Symposium

Management of large prostatic adenoma: Lasers versus bipolar transurethral resection of prostate

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ABSTRACT

Transurethral resection of prostate (TURP) has long been the most commonly performed surgical procedure for the management of benign prostate enlargement (BPE), but has several associated limitations. Over the years, laser techniques have developed as major contenders as alternative therapies for BPE. However, simultaneously, TURP has also flourished and with relatively recent development of resection in saline (bipolar TURP), the tussle between laser techniques and TURP has further gained momentum. A systematic search was performed on Medline using the various Medical subject headings related to the surgical management of BPE including TURP, bipolar, lasers, holmium laser enucleation of prostate (HoLEP), photo-selective vaporization of prostate (PVP), etc., All articles types including meta-analysis randomized controlled trials, review articles, guidelines from various urological associations, single center studies from 2002 onward were considered for review. Bipolar TURP, HoLEP, and PVP provide equivalent outcomes for large prostate adenoma (>60 g). For extremely large glands (>150 g), HoLEP is a very efficacious endoscopic alternative to open prostatectomy and has proven long-term results over more than a decade. Bipolar TURP and PVP are attractive with a minimal learning curves and equivalent short term durability. Surgical management of large prostate should be individualized based upon patient's comorbidities and surgeon's expertise.

Key words: Benign prostate enlargement, bipolar, holmium laser enucleation of prostate, laser, photo-selective vaporization of prostate, transurethral resection of prostate

INTRODUCTION

Benign prostate enlargement (BPE) is a common pathology affecting more than half the men by age of 60 years. Though, rarely being the direct cause of mortality these days, it causes considerable morbidity. Even though, it is quite prevalent, only 4% of the prostates in men more than 70 years old reach sizes greater than 100 g.[1] This group had not been studied well given the fact that large prostates (>80 g) had traditionally been treated with open prostatectomy. However over the last decade, this preference has gradually diminished in favor of endoscopic techniques, based largely on short term results for most new endoscopic techniques. This had been steered by holmium laser enucleation of prostate (HoLEP) technique leading from the forefront and showing equivalent or even better long-term results compared with open prostatectomy. In spite of the recent surge in the forms and modalities of surgical treatment of BPE, their remains a void in the existing literature because of absence of direct randomized trials over the long-term between various available modalities. Furthermore with the rapid pace at which various endoscopic modalities are developing, it calls for a frequent review of the subject at all levels. In this context, current literature needs to be interpreted in a wider and balanced perspective. Here, we review the literature to put forth the status of bipolar resection in saline (bipolar transurethral resection of prostate [TURP]), HoLEP and photo-selective vaporization of prostate (PVP) for management of BPE, with emphasis on large prostatic adenoma. The various potential concerns in large glands have been listed later and discussed individually.

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MATERIALS AND METHODS

A systematic search was conducted through Medline using the various Medical subject headings related to surgical

management of BPE including TURP, bipolar, lasers, HoLEP, PVP, etc. All articles over the last decade from 2002 onward were considered for the review including meta-analysis, randomized controlled trials and review articles, guidelines from various urological associations or single center studies. Isolated case reports and abstracts were not considered. Preference was given to articles focusing on large prostate size. A total of 150 articles were shortlisted from a pool of 6100 articles. The articles were further selected based upon their clinical relevance and year of publishing. All direct comparative studies between two or more surgical modalities and meta-analysis were included. Selected reviews on the subject from distinguished authorities were also included at the discretion of the authors. Overall 170 articles were evaluated for synthesis of the evidence in this review. Guidelines from American urological association, European association of urology, Canadian urology association and Japanese urology association (AUA, EAU, CUA and JUA) were also studied and included as part of the literature review. The evidence from available literature was assessed, analyzed and presented here in a concise fashion with an effort to put into perspective the pros and cons of various available surgical modalities, especially in relation to large prostatic adenoma. No effort was made to prepare a new meta-analysis by pooling data from various available studies. The objective was to reconcile evidence from various high level studies and to synthesize a short review with a balanced approach.

