Title

Randomized trial of bipolar resection vs. Holmium laser enucleation vs. Greenlight laser vapo-enucleation of the prostate for treatment of large sized benign prostate obstruction; 3-years outcome

By

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Abstract

Purpose

To assess the non-inferiority of transurethral resection in saline (TURis) and Greenlight laser Vapo-Enucleation of the prostate (GL.PVEP) to Holmium laser enucleation of the prostate (HoLEP) for controlling lower urinary tract symptoms secondary to large sized BPH with comparable 3-years-retreatment rate.

Methods

Eligible patients with BPH (80-150ml) were randomly assigned to one of the intervention groups.

Non-inferiority of retreatment rate was evaluated using a 1-sided test at 5% level of significance.

Results

At time of analysis, 60 GL.PVEP, 60 HoLEP and 62 TURis procedures were included.

Perioperative parameters were comparable between groups however; longer operative time (92+32, 73+30 and 83+28min, P=0.005) and less operative efficiency (1.2+0.4, 1.7+0.7 and 1.4+0.6gm/min, P=0.000) have been reported in GL.PVEP vs. HoLEP and TURis respectively.

Perioperative complications and need for auxiliary procedures were similar in the three groups however significantly higher rate of capsular violation 5, 8% was reported in TURis group compared to 1, 1.6% in GL.PVEP and none in HoLEP, p=0.01.

Significantly longer hospital-stay, catheter-time and higher rate of blood transfusion were reported following TURis.

There was significant comparable improvement in IPSS in 3 groups at different follow-up points.

At 3 years, retreatment for recurrent BOO was more after GL.PVEP and TURis. More redo surgeries for recurrent obstructing prostate adenoma was reported after GL.PVEP (4, 6.7%) and TURis (6, 9.7%) in comparison to HoLEP (none) (P=0.04).

Conclusion

The perioperative outcome of GL.PVEP and HoLEP surpasses that of TURIS for treatment of large sized prostate with significantly more operative time with GL.PVEP.

The three techniques achieve good functional outcome however 3-years retreatment rate following TURIS and GL.PVEP was inferior to HoLEP.

Introduction

Benign prostatic enlargement (BPE) leads to bothersome lower urinary tract symptoms (LUTS) in elderly males with significant negative impact on their daily life. For years, monopolar transurethral resection of the prostate (M-TURP) was considered worldwide standard surgical treatment for small to moderate sized benign prostate enlargement (BPE). Albeit higher morbidity and retreatment rate limit the use of M-TURP for treatment of large sized prostate [1].

Since first introduction of Holmium laser enucleation of the prostate (HoLEP) by Peter Gilling on 1998 [2], there was a great enthusiasm for use of endoscopic enucleation of the prostate as a minimally invasive approach suitable for all size prostate. This enthusiasm was supported by high quality evidence confirming its safety, efficacy and well-proven durability [3]. Therefore, HoLEP is currently guidelines endorsed standard treatment for large sized BPE [4, 5]. However the wide spread use of HoLEP and other transurethral enucleation procedures was hindered by learning difficulties [6]. Minimally invasive contenders of endoscopic enucleation of the prostate includes resection and vaporization techniques. Urologists would consider these techniques easier for learning than enucleation procedures. Enhancements of technology supporting these techniques open the door for these techniques to challenge large sized prostate.

In contrast to M-TURP, where prolonged resection should be avoided due to risk of transurethral resection (TUR) syndrome, transurethral resection of prostate in saline (TURis), particularly in large (over 80 grams) prostates is appealing step forward for urologist.

Prostate vaporization using greenlight laser (532-nm laser) has been limited to small and moderate BPE, based on data showing high retreatment rate associated with large sized prostate surface vaporization [7]. Greenlight laser photoselective vapo-enucleation of the prostate (GL.PVEP) using 180Watt power to vaporize partially enucleated prostate adenoma has been

shown to be non-inferior to HoLEP in control of lower urinary tract symptoms (LUTs) secondary to large BPE at one year however no long-term data was reported [8].

In the current trial, the tested hypothesis is that TURis and GL.PVEP are non-inferior to HoLEP in controlling LUTs secondary to large sized BPE with comparable retreatment rate at 3 years.

Patients and methods

After institutional review board approval (MS/16.04.79), eligible patients presented for intervention at the prostate unit were asked to participate in this trial after signing an informed consent form. ClinicalTrials.gov, NCT02332538.

