that HoLEP is size independent. The AUA updated their latest guidelines for the surgical management of LUTS attributed to BPH in 2018. These guidelines indicate laser enucleation procedures, such as HoLEP, can be considered as a prostate size-independent treatment option based on surgeon experience. This recommendation is based on literature showing size does not alter outcomes.[25,26] Humphreys et al performed a retrospective study that compared results across three groups, one with prostate size below 75 grams, another between 75 to 125 grams, and the last greater than 125 grams. Results showed that postoperative hospitalization, catheterization, AUA symptom score, average maximum flow rate, and average PSA all showed no statistical difference across the three groupings. Other complications, such as transient stress incontinence, transient dysuria, blood transfusion requirement, and stricture rates were also similar between the groups, highlighting multifunctionality of the technique independent of the clinical situation. Building on this, Krambeck et al preformed a retrospective study looking at patients with prostate volumes greater than 175 grams. They examined 57 patients with an average prostate size of 217.8 cc (range: 175-391 cc). Their findings showed similar results across objective and subjective outcomes, as well as reporting no patients with persistent incontinence or need for catheterization. When taken together, these two studies indicate that this procedure can be effectively utilized for glands of all sizes, with no increase in complications.

When assessing patient preference across the different procedures, the literature favors HoLEP.[27] Abdu-Mushin and colleagues used an independent third-party to administer a survey to all patients who underwent any surgical treatment for BPH over a six year time period. The third party received 479 responses (55.6% response rate), including patients receiving HoLEP (n = 214), TURP (n = 210), holmium laser ablation of the prostate (n = 21), photoselective vaporization (n = 18), transurethral incision of the prostate (n = 9), and open simple prostatectomy (n = 7). Validated questionnaires examined many domains, but HoLEP had the most favorable outcomes in terms of urinary intermittency, weak stream, straining, and overall quality of life. Notably, patients undergoing the HoLEP procedure had the lowest level of regret across all procedures. This highlights real life experience and patient satisfaction with HoLEP compared to all other BPH surgical procedures.

Durability and adverse events

As HoLEP is a newer technique than TURP, which has been around since 1926, the long term durability of this procedure has been in question, with EAU guidelines suggesting the retreatment rate of this procedure is 1%-2% per year,[28] which is much higher than the 0% retreatment rate in HoLEP at 7 years of follow up reported by Gilling et al.[21] Multiple studies have assessed durability, often by comparing long term HoLEP results to TURP for comparison. Gu et al did this, looking at data 3 years after the operations.[29] These results showed no difference in durability but did highlight that HoLEP had improved outcomes in terms of average Qmax (17.71 versus 15.92 mL/s), average International Index of Erectile Function-5 (IIEF-5) score (14.48 versus 13.40), average TRUS prostate volume (35.44 versus 37.80 mL), and average postoperative PSA (1.53 versus 1.96 ng/mL) when compared to TURP patients. Another group conducted a similar study, comparing HoLEP and TURP patients 3 years after their inclusion in a randomized control trial.[30] The study found that at 3 years after their operation, both HoLEP and TURP had similar, stable results which were significantly improved from baseline. The study noted that there was no difference in late complication rates and that reoperation rates were not statistically different. Gilling and colleagues published their experience comparing results at 7 years.[21] These results confirmed previous studies, showing high resected prostate volume, shorter catheter time, and shorter hospital time. At 7 years, results indicated that HoLEP is at least equivalent to TURP at 7 years when assessing AUA symptoms score, quality of life questioning, and Qmax. HoLEP did have lower reoperation rates than TURP, though both were rare. The longest follow up study currently found, to our knowledge, is a 10 year follow up looking at durability and complications, with no comparison to TURP.[31] With 949 patients, and a mean follow up of 62 months, this study showed that results lasted throughout the duration of follow up, and that complications rates were very low, with persistent incontinence in 1.5% of patients, stricture in 1.6%, contracture in 0.8%, and reoperation in 0.7% of patients.