Evolution of endoscopic modalities for surgical treatment of large prostate adenoma

Over several decades experience gained in TURP across all continents had firmly established this technique as the surgical procedure of choice for management of BPE. For large prostatic gland of more than 60 g, however standard TURP had its limitations, mostly related to absorption of irrigation fluid, bleeding and dilutional hyponatremia.[2] Long nursing contact time and post-operative irrigation requirement were other concerns. Thus for larger glands, faster resection efficiency and reduction of complications are two major issues to be tackled before accepting endoscopic surgery as an equivalent or better alternative to open prostatectomy. With refinements in the technique of TURP and related instruments (such as vapor resection, enucleation techniques or resection in saline), gradually larger and larger glands are now being dealt with TURP, particularly with vastly improved anesthetic and monitoring facilities compared with older times.[3-6] Transurethral vapor resection of prostate (TUVRP) using a thicker loop at higher current settings had been successfully reported to deal with glands larger than 100 g.[7] This study reported good perioperative results of 39 consecutive cases of large prostate gland (mean: 121.39 g, range: 101-232 g) performed in a single sitting with a minimal morbidity and average follow-up of 6 months. Enucleation techniques using the electrocautery have successfully been used similar to use of lasers for enucleation.[8] Zhang *et al*. have reported a significant difference in decline in Prostate specific antigen (PSA) (2.8 ± 3.0 vs. 0.8 ± 0.4 ng/ml; $P < 0.05$) and prostate volume (15.2 ± 7.7 vs. 10.5 ± 5.4 g; $P < 0.01$) favoring the enucleation-resection technique compared with standard resection technique.[8] Transurethral bipolar resection in saline (TURIS) or bipolar TURP is the recent most development in the growth story of TURP and is fast spreading among the users of TURP given its perceived minimal learning curve for those who are already practicing TURP. TURIS technique of resection remains the same and uses similar equipment as standard TURP with no major differences. Only fine nuances need to be adjusted before a surgeon can easily shift to this new technique. Alongside the evolution of TUR techniques, various laser resection procedures have evolved over last two decades and all have shown equivalent outcomes for small glands, HoLEP and PVP being frontrunners; though, they have still not replaced TURP as the reference standard. Contrast to TUR techniques, HoLEP and PVP involve a learning curve of altogether different method of dealing with prostate along with a new specialized set of equipment.[9] The laser techniques however, provide the advantage of less blood loss and safer usage in patients on anti-coagulants or patients with comorbidities compared with standard TURP.[10,11] Thus, the usage of TURP is gradually decreasing (nearly 5%/year)[12] with the emergence of laser techniques and bipolar TURP, which have provided less blood loss and hospital stay.[13-16] With proven reduction in associated morbidity and complications, the usage of all these newer techniques is logically increasing to include even the larger sized glands. HoLEP has certainly proven its worth for large glands compared with open prostatectomy over the long-term. However, randomized long-term trials continue to elude the current literature for other modalities because of rapid evolution of these procedures in the form of technique, instrumentation, energy etc. To this extent current literature needs to be interpreted in a wider and balanced perspective. In addition, none of these newer procedures have been subjected to rigorous evaluation against one another in multi-center randomized studies and even still so they continue to evolve at a rapid pace with the prime aim of reducing morbidity of standard monopolar TURP and possibly improving its long-term efficacy for large sized glands.

Current status and comparative evaluation of HoLEP, PVP and bipolar TURP for large glands

Many randomized trials have been reported over the last decade with various endoscopic laser techniques showing the equivalence of their efficacy over the mid- to long-term. Comparative results from some randomized trials comparing either of HoLEP, PVP or bipolar TURP with standard monopolar TURP or open prostatectomy are given in Table 1. Most of these studies are however limited in terms of gland size being treated, though gland sizes of up to

Table 1: Comparative results from some randomized trials comparing either of HoLEP, PVP or Bipolar TURP with standard monopolar TURP or open prostatectomy