Patients having refractory LUTS secondary to BPO or patients with acute urine retention secondary to BPO who failed medical treatment were eligible for inclusion in this study. Patients with TRUS estimated prostate volume between 80 and 150ml were only included. Patients were excluded from this trial if they have neurological disorder, bleeding tendency, ongoing anticoagulants or antiplatelet medications. Patients with history of previous prostate surgery and patients diagnosed with prostate cancer were excluded.

Patients were randomly allocated to one of the 3 treatment options in 1:1:1 ratio. Random allocation was done by stratified blocked randomization using computer generated random tables. Preoperative catheterization was used as stratifying criterion to ensure parity among treatment groups.

Urinary symptoms assessment by IPSS (international prostate symptom score), QOL (quality of life), Uroflowmetry and PVR (post void residual urine) were performed at enrollment and 1, 4, 12, 24 and 36 months postoperatively. PSA (prostate specific antigen) was done at enrollment, 4 months and then annually.

Erectile function (EF) assessment using IIEF-5 score (international index of erectile function) was done at enrollment, 4 months and then annually.

Intervention

After initial cystoscopy, patients were offered assigned intervention. All procedures were performed by dedicated expert surgeons who passed learning curve of each procedure, each surgeon had an experience of at least 300 similar procedures done before the start of the trial.

GL.PVEP was performed as previously described [9] with vaporization of partially enucleated adenoma. Green light laser system (AMS, Minnetonka, MN) with 180 Watt (XPS^{TM}) and side-firing fiber (MoXy^{TM}).

TURis was performed classically according to Mauermayer`s technique. Olympus UES-40 surgmaster generator (Olympus Europe, Hamburg, Germany) using power of 280 Watt for resection and 140 Watt for coagulation were used.

HoLEP was performed as previously described [10]. The equipment used includes a 100W Holmium: YAG laser (Versapulse, Lumenis Inc., Santa Clara, CA, USA), 550-um end-firing flexible fiber and Piranha tissue morcellator with reusable blades (Richard Wolf Inc.).

A 22Fr 3-way Foley`s catheter was inserted, and intermittent bladder irrigation was delivered. Catheter was taken out 6 hours after cessation of bladder irrigation.

Outcome measures

The primary endpoint of this study is the need for retreatment for bladder outlet obstruction (BOO) at 3 years. Retreatment includes medical (alpha blockers; non-bladder targeting medicines) or interventional treatment for recurring prostate adenoma, bladder neck contracture and urethral stricture.

Secondary outcome measures include, operative parameters as operative efficiency; preoperative prostate weight divided by operative time (from insertion until removal of the resectoscope) in gm/min, need for auxiliary measures (Monopolar TUR), perioperative blood changes, hospital stay and time to catheter removal.

Postoperative dysuria was assessed by reporting pain during voiding on dysuria visual analogue scale (DVAS; zero to 10)[8] one month after catheter removal. Peri-procedure adverse events were reported (Clavien classification) and compared. IPSS, QOL, Q.max (peak urine flow rate) and PVR were reported. PSA level was measured at 4 and 12 months, percent change of mean postoperative PSA (preoperative PSA minus mean postoperative PSA divided by preoperative PSA) was estimated and compared. EF changes among sexually active men was reported as per IIEF-5 score at 4 and 12 months postoperatively and compared.

Patients who reported persistent urine leak at 12 months was examined by the standardized 1-hour pad test. Urine incontinence was objectively reported as grade 0 to 4 [11].

Sample size Data analysis

We hypothesized that GL.PVEP and TURis would control LUTs secondary to large sized BPE with comparable retreatment rate to HoLEP at 3 years. Type 1 statistical error less than 5% and type 2 statistical error less than 20% were considered. Furthermore, based on previous reports [12, 13] assessing medical (22%) and surgical (9.3%) retreatment after BPE surgery (resection /vaporization) with expected 5% annual dropout rate; a total sample size of 180 patients was considered.

Data analysis was conducted using SPSS® 20 for Mac. Descriptive statistics were reported in terms of number (percentages) or medians (range)/means (SD) for categorical and continuous variables, respectively. The Chi-Square test was used to compare categorical variables and ANOVA test with post HOC analysis using Bonferroni or Games-Howell tests were used as appropriate to compare continuous variables.

Results

Between March 2014 and July 2016; GL.PVEP was performed in 60, HoLEP in 60 and TURis in 62 legible patients. Baseline patients` demographics, prostate size and indications of intervention were comparable. All perioperative parameters were comparable between groups (**table 1**) however; longer operative time (92+32, 73+30 and 83+28 min, P=0.005) and less operative efficiency (1.2+0.4, 1.7+0.7 and 1.4+0.6gm/min, P<0.001) have been reported in GL.PVEP vs. HoLEP and TURis respectively. Significantly longer hospital stay and catheter time were reported following TURis **table 1**.

