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Original Article

HoLEP: the gold standard for the surgical management of BPH in the 21st Century

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Abstract: *Introduction:* For many years, transurethral resection of the prostate (TURP) has been accepted as the gold standard to surgically alleviate obstructive voiding dysfunction in men with benign prostatic hyperplasia (BPH). This historical standard has been challenged repeatedly over the last decade by consistent data demonstrating the superiority of Holmium enucleation of the prostate (HoLEP). This review summarizes the literature comparing HoLEP and traditional therapies for BPH that are widely used and have long term efficacy data, primarily TURP, open prostatectomy (OP), and alternative laser therapies (PVP, ThuLEP, etc). *Results:* Patients undergoing HoLEP have greater improvements in post-operative Qmax, greater reduction in post-operative subjective symptom scores, and lower rates of repeat endoscopic procedures for recurrent symptoms at 5-10 year follow up compared with TURP, OP, and other laser therapies. Furthermore, patients undergoing HoLEP benefit from significantly shortened catheterization times, decreased length of hospital stay (LOS), and fewer serious post-operative complications. In particular, randomized controlled trials (RCT) have demonstrated that HoLEP can be used to resect adenomas greater than 100 grams with equivalent efficacy to open prostatectomy, but with radically decreased morbidity. *Conclusion*: Numerous large, RCTs demonstrate HoLEP to be objectively superior to other surgical therapies for BPH. The urologic community should embrace HoLEP as the new gold standard for surgical BPH therapy, especially in men with large prostates who would otherwise be considered for an OP or staged TURP. The only obstacle to widespread implementation of HoLEP remains its difficult learning curve when compared with traditional transurethral resection. Further allocation of resources towards appropriate mentoring and teaching of HoLEP is warranted, particularly in residency training programs.

Keywords: HoLEP, holmium, laser, enucleation, benign prostatic hyperplasia, transurethral resection of prostate, open prostatectomy

Introduction

TURP is the historical gold standard to which all surgical modalities for BPH are compared. Other interventions, such as OP, PVP, and various laser therapies have demonstrated efficacy in relieving BPH related LUTS. HoLEP is poised to replace all of these modalities as the new standard, based on nearly two decades of data that consistently demonstrate its superior outcomes and lower morbidity. This review summarizes the available literature comparing HoLEP and traditional therapies for BPH that are widely used and have long-term efficacy data.

Patients undergoing HoLEP have greater improvements in post-operative Qmax, greater improvement in post-operative subjective symptom scores, and lower rates of repeat endoscopic procedures for recurrent symptoms at 5-10 year follow-up (< 1% [6-8] vs 7.4% for TURP [3] and 5.6% for PVP [4]). Furthermore, patients undergoing HoLEP benefit from significantly shortened catheterization times and decreased length of hospital stay (LOS) (see **Tables 1**-**3**). Urologists often recommend men with very large prostates undergo open prostatectomy in an attempt to avoid staged TURPs and TUR syndrome. The problem with this recommendation is the exceptional morbidity associated with OP. The advantages of HoLEP over OP are obvious and well documented. RCTs [9] have demonstrated that HoLEP can enucleate adenomas greater than 100 grams with similar efficacy as open prostatectomy, but with radically decre-