Study	Procedures	No. of cases	Follow-up (year)	Surgeons	Surgical time (min)	Prostate volume (ml)	Resected weight (g)	Prostate volume at 6 month (ml)	S sodium decrease (mmol/ml)	Hb decrease (g/dl)	Bladder irrigation time (min)	Catheter time (days)	AUA symptom score relief at 3 month	Stricture/ bladder neck contracture	Redo cases
Mamoulakis *et al.* 2012[17,18]	Bipolar TURP versus TURP	141 versus 138	3	Multicenter, double blind	52 versus 50.8, *P*=0.7	64 versus 63.2, *P*=0.76	-	-	0.8 versus 2.5, *P*=0.003	0.8 versus 0.9, *P*=0.55	-	3.1 versus 3, *P*=0.44	13.8 versus 13.5, *P*=0.68	2 versus 5 early strictures, *P*=0.28, 10 versus 10 late strictures, *P*=0.96, 8 versus 2 BNC, *P*=0.11	-
Autorino *et al.* 2009[19]	Bipolar TURP versus TURP	35 versus 35	4	Single blinded, singles surgeon	49 versus 53, *P*=0.07	51.6 versus 47.5, NS	24 versus 20, *P*=0.08	22.1 versus 19.3, *P*=0.32	0.6 versus 0.9, *P*=0.07	0.8 versus 1, *P*=0.09	-	-	20.3 versus 20.5, *P*=0.9	2 versus 3, *P*=0.7	1 versus 1, *P*=0.8
Méndez-Probst *et al.* 2011[20]	Bipolar TURP versus TURP	22 versus 21	6 month	Multicenter, single blind	60.8 versus 47.5 *P*=0.08	57.9±25.6 versus 50.23±20.7, NS	22.5 versus 19.3, NS	-	1 versus 4 cases with value <135, no TUR syndrome	12.6 versus 9.1 mmol/L, NS	876 versus 776, NS	1.5 versus 1.1, NS	15.9 versus 17.9, NS	3 versus 3	None
Xie *et al.* 2012[21]	Bipolar TURP versus TURP	110 versus 110	5	Singles blinded	55 versus 60, *P*=0.03	65.9 versus 67, *P*=0.83	55.4 versus 52.2, *P*=0.014	-	1.6 versus 2, *P*=0.014	1.22 versus 1.58, *P*=0.014	15.8 versus 24.5 h, *P*<0.001	2.7 versus 3.6, *P*<0.001	17.3 versus 16, *P*<90.001	4 versus 4 stricture, 4 versus 8 BNC, *P*=0.4	3 versus 3
Zhao *et al.* 2010[22]	Bipolar enucleation versus TURP	102 versus 102	3	Single blind, 3 surgeons	62.8 versus 55.3, *P*=0.13	69.2±13.5 versus 67.5±11.8, NS	56.4 versus 43.8, *P*<0.001	20.7 versus 29.3, *P*<0.001	1.36 versus 1.67, *P*=0.12	0.74 versus 1.88, *P*<0.001	996 versus 1518, *P*<0.001	51.7 versus 80.5 h, *P*<0.001	17.7 versus 17.1, NS	0 versus 3	1 VIU versus 2 redo TURP
Ahyai *et al.* 2007[23,24]	HoLEP versus TURP	100 versus 100	3	Unblinded, many surgeons	94.6 versus 73.8, *P*<0.0001	53.5±20 versus 49.9±21.1, *P*=0.15	32.6 versus 37.2, *P*=0.17	-	1.1 versus 1.8, *P*=0.28	1.3 versus 1.8, *P*=0.01	-	27.6 versus 43.4, *P*<0.0001	17.8 versus 15.9, *P*=0.04	3 versus 1	None
Montorsi *et al.* 2008[25]	HoLEP versus TURP	52 versus 48	1	Multicenter, unblinded, many surgeons	74 versus 57, *P*<0.05	70.3 versus 56.2, *P*<0.05	36.1 versus 25.4, *P*<0.05	-	-	1.3 versus 1.2, NS	-	31 versus 57.8 h, *P*<0.001	16.7 versus 17.2, *P*=0.14	1 versus 4, NS	-
Capitán *et al.* 2011[16]	PVP (120 W) versus TURP	50 versus 50	2	Unblinded, senior surgeons	54.1 versus 48.2, *P*=0.005	51.3±14.8 versus 53.1±13.8, *P*=0.5	-	26.9 versus 21.3, p=?	2.2 versus 7.2, *P*<0.0001	0.65 versus 2.3, *P*<0.0001	-	23 versus 72 h, *P*<0.0001	11.5 versus 13.9, *P*=?	3 versus 6	-

contd...

Table 1: Contd...