All perioperative complications and need for conversion were similar in the three groups however significantly higher rate of capsular violation 5 (8%) was reported in TURis group compared to 1 (1.6%) in GL.PVEP and none in HoLEP, P=0.01.

Furthermore, significantly more drop in post-operative Hemoglobin and haematocrit value was reported following TURis with subsequent higher rate of blood transfusion was depicted in TURis group **table 2**.

Figure 1 depicts evaluable patients at each follow up. At one month, patients reported mean DVAS 4.2+1.6, 3+1.6 and 3.3+1.7 (P=0.12) following GL.PVEP, HoLEP and TURis respectively. There was no statistically significant difference in the mean IPSS at 3 years between the 3 groups. The IPSS mean difference between HoLEP and GL.PVEP was <0.001 (SE 1.5, 95%CI -3.8:3.9, P=1) and between HoLEP and TURis was -0.95 (SE 1.3, 95%CI -4.1:2.8, P=0.73). The mean IPSS obstructive subdomain score was significantly lower in HoLEP

compared to GL.PVEP at one year, mean difference was -1.6 (SE 0.55, 95%CI 0.27:2.9, P=0.014). The mean Q.max was significantly higher in HoLEP than TURis at 2 years, mean difference was 7.2 (SE 2.8, 95%CI 0.55:14, P=0.031). Otherwise, there were no statistically significant differences (P>0.05) in IPSS & its subdomains, QOL, Q.max and PVR between the 3 groups at all reported follow-ups **figure 2.** There were no statistically significant differences in the IIEF-5 between the 3 groups at different follow-ups (**figure 2.g**), with only 76, 52 and 33 patients reported sexual activity at 1, 2 and 3 years respectively. At one year, patients reported ejaculatory dysfunction significantly more following HoLEP (81%) compared to GL.PVEP (62%, P=0.04) and TURis (59%, P=0.01). **Figure 2.i.** depicts changes in the PSA level at different follow ups. At one year, the mean postoperative reduction in PSA was significantly higher in HoLEP 77.8%, (mean difference from GL.PVEP was 24.1%, SE 7.9, 95%CI 4.7:43.6, P=0.01) and (mean difference from TURis was 27%, SE 9.4, 95%CI 4.09:50, P=0.015).

After 3 years, overall retreatment for recurrent BOO was significantly higher following GL.PVEP 16 (26.7%) and TURis 17 (27.4%) in comparison to HoLEP 3 (5%), P=0.03. In comparison to HoLEP, more patients restart alpha blockers therapy after GL.PVEP and TURis (P=0.01) with more redo surgeries for recurrent obstructing prostate adenoma (P=0.04) were reported (**table 2**). In GL.PVEP, mean energy delivered per ml prostate volume was 4.77+1.42 KJ/ml with no significant correlation with need for retreatment (P=0.9).

There were no reported significant differences in urine incontinence rate following the 3 procedures (**table 2**).

Discussion

Over the past 10 years, evidence is growing, suggesting a superior role for endoscopic enucleation of the prostate in management of large sized BPH, with HoLEP on the top list of these techniques. Despite being endorsed by guidelines for the past 10 years [14], data suggests underutilization of endoscopic enucleation techniques. HoLEP rates were reported as low as 4% of all BPH treating procedures in USA with large regional care gaps exist [15].

A recent systematic review has looked at the available clinical trials assessing the management of patients with large sized prostates more than 80ml [16]. Nine clinical trials were included and data concerning long term efficacy is lacking. The pending concern, does non-enucleation techniques compromise treatment durability in large sized prostate?

Zhu et al, compared bipolar enucleation and resection for management of prostates more than 70ml, their data suggests superior perioperative outcome for enucleation. At 60 months, 76.3% of their patients were evaluable with no depictable difference in need for retreatment, however this study was underpowered to detect long term differences in the retreatment rate [17]. Huang et al reported 30 months data after bipolar resection of prostate for 120 patients with prostate more then 80ml. The mean operative time was 112 minutes and mean time to catheter removal was 83.05 hours with no reported retreatment at 30 months [18]. In a study by Zhang et al, diode laser enucleation of the prostate and bipolar resection had comparable urinary function outcome at 12 months. However, enucleation was associated with less perioperative bleeding, operative time, time to catheter removal and hospital stay. [19] A recent systematic review including a Fourteen comparative studies between bipolar enucleation and resection. Similar to our findings, significantly more hemoglobin loss, more resected tissue, catheter time, hospital stay and PSA reduction were reported after resection [20]. However, only 5 of the included studies were RCTs. Furthermore, all included studies vary significantly in their endpoints and follow up durations and none of them were powered to detect difference in long term retreatment [20].