Table 1. Comparison of HoLEP and TURP

	Kuntz, et al 2004 [12] (RCT)		Gilling, et al 2012 [13] (RCT)		Montorsi et al 2004 [25] (RCT)		Gupta et al 2006 [26] (RCT)	
	HoLEP	TURP	HoLEP	TURP	HoLEP	TURP	HoLEP	TURP
Length of stay (d)	2.2 *p ≤ 0.001*	3.6	1.2 *p ≤ 0.001*	2.1	2.5 *p = 0.001*	3.6	-	-
Catheter time (d)	1.1 *p ≤ 0.001*	1.8	0.7 *p ≤ 0.01*	1.9	1.3 *p = 0.001*	2.4	1.2 *p = 0.001*	1.9
Tissue removed (g)	32.6	37.2	40.4 *p ≤ 0.05*	24.7	36.1 *p ≤ 0.05*	25.4	17.2	24.2 *p ≤ 0.004*
Procedure time (min)	94.6	73.8 *p = 0.001*	62.1	33.1 *p = 0.001*	74	57 *p ≤ 0.05*	75.4	62.6 *p ≤ 0.001*
Transfusion rate (%)	0	2	0	3	0	2	0	2
Blood loss (mL)	-	-	-	-	-	-	40.6 *p = 0.001*	140.5
Change in Qmax	+20.2	+21.8	+13.8	+9.5	+16.9	+15.9	+19.9	+19.2
Change in AUASS/IPSS	-19.9	-17.7 *p = 0.006*	-18.4	-13.4	-17.5	-19	-18.2	-17.7

ased hospitalization stay, catheterization times, blood loss, and transfusion rates.

This review article contains a broad cross section of the best randomized data directly comparing HoLEP with alternative surgical therapies. Although by no means an exhaustive list, the data contained within gives a clear demonstration of the superior efficacy of HoLEP for surgical BPH therapy.

HoLEP and TURP

TURP is the historical gold standard to which all surgical modalities for BPH are compared. HoLEP is poised to replace TURP as the standard, based on years of data that consistently demonstrate equivalent or superior outcomes with fewer post-operative complications and longer durability based on re-operation rates [5]. There is an abundance of level 1 data directly comparing outcomes and complications for HoLEP and TURP. Ahyai et al [22] performed a meta-analysis of 23 RCTs comparing monopolar TURP, bipolar TURP, OP, HoLEP, and PVP from 2,245 patients. Not only did HoLEP demonstrate a statistically significant improvement over TURP in IPSS ($p = 0.005$) and post-operative Qmax ($p = 0.012$), it was the *only* endoscopic procedure to do so. Regarding durability, HoLEP was the only procedure that did not require re-operation for adenoma regrowth within 5 years. An argument against HoLEP is that operative times are significantly longer than with TURP. However, Ahyai [22] also found that the mean tissue resection rate (g/min) for HoLEP and TURP was statistically similar (0.52 g/min vs 0.57 g/min), making them equally time-efficient procedures. Post-operative complications tend to be lower for HoLEP compared to TURP, and post-HoLEP TUR syndrome has never been reported-even for adenomas hundreds of grams in size [22].

In 2013, Yin et al [23] published a meta-analysis comparing six HoLEP vs M-TURP RCTs. HoLEP bested TURP in both Qmax and IPSS scores at one year ($p < 0.0001$ and $p = 0.01$, respectively). Furthermore, HoLEP patients benefited from less intraoperative blood loss ($p = 0.001$), shorter catheterization time ($p < 0.001$), shorter hospital LOS ($p = 0.001$), and lower transfusion rates ($p = 0.04$). HoLEP procedures did, however, require longer operating time ($p = 0.001$).

Gilling et al [13] reported outcomes data after following prospective cohorts for 92 months. They reported HoLEP on average resulted in an increased amount of tissue removed, decreased catheter time, and decreased hospital LOS-all of which were statistically significant (*P* value < 0.05). Furthermore, patients who underwent HoLEP had greater reductions in AUA SS and greater improvements in post-operative Qmax when compared to pre-operative values. Like others in the literature, Gilling also reported similar outcomes for erectile function, orgasmic function, and sexual desire between the HoLEP and TURP cohorts. Finally, zero patients in the HoLEP arm required reoperation