Study	Procedures	No. of cases	Follow-up (year)	Surgeons	Surgical time (min)	Prostate volume (ml)	Resected weight (g)	Prostate volume at 6 month (ml)	S sodium decrease (mmol/ml)	Hb decrease (g/dl)	Bladder irrigation time (min)	Catheter time (days)	AUA symptom score relief at 3 month	Stricture/ bladder neck contracture	Redo cases
Lukacs *et al.* 2012[15]	PVP (120 W) versus TURP	69 versus 70	1	Multicenter, senior surgeons, unblinded	71 versus 55, *P*=0.0001	50.5 versus 50.1, NS	-	30 versus 24.7, *P*=0.09	-	-	-	-	15 versus 12, NS	-	6 PVP cases converted to TURP, 1 reoperated for hematuria
Kuntz *et al.* 2007[26]	HoLEP versus open prostatectomy	60 versus 60	5	Unblinded	136 versus 91, *P*<0.0001	114.6 versus 113, *P*=0.6	94 versus 96, *P*=0.99	-	-	1.9 versus 2.8, *P*<0.0001	-	30 versus 194 h, *P*<0.0001	19.8 versus 18.7, *P*=0.94	3 versus 4, *P*=0.6	5 versus 6.7%, *P*=1 (all were VIU or BNI)

NS=Not significant, BNC=Bladder neck contracture, VIU=Visual internal urethrotomy, BNI=Bladder neck incision, TURP=Transurethral resection of prostate, HoLEP=Holmium laser enucleation of prostate, PVP=Photo-selective vaporization of prostate, Hb=Hemoglobin, AUAS=American Urological Association

120-150 g are now frequently being managed by endoscopic means, wherein lies the current inadequacy of literature support for treatment of large glands.

HoLEP technique is one particular procedure, which has firmly proved to be a worthy alternative for large glands and has shown good long-term outcomes compared with open prostatectomy in several randomized trials in terms of reduction of International Prostate Symptom Score (IPSS), improvement in quality-of-life indices and rate of flow of urine.[27-29] Elmansy *et al.* presented 10 years follow-up of cases after HoLEP showing durability of outcomes. 563 and 89 cases had completed 5 years and 10 years follow-up, respectively. Bladder neck contracture and urethral stricture developed in 0.8% and 1.6% of patients, respectively. The reoperation rate as a result of recurrent obstruction from residual adenoma was 0.7%.[27] These results compare favorably with those of contemporary open prostatectomy series. HoLEP is the technique considered as being most similar to enucleation of open prostatectomy with less blood loss and early recovery compared with its open counterpart.[26,29] It is also the only technique to have been shown to achieve statistically significant higher reduction of IPSS compared with TURP.[10]

Use of PVP for large glands is also fast growing and is easier to learn, but with the rapid emergence of higher power machines, the data is not quite as robust as for HoLEP. However, in the short term PVP with 120 W or 180 W machine has shown comparable outcomes.[30,31] Presently, there are very few studies addressing the efficacy of PVP in large size glands. Gu *et al.* have shown good functional outcomes with no increased morbidity for gland size >80 g compared with those with <80g musing 120 W system.[30] Similarly Ruszat *et al.* report good functional outcomes for gland size >80 g sustained over 2 years follow-up with this technique.[32] However, this procedure certainly lags from others in terms of resection efficiency for large glands.[31] Use of much higher power systems (120 W or 180 W) aims at faster tissue vaporization to make this technique comparable in terms of overall surgical time to other endoscopic techniques. Proponents of HoLEP continue to suggest inadequacy of tissue removal with vaporization techniques and remain skeptical of long-term redo procedures rate with PVP, which is yet to be determined.[33] In this recent single center randomized trial between 120 W PVP and HoLEP by Elmansy *et al.* for large prostates (mean: 90 g), the residual prostate weight at 6 months of surgery was twice as more for PVP (41.2 ± 13.3 vs. 20.7 ± 7.7 g, $P < 0.0001$).[33] Because of more aggressive PSA-based prostate cancer detection efforts, the absence of tissue analysis in PVP is no longer considered a disadvantage to this technique.

Bipolar TURP is another relatively new entrant and has promised good efficacy for large sized glands.[34-38] Its appeal lies in its similarity to conventional TURP while reducing the

complication of dilutional hyponatremia and being safer to use in patients on pacemakers.[39] Many studies have reported less blood loss, fewer clot retention episodes and shorter catheterization time and hospital stay.[40] Fluid absorption however still remains a concern[41] and its usability for very large glands is inconspicuous and needs to be proven although hybrid enucleation resection techniques[8] are evolving and may further complicate the choice of modality for larger glands. In a recent comparative randomized study, bipolar TURP was compared with open prostatectomy.[42] Post-operative hemoglobin levels, catheterization time, hospital stay and 3-years overall surgical re-treatment-free rate were significantly better in the bipolar group while the two groups were comparable in other terms. In another very recent randomized controlled trial, 280 cases were randomized into bipolar TURP or HoLEP groups.[43] Mean prostate size was equivalent in both groups at 60.3 and 56.7 g, respectively. HoLEP was found to be superior to bipolar TURP with respect to bladder irrigation, catheter time and hospital stay, but the procedure required more time to perform. HoLEP group also demonstrated significantly higher resected prostate weight and less drop in hemoglobin levels, whereas serum sodium levels were similar between the groups.