Endeavors to treat large sized prostate using Greenlight (532nm laser) PVP have been attempted using its different generations. Using the 80Watt KTB laser, disproportional functional outcomes between small and large prostates >80 ml and higher retreatment rate were reported in large glands (23.1 vs. 10.4 %) [7]. With introduction of the 2nd generation HPS 120W, Greenlight PVP was attempted again in large prostates. When treating prostates >80ml Greenlight PVP was equally effective in controlling LUTs at 18 months to open prostatectomy. Despite having much lower prostate volume reduction, greenlight PVP was favoured by higher perioperative safety profile compared to open prostatectomy [21]. Another RCT of Greenlight HPS/120W PVP against HoLEP for prostates >60ml, similar IPSS with significantly higher Q.max and lower PVR were noted in HoLEP. More prostate volume and PSA reduction were noted following HoLEP (78% and 88% respectively) compared to (52% and 60% respectively) in the vaporization group [22]. Long term data on the need of retreatment is missing in both trials.

The advent of the XPS 180W and its renovated MoXy fiber furthers the expectations for Greenlight PVP. A multicenter study assessing long term outcome of Greenlight (180W) PVP for prostates larger than 100ml, redo intervention for recurrent adenoma was 5.4 and 9.3% at 2 and 3 years respectively. The need for retreatment was associated with less energy to prostate

ratio 2.4 vs. 3.4 kJ/ml of prostate (p= 0.02) and less PSA reduction at one year 26 vs. 51% (p = 0.02) [12]. It seems that it is not only a matter of power rather than endpoints of vaporization. This encourages the adoption of the enucleation principle, it seems that with increasing the prostate size, prostate vaporization alone might not be sufficient, and the vapoenucleation/enucleation principle need to be adopted. In a study by McGill group, GL.PVEP was shown to be non-inferior to HoLEP in controlling LUTs at one year. However, this study was limited by including wide range of prostate sizes (40 to 150ml) and lack of long term data [8].

In the current study, surgical retreatment for recurrent adenoma was 6.7% following GL.PVEP compared to 9.3% in Meskawi study [12]. Furthermore, 4.77 KJ were delivered for each ml of prostate tissue during G.PVEP in our study with no difference among retreated group. No redo surgery for recurrent adenoma was reported after HoLEP in the current study. Large single center study has shown that for recurrent adenoma, the 10 years reoperation-free probability was 95% after HoLEP [23]. Gilling et al reported the 7 years outcome of their RCT of HoLEP vs. M.TURP, no retreatment in HoLEP arm vs. 3 out of 17 evaluable patients (17.6%) required re-operation for recurrent adenoma in the TURP arm [24]. Gilling's study included prostates ranging from 40 to 200ml [24]. In the current study the need for re-operation for recurrent adenoma in the TURis arm was 9.7%. Zhu et al reported 6.6% re-operation for recurrent adenoma after TURis in 30 evaluable patients at 60 months after surgery [17].

Patients seeking surgical intervention for BPE related LUTs are not willing to keep lifelong commitment to medical therapy. Furthermore, reuse of BPE treating medications after surgery represents a significant burden for patients and insurers nevertheless it is poorly reported in clinical trials. Thus, the effectiveness of a procedure should include a measure of whether medication therapy was used after surgery [13]. The rate of reuse of alpha blockers therapy was 20, 3.3 and 17.7% following GL.PVEP, HoLEP and TURis respectively and the difference is statistically favoring HoLEP.

GL.PVEP has early promising results, with enthusiasm in vaporizing partially enucleated adenoma with highest power of the greenlight laser 180W rather than complete detachment and intravesical morcellation as a second step [8]. The procedure resembles HoLEP in the pre-morcellation era, where mushroom technique was adopted with resection of partially enucleated prostate adenoma [25]. However, in GL.PVEP the enucleation is much less to keep the adenoma vascularized to maintain vaporization efficiency of the Greenlight laser. The procedure ends up

by HoLEP like cavity in small to moderate sized prostate, however less tissue is removed, and more operative time is needed when tackling larger glands with more need for retreatment. Our data support Greenlight laser to move for pure enucleation when tackling large glands [26].