Table 2. Comparison of HoLEP and OP

	Kuntz, et al 2008 [9] (RCT)		Naspro, et al 2006 [14] (RCT)	
	HoLEP	Open	HoLEP	Open
Length of stay (d)	2.9 *p ≤ 0.0001*	10	2.7 *p ≤ 0.0001*	5.4
Catheter time (d)	1.3 *p ≤ 0.0001*	8.1	1.5 *p ≤ 0.0001*	4.1
Tissue removed (g)	93.7	96.4	59.3	87.9 *p = 0.005*
Procedure time (min)	135.9	90.6 *p ≤ 0.0001*	72.1	58.3 *p ≤ 0.0001*
Transfusion rate (%)	0 *p = 0.003*	13.3	4 *p ≤ 0.007*	17.9
Hemoglobin loss (gm/dL)	1.9 *p ≤ 0.0001*	2.8	2.1 *p = 0.007*	3.1
Prostate size (g)	> 100	> 100	> 70	> 70
Change in Qmax	+20.6	+20.7	+11.4	+11.8
Change in AUASS/IPSS	-19	-18	-12.2	-13.5

for BPH compared to 18% re-operation rate in the TURP arm.

See **Table 1** below for a sample of outcome data from several RCTs comparing HoLEP and TURP.

HoLEP and OP

Since the origin of HoLEP in the early 1990s, it has revolutionized the surgical treatment of men with large prostates. Men with adenomas deemed too large to resect endoscopically are often advised to undergo open prostatectomy-a surgery associated with high transfusion rates, lengthy catheterization times, and hospital stays averaging as many as 5.4-10 days [9, 14].

Contrary to TURP, HoLEP is a *size-independent* procedure. The consequence of this is that HoLEP will eventually make OP all but a historical operation for even the largest of prostates. HoLEP has been used to successfully enucleate adenomas as large as 800 g [5]. Numerous well-designed studies have demonstrated that HoLEP outcomes, catheterization time, and hospital length of stay are independent of preoperative TRUS volume. Lingeman, et al [1] retrospectively reviewed 507 patients who were stratified into three groups based on preoperative TRUS measurement - < 75 g, 75-125 g and > 125 g. They found no significant difference in hospital stay, catheterization time, post-operative AUA-SS, and post-operative Q max among the three groups. Similarly, Kuntz, et al [11] prospectively followed 389 patients who were stratified into three subgroups (< 40 g, 40-79 g, and > 80 g). They found no differences in catheter time, hospital stay, complication rate, or post-operative symptom score across the cohorts. Furthermore, the blood transfusion rate was zero in all three subgroups.

HoLEP and OP outcomes have been directly compared in multiple, well-designed, RCTs. Kuntz [9] demonstrated that HoLEP could be used to resect adenomas greater than 100 grams with similar efficacy as OP, but with radically decreased hospitalization stay, catheterization times, blood loss, and transfusion rates (see **Table 1**). Naspro, et al [14] performed a similar randomized, prospective study comparing HoLEP to OP in 80 patients with prostates > 70 g at 2 years of follow up. They found almost equivocal functional outcomes but a lower transfusion rate (4% vs 17.9%), decreased catheterization time (1.5 vs 4.1 days), and shorter hospital LOS (2.7 vs 5.4 days) in patients who underwent HoLEP vs OP, respectively. Moody and Lingeman, et al [15] retrospectively compared HoLEP to OP in prostates greater than 100 gm and found that patients who underwent HoLEP benefitted from a minimal change in postoperative hemoglobin (1.3 vs 2.9 gm/dl), a shorter length of stay (2.1 vs 6.1 days) and greater amount of adenoma resected (151 vs 106 gm). Furthermore, efficiency and efficacy of the operation were not compromised; procedure duration and AUS-SS improvement between the two cohorts were equivalent.

Table 2 demonstrates the staggering reduction in LOS, catheter time, and transfusion rate that HoLEP patients enjoy.