Overall, presently bipolar TURP, HoLEP and PVP have been recommended as the endourological alternative procedures for dealing with large prostatic adenoma as per various guidelines. Currently, HoLEP scores over others given its proven long-term results. It's difficult to project one procedure as the standard of treatment either because of insufficient good quality evidence, surgeon's expertise or variability of patient preferences. Most available randomized studies compare new endoscopic modalities against standard monopolar TURP or open prostatectomy, rather than being put to trial against each other. Also in the absence of proper randomized trials, conclusions are often drawn based on non-concurrent or historical comparisons or non-validated assumptions. There are no direct good quality head to head randomized comparative trials available for these newer endoscopic modalities since rapid evolution of technologies and power levels precludes long-term direct comparison between various techniques for large adenomas. Results from a few available randomized head-to-head studies have already been discussed and are presented in brief in Table 2.

Issue specific considerations for large glands

Perioperative complications

TUR syndrome and intra-operative parameters

The laser techniques and bipolar TURP have virtually eliminated TUR syndrome as a complication of endoscopic resection of large prostates because of use of saline as an irrigant solution along with reduced absorption due to simultaneous robust coagulation underneath while cutting or vaporizing. However, the risk remains particularly for large glands with standard monoplar TURP. Overall mortality following prostatectomy has decreased significantly within the past two decades and is <0.25% in contemporary series.[45-47] The risk of a TUR-syndrome (fluid intoxication, serum Na+ <130 nmol/L) is in the range of 2%. Risk factors for the development of the TUR-syndrome are excessive bleeding with opening of venous sinuses, prolonged operation time, large glands and past or present smoking.[48,46] Blood transfusion rate following TURP is in the range of 2-5%. Higher percentages have been reported following open prostatectomy.[49]

A detailed meta-analysis performed recently by Ahyai *et al*. evaluated the functional outcomes and complications of various transurethral procedures for BPE.[10] They reported an overall treatment specific intra-operative complications to the tune of 3-3.5% for TURP, PVP and HoLEP, which include bleeding, capsular perforation, conversion to TURP, injury of the mucosa, blood transfusion or TUR syndrome.[10] Bipolar TURP reportedly had a lower intra-operative complication rate of 1.9% in this review. For PVP, conversion to TURP constituted a major part of intra-operative complications. For HoLEP, bladder mucosal injury and perforation is an added risk due to use of morcellation instruments. In the early part of the learning curve, the complication rate may be higher.[50] For HoLEP, both very large and very small glands should be avoided in the early part of the learning curve.[9]

Early complications

Treatment specific perioperative complications such as clot retention, re-catheterization, secondary bleeding, urinary tract infection (UTI), fever, sepsis and need for secondary procedure occur to the tune of 15-20% after TURP and 10-15% after bipolar TURP, both of which have a similar complication profile.[51,10] Catheterization time is the longest for TURP. PVP reportedly had the highest UTI and re-catheterization rates amounting to a total of 20-25% early complication rate.[10] HoLEP had the lowest reported early complication rate up to 10%.[10] The literature remains largely silent whether cases with large glands are at higher risk of early complications or not.

Incontinence

Nearly, 1% risk of urinary incontinence has been reported after TURP in the Veterans Affairs Cooperative Study,[52] with a similar incidence in the watchful waiting group. Ahyai *et al*., have reported incidence of 0.6% (range: 0-5) in a recent review of literature for standard TURP compared with 0.9% (range: 0-3) for HoLEP.[10] Incontinence as complication following PVP remains poorly reported in recent literature along with the degree and type of incontinence to make any conclusive judgments in this regard. Overall, there seems to be no significant difference between various techniques in terms of incidence of incontinence.[10] Furthermore, there is no clear indication that the incidence is affected by patient age or (resected) prostatic volume.