BPE interventions are growing and prostates larger than 80ml are always a challenge. Aquablation has been introduced, data on 80 to 150ml prostate showing promising early results. However, a reported 38% PSA reduction at one year may question the long-term durability in such gland size [27]. Prostate artery embolization has been tried as well for prostates >80ml with short term clinical improvement and no long term data is available [28].

Our study has potential limitations, 1st being single center study, 2nd is limiting the included prostate size to less than 150ml. However, we felt from the start that pure enucleation is the safest approach for the huge glands. Lastly that this study is powered only for single outcome measure. Nevertheless, to the best of our knowledge this is the only study in the literature comparing the 3 techniques looking at the 3 years retreatment rate as primary outcome.

Eventually, our data suggests endoscopic enucleation, namely HoLEP, followed by intravesical morcellation to be the treatment with the best long-term retreatment rate. Data could be extrapolated to other energies attempting HoLEP principles.

Conclusion

The perioperative outcome of GL.PVEP and HoLEP surpasses that of TURis for treatment of large sized prostate with significantly more operative time with GL.PVEP.

The three techniques achieve good functional outcome however 3-years retreatment rate following TURis and GL.PVEP was inferior to HoLEP.

Conflicts of Interest

None declared

References

1. Reich, O., Gratzke, C., Bachmann, A. et al.: Morbidity, mortality and early outcome of transurethral resection of the prostate: a prospective multicenter evaluation of 10,654 patients. J Urol, **180:** 246, 2008
2. Tan, A. H., Gilling, P. J., Kennett, K. M. et al.: Long-term results of high-power holmium laser vaporization (ablation) of the prostate. BJU Int, **92:** 707, 2003
3. Cornu, J. N., 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, 2014
4. American-Urological-Association.: Guideline on the management of benign prostatic hyperplasia (BPH). vol. 2012, p. Results of the Treatment Outcomes Analyses, 2010
5. Gravas, T. B., A. Bachmann, M. Drake, M. Gacci, C. Gratzke, S. Madersbacher, C. Mamoulakis, K.A.O. Tikkinen: Guidelines on the Management of Non-Neurogenic Male

Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO): European association of Urology, vol. 2018, 2015

6. Elshal, A. M., Nabeeh, H., Eldemerdash, Y. et al.: Prospective Assessment of Learning Curve of Holmium Laser Enucleation of the Prostate for Treatment of Benign Prostatic Hyperplasia Using a Multidimensional Approach. J Urol, **197:** 1099, 2017
7. Pfitzenmaier, J., Gilfrich, C., Pritsch, M. et al.: Vaporization of prostates of > or =80 mL using a potassium-titanyl-phosphate laser: midterm-results and comparison with prostates of <80 mL. BJU Int, **102:** 322, 2008
8. Elshal, A. M., Elkoushy, M. A., El-Nahas, A. R. et al.: GreenLight laser (XPS) photoselective vapo-enucleation versus holmium laser enucleation of the prostate for the treatment of symptomatic benign prostatic hyperplasia: a randomized controlled study. J Urol, **193:** 927, 2015
9. Elshal, A. M., Laymon, M., Ghobrial, F. K.: Greenlight (532 nm) Laser (XPS™) Photoselective Vapo-Enucleation of the Prostate: Technical Consideration and Short-Term Outcome. Videourology, **30**, 2016
10. Elshal, A. M., Elhilali, M. M.: Holmium Laser Therapy of the Prostate. In: Smith's Textbook of Endourology, 4th ed. Edited by A. D. Smith, G. M. Preminger, L. R. Kavoussi et al.: John Wiley & Sons, Ltd, pp. 1681-1692, 2019
11. Abrams, P., Cardozo, L., Fall, M. et al.: The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology, **61:** 37, 2003
12. Meskawi, M., Hueber, P. A., Valdivieso, R. et al.: Multicenter international experience of 532 nm-laser photo-vaporization with Greenlight XPS in men with large prostates (prostate volume > 100 cc). World J Urol, **35:** 1603, 2017
13. Strope, S. A., Vetter, J., Elliott, S. et al.: Use of Medical Therapy and Success of Laser Surgery and Transurethral Resection of the Prostate for Benign Prostatic Hyperplasia. Urology, **86:** 1115, 2015
14. McVary, K. T., Roehrborn, C. G., Avins, A. l. et al.: American Urological Association Guidelines; Managment of BPH, vol. 2018, 2010