HoLEP and PKRP, ThuLEP, PVP

In addition to HoLEP and TURP, numerous other minimally invasive therapies exist for the treat-

Table 3. Comparison of HoLEP and PVP, PKRP, ThuLEP, and PKEP

	Elmansy, et al 2012 [20] RCT		Chen, et al 2013 [18] RCT		Zhang, et al 2012 [27] RCT		Neill et al 2006 [28] RCT	
	HoLEP	PVP	HoLEP	PKRP	HoLEP	ThuLEP	HoLEP	PKEP
Length of stay (d)	-	-	3.55 *p ≤ 0.01*	4.37	-	-	1.4	1.3
Catheter time (d)	1.2	1.4	3.3 *p ≤ 0.05*	3.5	2.5	2.4	1.0	1.0
Tissue removed (g)	-	-	48.5 *p ≤ 0.01*	41.1	40.4	37.6	21.7	20
Procedure time (min)	107	110	86.6	60.4 *p ≤ 0.01*	61.5 *p = 0.03*	72.4	43.6 *p ≤ 0.05*	60.5
Transfusion rate	0	0	0	0	0	0	0	0
Prostate size (g)	91.3	89.3	56.7	60.3	43.5	46.6	57.0	51.0
Change in Qmax	+22.4 *p = 0.02*	+20.3	+16	+15.8	+16.7	+16.2	+11.6	+14.6
Change in AUASS/IPSS	-19	-18	-15.4	-15.2	-16.6	-19.4	-18.2	-17.1

V. Durability, sexual function, learning curve, and cost-effectiveness.

ment of symptomatic BPH, including greenlight PVP, ThuLEP, and PKRP. Few studies are available that directly compare HoLEP to these alternative modalities.

Greenlight PVP is the most well established laser alternative to traditional transurethral resection of the prostate that allows for quick and efficient vaporization of prostatic adenoma. Recent advances in the PVP laser have allowed for the treatment of larger adenomas [29]. Elmansy, et al [20] performed the only RCT comparing HoLEP with PVP. Average preoperative TRUS volume was 91.3 g and 89.3 g in the HoLEP and PVP cohorts, respectively. A significantly higher post-operative Qmax and lower PVR were noted in the HoLEP cohort at one year of follow up (p = 0.02). There was no significant difference in IPSS, quality of life, or sexual function at one year. However, 22% of patients undergoing PVP required conversion to either HoLEP or TURP; the authors attributed this to impaired vision from bleeding that could not be controlled with the PVP laser. They also noted that ~33% of PVP cases required multiple laser fibers to complete the operation and required higher energy settings than the HoLEP procedures.

PKRP is similar to bipolar TURP. Chen, et al [18] compared HoLEP and PKRP in a RCT and found HoLEP procedures had significantly more tissue resected and shorter hospital LOS and catheter time. HoLEP procedures on average were 86.6 minutes vs 60.4 for PKRP. Chen concluded that, compared with PKRP, HoLEP was applicable to all prostates regardless of size, and had lower risk of hemorrhage and intraoperative bleeding, with reduced need for post-operative bladder irrigation and reduced catheter times and hospital LOS. Neill et al [28] randomized 40 patients to either HoLEP or PKEP. They found reduced operative time (43.6 vs 60.5 min) and reduced bladder irrigation requirement (5% versus 35%) for HoLEP. All other functional outcomes were statistically similar.

The thulium: YAG laser (ThuLEP) works at a wavelength of 2013 nm in continuous wave mode, and boasts excellent vaporization and hemostatic capabilities with outcomes and complication rates similar to that of HoLEP. However, as a pulsed laser, HoLEP offers greater versatility to the urologic surgeon; patients undergoing endoscopic de-obstruction for BPH frequently require cystolitholapaxy, stricture ablation, or tumor remova-all of which can be accomplished using the holmium laser. Zhang, et al [27] compared HoLEP and ThuLEP in a RCT and found similar functional objective outcomes with significantly reduced operative time for HoLEP but more blood loss, both of which they found to be clinically insignificant.

Table 3 below summarizes the data of these four trials.