Table 2: Results from randomized trials comparing HoLEP, PVP and Bipolar TURP. This excludes randomized trials which compare these procedures to standard monopolar TURP or open prostatectomy

Study	Procedures	No. of cases	Follow-up (year)	Surgeons	Surgical time (min)	Prostate volume (ml)	Prostate volume at 6 month (ml)	S sodium decrease (mmol/ml)	Hb decrease (g/dl)	Stricture/ bladder neck contracture	Redo cases
Chen *et al*., 2013[43]	HoLEP versus bipolar TURP	140 versus 140	2	Different for two procedures	86.57±31.48 versus 60.38±20.87 *P*<0.01 (significant)	56.70±28.41 versus 60.31±22.41 *P*=0.24	29.61±6.81 versus 34.84±6.03 *P*<0.01 (significant)	3.04±1.50 versus 3.16±1.58 *P*=0.54	1.08±0.53 versus 1.32±0.65 *P*<0.01 (significant)	1 versus 2	-
Elmansy *et al*., 2012[33]	HoLEP versus PVP (120 W)	43 versus 37	1	Supervised by one senior surgeon	107±35.1 versus 110±41.5 *P*=0.7	91.3±23.2 versus 89.3±16.6 *P*=0.6	20.7±7.7 versus 41.2±13.3 *P*<0.0001 (significant)	-	No blood transfusions, 8 cases in PVP group were converted to TURP/HoLEP for bleeding	None	0 versus 2
Neill *et al*., 2006[44]	HoLEP versus Bipolar enucleation	20 versus 20	1	3 surgeons doing both type cases	43.6±5.3 versus 60.5±6.1 *P*<0.05 (significant)	57.0±5.1 versus 51.0±3.9 *P*=0.366	29.7±3.1 versus 33.3±2.9 *P*=0.523	-	-	1 versus 1	0 versus 1

TURP=Transurethral resection of prostate, HoLEP=Holmium laser enucleation of prostate, PVP=Photo-selective vaporization of prostate, Hb=Hemoglobin

Long-term complications

Most of current innovations and research focuses on improving the intra and per-operative complications or morbidity of TURP or open prostatectomy. Long-term outcomes are equally important for all concerned and must not be forgotten in the enthusiasm of introducing newer technologies or methods. These consist of the problems that the patient must live with or the surgeon has to deal with after the initial period of convalescence has long passed. Bladder neck contracture, urethral stricture, persistent urgency or dysuria and retreatment constitute the long-term complications for all procedures. Cases with large glands may be particularly susceptible to long-term complications given the long duration of endoscopic urethral manipulation. Use of smaller sized scopes for pure vaporization techniques may be an advantage if the overall procedure time is also reduced. As per existing literature, PVP has the highest cumulative late complications, consisting of the bladder neck contracture, surgical re-intervention and transient dysuria.[53,10] However, despite minor differences and some trends toward safety profiles, overall there is insufficient evidence for making any judgments regarding long-term complications. Ahyai *et al.* suggest, there is no significant difference in the long-term morbidity of any of the endoscopic procedures presently.[10] As more and long-term data gets collected we may be able to evaluate better in the future with focused studies. Presently one has to contend with data available from individual non-comparative studies.

Sexual/erectile dysfunction

Briganti *et al.* demonstrated no clinical significant difference between the degree of retrograde ejaculation caused by TURP and HoLEP in a prospective randomized trial.[54] Furthermore, there was no significant difference between the deterioration of IIEF orgasmic function domain due to retrograde ejaculation in TURP and HoLEP groups. Overall minor improvement in the erectile function was noted in both groups. Similarly, PVP and bipolar TURP have been shown to have minimal impact on the sexual function.[55-57] Following PVP, a relative preservation of retrograde ejaculation has been shown by some authors compared with standard TURP,[58,16] but the reasons remain unexplained so far. There are other studies, which conflict these results on preservation of retrograde ejaculation.[59]

Effect of size and shape of gland

For vary large glands (>150 g) HoLEP may presently be considered as the best endoscopic alternative to open prostatectomy at centers where the expertise is available.[60,61] It has been shown that the resection efficiency for HoLEP increases linearly with the increase in size of the gland.[62] PVP with higher power settings (180 W) has shown some encouraging early results,[63] but still very large glands may presently be considered out of the purview of pure vaporization techniques. Vaporization enucleation/ resection combining benefits of hemostasis of PVP laser with enucleation technique of HoLEP may be options for further research.[64] Similarly, bipolar TURP for enucleation has also been tried with reasonable results.[44]

Though 5 alpha reductase inhibitors (5-ARIs) have been shown to reduce microvessel density in the suburethral zone of prostate as per 2010 AUA BPH guidelines,[65] the evidence is insufficient for recommending regular use of 5-ARIs before TURP to reduce intraoperative bleeding. Reduction in the need for blood transfusions has not been reported. However, a positive correlation between blood loss and resection weight in finasteride treated patients does

exist. The duration for which 5-ARIs are recommended must be balanced against cost and adverse effect profile to optimize the benefit.