15. Robles, J., Pais, V. M., Jr., Miller, N.: Mind the Gaps: Adoption and Underutilization of Holmium Laser Enucleation of the Prostate (HoLEP) in the United States from 2008-2014. J Endourol, 2019
16. Leonardo, C., Lombardo, R., Cindolo, L. et al.: What is the standard surgical approach to large volume BPE? Systematic review of existing randomized clinical trials. Minerva Urol Nefrol, **72:** 22, 2020
17. Zhu, L., Chen, S., Yang, S. et al.: Electrosurgical enucleation versus bipolar transurethral resection for prostates larger than 70 ml: a prospective, randomized trial with 5-year followup. J Urol, **189:** 1427, 2013
18. Huang, J. Y., Li, S., Yang, Z. H. et al.: Efficacy and Safety of Plasmakinetic Resection of the Prostate in Patients with a Prostate Gland Larger than 80 cc: 30-Month Follow-Up Results. J Endourol, **29:** 925, 2015
19. Zhang, J., Wang, X., Zhang, Y. et al.: 1470 nm Diode Laser Enucleation vs Plasmakinetic Resection of the Prostate for Benign Prostatic Hyperplasia: A Randomized Study. J Endourol, **33:** 211, 2019
20. Arcaniolo, D., Manfredi, C., Veccia, A. et al.: Bipolar endoscopic enucleation versus bipolar transurethral resection of the prostate: an ESUT systematic review and cumulative analysis. World J Urol, 2019
21. Skolarikos, A., Papachristou, C., Athanasiadis, G. et al.: Eighteen-month results of a randomized prospective study comparing transurethral photoselective vaporization with transvesical open enucleation for prostatic adenomas greater than 80 cc. J Endourol, **22:** 2333, 2008
22. Elmansy, H., Baazeem, A., Kotb, A. et al.: Holmium laser enucleation versus photoselective vaporization for prostatic adenoma greater than 60 ml: preliminary results of a prospective, randomized clinical trial. J Urol, **188:** 216, 2012
23. Elkoushy, M. A., Elshal, A. M., Elhilali, M. M.: Reoperation After Holmium Laser Enucleation of the Prostate for Management of Benign Prostatic Hyperplasia: Assessment of Risk Factors with Time to Event Analysis. Journal Of Endourology, **29:** 797, 2015
24. Gilling, P. J., Wilson, L. C., King, C. J. et al.: Long-term results of a randomized trial comparing holmium laser enucleation of the prostate and transurethral resection of the prostate: results at 7 years. BJU Int, **109:** 408, 2012

25. Hochreiter, W. W., Thalmann, G. N., Burkhard, F. C. et al.: Holmium laser enucleation of the prostate combined with electrocautery resection: the mushroom technique. J Urol, **168:** 1470, 2002
26. Gomez Sancha, F., Rivera, V. C., Georgiev, G. et al.: Common trend: move to enucleation-Is there a case for GreenLight enucleation? Development and description of the technique. World J Urol, **33:** 539, 2015
27. Bhojani, N., Bidair, M., Zorn, K. C. et al.: Aquablation for Benign Prostatic Hyperplasia in Large Prostates (80-150 cc): 1-Year Results. Urology, **129:** 1, 2019
28. Bhatia, S., Sinha, V. K., Harward, S. et al.: Prostate Artery Embolization in Patients with Prostate Volumes of 80 mL or More: A Single-Institution Retrospective Experience of 93 Patients. J Vasc Interv Radiol, **29:** 1392, 2018