Regarding durability, HoLEP is far and away the most durable minimally invasive procedure for

the treatment of BPH. Several studies have followed HoLEP patients for between 5 and 10 years, with a re-operation rate of less than 1%. Note this is in stark contrast to TURP with a reported average re-operation rate of 7.4% and PVP with a re-operation rate of 5-6% [5]. In a RCT of HoLEP vs TURP, Gilling et al [13] reported a re-operation rate of zero vs 18% at 7 years in the HoLEP and TURP cohorts, respectively. Note that pre-operative TRUS volumes in this study ranged from 40-200 mL, suggesting that the durability of HoLEP is size independent. Kuntz et al in 2008 also reported a reoperation rate of zero at 5 years for men with prostates > 100 g who underwent HoLEP. In a retrospective review of 507 patients who underwent HoLEP, Lingeman et al reported a stricture rate of 2.2%, significantly lower than the 7.4% rate reported for TURP [1].

Regarding sexual function, HoLEP appears to offer no distinct advantage over TURP. Frieben et al [30] reviewed eight RCTs for HoLEP and found that 7.5% and 7.7% patients reported decreased erectile function after HoLEP and TURP, respectively. Interestingly, 7.1% and 6.2% (0-19%) reported increased erectile function, respectively. Retrograde ejaculation was equally common after HoLEP (50-96%) and TURP (50-86%). In a Danish study of 108 HoLEP patients, 70% had retrograde ejaculation at 6 months post-operatively, but the incidence of early morning erections increased from 45% to 62% [31]. They found that HoLEP did not significantly affect libido, erections, or sexual satisfaction. Finally, in a study of 191 sexually active men who underwent either HoLAP, PVP, or HoLEP, Elshal et al found those patients who underwent HoLEP had significant improvements in erectile function, sexual desire, and intercourse satisfaction [32]. Those who underwent HoLAP or PVP did not demonstrate these same improvements.

Regarding cost-effectiveness, it seems obvious that HoLEP patients would generate decreased hospital bills, based purely on shorter average LOS. Several studies have attempted to compare the cost-effectiveness of HoLEP with TURP. Fraundorfer, et al found that HoLEP and TURP had equivalent clinical outcomes at one year, but HoLEP cost 24.5% less than TURP [35]. When comparing HoLEP to OP, Salonia, et al found that average costs were $2,919 vs. $3,556, respectively [21]. They attributed the reduction in cost for HoLEP to shortened hospital LOS. Other studies, however, have been inconclusive and suggested that further research and analysis is needed [19].

Perhaps the greatest obstacle to widespread implementation of HoLEP at academic and private centers worldwide remains the procedure's steep learning curve. There are multiple publications describing self-taught learning experiences, with time to expertise reportedly requiring as many as 50 cases [33]. Al-Hakim and Elhilali reported that the two most difficult technical steps were the initial apical enucleation and the incision of the antero-apical mucosal attachment of the lateral lobes [34]. They reported that surgical proficiency with HoLEP was achieved after a mean of 20 patients.

Conclusion

Based on all available evidence, HoLEP offers patients a safer, more efficient, and at least equally efficacious, if not more efficacious, treatment for BPH related LUTS when compared to other surgical therapies. When compared with TURP, currently the reference gold standard, patients undergoing HoLEP benefit from a shorter catheterization time, shorter hospital LOS, and fewer complications.

In centers where HoLEP is available, OP is an unnecessary and historical operation fraught with high transfusion rates, long hospital stays, and lengthy catheterization times. Despite the well-documented superiority of HoLEP over more traditional therapies, widespread implementation remains to be realized. The standard argument that HoLEP is too time consuming or too difficult to learn is not well supported in the literature. Unfortunately, only a handful of urology training programs appear to offer experience in HoLEP to residents.

In summary, HoLEP is at least as effective as other surgical therapies, including TURP, OP and other laser modalities, with fewer complications, shorter hospital stays, and decreased catheter time. These benefits make HoLEP the procedure of choice for men seeking surgical relief for BPH related LUTS and the gold standard for the 21st Century.

Abbreviations

HoLEP (Holmium enucleation of prostate), TURP (transurethral resection of prostate), OP (open prostatectomy), PVP (photovaporization of prostate), ThuLEP (Thulium laser enucleation of the prostate), PKRP (plasmakinetic resection of the prostate), PKEP (plasmakinetic enucleation of the prostate), RCT (randomized controlled trial), length of stay (LOS).

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