Shape of the gland may be a minor concern particularly at the apex and bladder neck. Overhanging lobes, projecting distally beyond the verumontanum, put the external sphincter at risk. Holmium laser with its penetration depth of only 0.4 mm and cutting from distal to proximal direction is theoretically the best bet to save external sphincter in such situations. However, surgeon's expertise counts as a major factor other than the procedure opted for. Intravesical protrusions of the lateral lobe or median lobe are perhaps more easily dealt with traditional cutting with loops as in TURP or bipolar TURP. It also theoretically saves ureteric orifices better because of the nature of direction of cutting.

Simultaneous management of stones

HoLEP procedure can easily be combined for holmium laser lithotripsy for simultaneous management of vesical stones.[66] Laser for PVP is not a pulsed laser and unsuitable for stone fragmentation. Similarly, one has to make do with the use of other form of energy for stone fragmentation like holmium laser or pneumatic lithotripsy during TURP or TURIS.

Coagulation disorders

Cases of large glands with coagulation disorders or on anti-coagulation therapy pose a great challenge. Most studies focusing on coagulation disorders have studied upon relatively small glands. Both PVP and HoLEP have been shown to be relatively more effective in patients on anti-coagulant treatment.[67-70] As per EAU guidelines PVP (Grade of recommendation: B, Level of evidence: 4) and HoLEP (Grade of recommendation: B, Level of evidence: 2b) can be offered to patients using anti-coagulation medication.[47] Diode laser, though not a standard treatment option for BPE considering its higher retreatment rate and transitory or permanent incontinence rate, provides a viable option for patients on anti-coagulation (Grade of recommendation: C, Level of evidence: 1b). Bipolar TURP is yet to prove itself in terms of reduced blood loss in-patients on anti-coagulants.[71]

Which procedure is faster?

For large glands duration of surgery may become a concern, especially in patients with various comorbidities with risks of increased anesthesia time as well as problems of irrigant absorption, hemolysis, TUR syndrome etc. HoLEP and PVP have been considered by many as procedures requiring long operation time compared with TURP/bipolar TURP/TUVRP.[72] Interestingly in one study, when compared objectively using a match pair analysis for the amount of tissue resected in TURP, open prostatectomy and HoLEP, it was found that the resection speed was statistically significantly faster for HoLEP than TURP (0.61 vs. 0.51 g/min and 62 vs. 73 min, $P < 0.01$).[73] This included the time needed for morcellation during HoLEP. The time speed for HoLEP was comparable with those achieved with simple open prostatectomy (0.92 vs. 1.0 g/min and 101 vs. 90 min, respectively, $P \geq 0.21$).

Redo procedure

Redo procedures in early post-operative period have been reported in early experiences with PVP.[74] Furthermore few patients may require a redo procedure over long-term due to regrowth of adenoma. These cases have frequently been dealt with TURP or more recently with bipolar TURP. However, laser treatments have also now been shown to be feasible for redo cases.[75] HoLEP has been shown to have favorable durable results in a wide range of prostate volumes, especially for gland size >100 g with virtually no erosion of symptomatic or urodynamic results over time up to 7 years.[26,28,76]