Additional studies have compared HoLEP to other, more invasive techniques as well, such as open prostatectomy (OP) and robotic simple prostatectomy (RSP). Data here shows that OP and HoLEP are equally good 5 years after the operations, with similar improvements in average urinary function (Qmax: 24.4 mL/s for HoLEP and OP; PVR: 11 mL in HoLEP, 5 mL in OP) , and similarly low reoperation rates (5% in HoLEP, 6.7% in OP).[32] To date, no long term data are available comparing HoLEP to RSP. However, short term results show both as efficacious, with HoLEP showing many notable advantages compared to RSR.[33] HoLEP had lower average operative times (103 versus 274 min), less average postoperative hemoglobin drop (1.8 versus 2.5 g/dL), lower transfusion rates (1.8% versus 9.4%), shorter average hospital stay (1.3 versus 2.3 days), and decrease average catheterization time (0.7 versus 8 days). Though these studies do not include long term results, this shows short term results highlighting HoLEP's advantages in blood loss, hospital stay, and catheterization times when compared to RSP.

One major concern many patients have regarding prostate surgery is the risk of sexual side effects. Several studies have examined the impact of HoLEP on erectile function.[34] One retrospective analysis of 393 patients compared their preoperative and postoperative IIEF-5 scores. Though there was a small decrease in average IIEF-5 score after the procedure, there was no statistical difference from preoperative scores to postoperative score taken 3 months, 6 months, 12 months, and 36 months. Interestingly, 8.9% of the patients surveyed reported improved erectile function after undergoing HoLEP. However, retrograde ejaculation is a common complication with this procedure, with multiple studies reporting an incidence of over 65%, and up to 90% of patients.[35-37] Placer et al showed that 70.3% of men undergoing HoLEP reported a loss of antegrade ejaculation, while 21% report a reduction in semen quality. These results highlight a significant concern with HoLEP, and patients must be appropriately counseled about this complication and their subsequent fertility potential.

One concern for many surgeons is the well-documented steep learning curve associated with learning HoLEP. The learning curve has been estimated at anywhere from 20-50 cases.[38-40] It appears that such a steep learning curve has limited the widespread adoption of this technique amongst US surgeons, with very few receiving HoLEP training, and seemingly even less interested in acquiring such training after completing residency. The recent systematic review by Kampantais et al showed that this procedure has an acceptable learning curve at around 50 cases with careful selection, which can fall to 25 or fewer when in a structured mentorship program or with the use of simulation. We feel that despite this learning curve, the benefits of the operative outcomes justify this surgery being utilized. There are additional concerns based on insurance reimbursement for the surgeon, which is an area of debate.

Conclusions

Overall, HoLEP is an extremely durable and effective treatment for patients suffering from LUTS due to BPH. The AUA guidelines highlight this by recommending HoLEP as a size-independent treatment option for those with moderate to severe symptoms from BPH. The literature shows HoLEP to be a superior surgical solution to TURP and OP in many respects and a growing body of research comparing HoLEP favorably to other techniques such as RSP. Specific objective postoperative outcome measures that were superior to TURP include Qmax, erectile function, and prostate volume after resection when compared to TURP. Subjective results favor HoLEP as well, with patient surveys showing increased happiness for those undergoing HoLEP compared to other procedures. Critically, HoLEP has proven to be more durable than TURP, with studies showing similarly stable results to OP over time, with studies out to greater than 10 years. While there are some limitations to this technique, such as the steep learning curve and high rate of retrograde ejaculation, this procedure has a large body of literature showing its efficacy, durability, and favorable risk profile. The research shows HoLEP is an option with many patients who may not be good candidates for other procedures based on prostate size, age, or bleeding risk. HoLEP is the endoscopic procedure of choice and is considered the gold standard for the surgical treatment of BPH.

Disclosures

Dr. Akhil K. Das is a consultant for Lumenis and Richard Wolf.
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