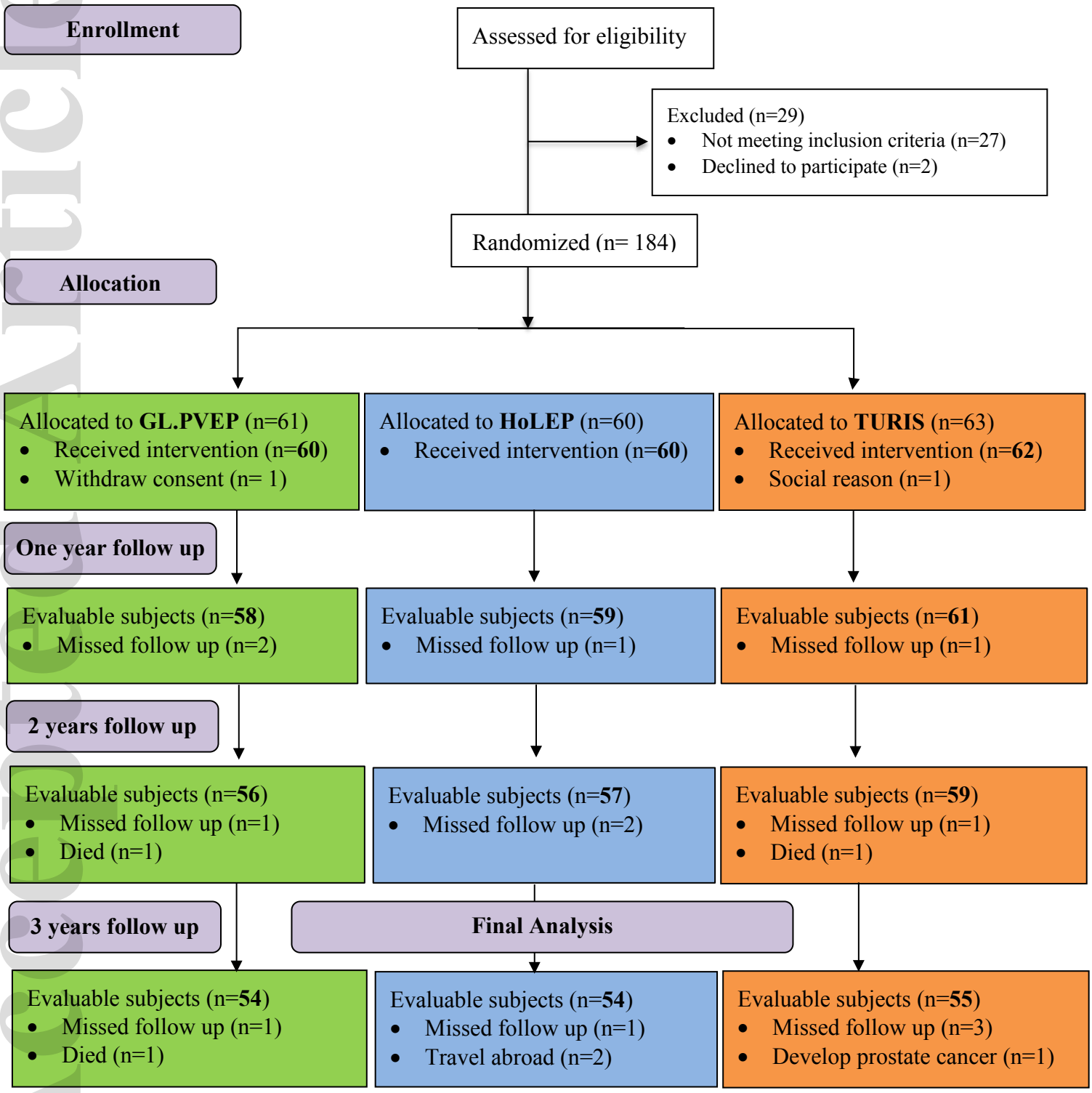
Table 1; perioperative data	GL.PVEP	HoLEP	TURIS	P
Number of patients	60	60	62	
• **Preoperative data**				
Mean age at time of surgery (+SD) years	64.5+6	66.2+7	66.1+7	0.3
Mean PSA (+SD) ng/ml	8.36+3.6	8.2+4.1	8.7+3.8	0.9
Mean TRUS-estimated prostate volume (+SD) ml	103+25	107+21	106+23	0.6
Number of preoperatively catheterized patients (%)	25(42)	32(53)	21(39)	0.09
• **Operative data**				
Mean operative time (min +SD)	92+32	73+30	83+28	**0.005**
Mean operative efficiency (preoperative prostate weight divided by operative time) (gm/min +SD)	1.2+0.4	1.7+0.7	1.4+0.6	**<0.001**
Mean resected prostate tissue weight (gm +SD)	--	80.4+14.9	54.8+21.6	**<0.001**
Mean volume of intraoperative irrigation (+SD) Liters	38+11	37+13	33+14	0.17
• **Auxiliary measures (Monopolar TUR)**				
For hemostasis	1	1	--	0.3
Machine failure	--	--	2	
• **Perioperative outcome**				
Median hospital stay in days (range)	1(1:8)	1(1:5)	2(2:10)	**<0.001**
Median time to catheter removal in days (range)	1(1:5)	1(1:4)	2(2:7)	**0.01**
Median dysuria analogue scale (range) at 2 weeks	4(0:10)	2(0:10)	2(0:10)	0.1
Median HB-Deficit gm/dl (range)	0.5(0.1:2.7)	0.65(0.1:5)	1.2(1:4)	**0.002**
Median HCV-Deficit % (range)	5.7(-12:57)	5.4(-8:90)	9.1(-14:90)	**0.047**