Learning curve and cost

HoLEP technique is perceived to have a longer and steeper learning curve compared with other techniques;[77-79] though, there is no yet comparable clinical standard for the learning curve of established procedures like TURP or open prostatectomy in the existing literature, mentored or otherwise. Learning curve for HoLEP has been suggested to be 20-30 cases.[80] In a systematic review of cases performed at their center, Shah *et al.* reported that an endourologist in experienced with HoLEP can perform the procedure with reasonable efficiency after about 50 cases with an outcome comparable with that of experts.[77] Dusing *et al.* Reviewed their experience of HoLEP in 949 consecutive cases over 9 years and reported a constant improvement in overall lasing time for glands >100 g over the study duration.[81] They also reported that in contrast to glands of other sizes, overall enucleation was significantly more efficient in larger than in medium and small glands (1.71 vs. 0.77 g/min, $P < 0.001$). The learning curve for bipolar TURP is perceived to be lower because of the similarity of resection technique to standard monopolar TURP. One recent study, which used enucleation resection technique has hinted at a learning curve of about 30 cases with this technique when efficiency of enucleation and rate of conversion to standard monopolar TURP stabilize.[82] Added perceiveddisadvantages of laser techniques include additional set-up cost and recurrent cost for laser fibers.[83] However, direct comparison of costs is difficult because both holmium and bipolar energy find many other usages in the operation theater. The PVP procedure using KTP laser has a distinct disadvantage on this front with its fiber also being a single use disposable. As regard overall surgical time and hospital stay, present data favors HoLEP over PVP or bipolar resection particularly for large glands.[73]

OTHER PROCEDURES AND LASERS

Laser procedures continue to evolve by day and many surgeons have tried combining properties of one laser with

technique of resection of the other. Vaporization resection using the high power green light laser has been described with good early results.[64] Thulium laser and diode laser have also been used at relatively few centers in the world and have shown reasonable results. Thulium laser has properties very similar to holmium laser and enucleation with it has been proven to be safe, effective and prostate size independent.[84] However, these newer lasers are yet to achieve mass appeal and usage given their limited usability only for prostate resection unlike holmium laser.

As with other procedures bipolar TURP is also evolving with integration of this energy source with resection techniques of others. Early experience with the bipolar TURIS enucleation showed equivalent short term outcomes, but with somewhat longer surgical time and more need for post-operative irrigation.[44,22] TURIS vaporization technique is also coming up using a button shaped bipolar electrode for vaporization, somewhat similar to PVP and has shown promising results, but may be a time consuming procedure for large glands.[85] Bipolar TURP has also been studied in combination with the high-intensity diode laser as an alternative for gland sizes larger than 80 g.[86] In this retrospective study, the authors found a shorter catheterization time and hospital stay in favor of the combination group ($P < 0.001$), though the TURP group had significantly shorter operative time. Similarly, enucleation-morcellation technique of HoLEP has been tried using the PVP laser for large glands, hoping to utilize the blood less advantage of PVP laser while retaining the efficacy of enucleation technique for large glands with reasonable early results.[87] However, larger well-structured studies at multiple centers can only provide answers in the near future.

Laparascopic prostatectomy and robotic assisted prostatectomy remain viable options for large prostates at centers where expertise is available,[88] but cannot presently be recommended as standard endoscopic minimally invasiveoptions.

CURRENT STANDARDS AND GUIDELINES

As per the AUA clinical guideline[73,89] and CUA clinical guideline[90] for management of BPE, the choices of surgical approach (open or endoscopic and energy source-electrocautery versus laser) are technical decisions based on the patient's prostate size, the individual surgeon's judgment and the patient's comorbidities.

For larger prostates, the choice of procedure is more difficult than for small glands because of no benchmark procedure to compare with. Most guidelines remain silent on the procedure of choice for large glands. Open prostatectomy was considered the procedure of choice for prostate size more than 80-100 g as recently as the last EAU guidelines in 2004, with its associated more morbidity and longer catheterization time and hospital stay.[46] It is still recommended as the standard therapy for large glands as per EAU guidelines, 2012.[47] All endoscopic procedures remain alternative to open prostatectomy where expertise and technology are available. Irrespective of the final choice of modality, information on the potential benefits and harms of surgical treatment alternatives for BPE should be explained to patients with individualization of treatment based upon patient's comorbidities, surgeon expertise, gland size and associated complications such as stones, renal failure, very large median lobe, etc.

CONCLUSION

In conclusion, it may be reiterated that for large prostate adenoma (>60 g) bipolar TURP, HoLEP and PVP provide equivalent outcomes. For extremely large glands, HoLEP is a very efficacious endoscopic alternative to open prostatectomy and has proved its versatility irrespective of the size of the prostate. As of now, HoLEP technique has been best studied and has shown equal or better outcomes over more than a decade. It can be used for simultaneous management of stones, but has a longer learning curve. Other techniques are yet to substantiate their results over the long-term. Bipolar TURP and PVP are attractive with a minimal learning curves and proven short term results. Surgical management of large prostate should be individualized based upon patient's comorbidities and surgeon's expertise.

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