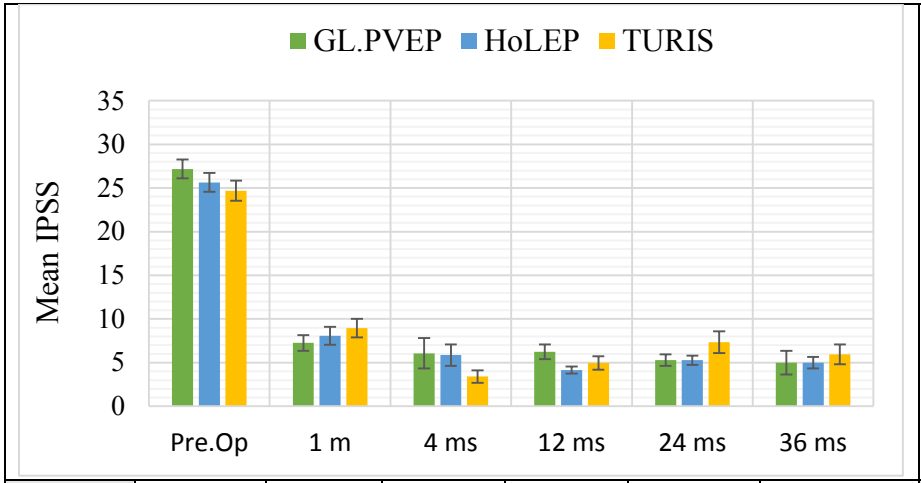
Table 2: Perioperative complications (intraoperative and 1st 30 days)	**Clavien-Dindo grade**	**Management**	**GL.PVEP No (%)**	**HoLEP No (%)**	**TURIS No (%)**	**P**
Capsular violation	I	Prolonged catheter drainage	1 (1.6)	--	5 (8)	**0.01**
Bladder wall injury	I	Prolonged catheter drainage	1 (1.6)	--	--	1
Retention/ re-catheter	I	Catheterization & repeat voiding trial	2 (3.3)	--	1 (1.6)	1
Epididymo-orchitis	II	Antibiotics & lead-subacetate foments	1 (1.6)	--	--	1
Uro-sepsis	II	Systemic antibiotics & ICU measures	1 (1.6)	--	--	1
Anemia necessitating blood transfusion	II	Blood transfusion	--	--	4 (6.5)	**0.03**
Postoperative hematuria			5 (8.3)	4 (6.6)	3 (4.8)	0.1
• Conservative	II	Continuous bladder irrigation	5 (8.3)	3 (5)	3 (4.8)	
• Hemostasis	IIIa	Cystoscopic hemostasis	--	1 (1.6)	--	

Table 3: Delayed postoperative (after 30 days) complications	Clavien-Dindo grade	Management	GL.PVEP No (%)	HoLEP No (%)	TURIS No (%)	P
Recurrent BOO No (%)			16(26.7)	3(5)	17(27.4)	**0.03**
• Residual/ recurrent obstructive LUTs	II	Alpha blockers controlled LUTs	12(20)	2(3.3)	11(17.7)	**0.01**
• LUTs with residual prostate adenoma	IIIa	Redo for adenoma (TURP)	4(6.7)	--	6(9.7)	**0.04**
• Bladder neck contracture	IIIa	Bladder neck incision	--	1(1.6)	--	0.3
Persistent urge urine incontinence	II	anticholinergic medicines	7(11.7)	6(10)	6(9.7)	0.3
Persistent (>/= one year) Stress urine incontinence; patient subjective reporting			4(6.7)	9(15)	2(3.2)	0.2
• 1-hour pad test*, Grade Zero (dry pad)	I	Pelvic floor exercise	2(3.3)	7(11.7)	1(1.6)	
• 1-hour pad test*, Grade I (< 10gm)	I	Pelvic floor exercise	1(1.6)	1(1.6)	--	
• 1-hour pad test*, Grade II (11-50gm)	IIIa	Anti-incontinence surgery	1(1.6)	1(1.6)	--	
• 1-hour pad test*, Grade III (51-100gm)	IIIa	Anti-incontinence surgery	--	--	1(1.6)	

BOO: bladder outlet obstruction, **LUTs**: lower urinary tract symptoms, * Abrams P et al 2003

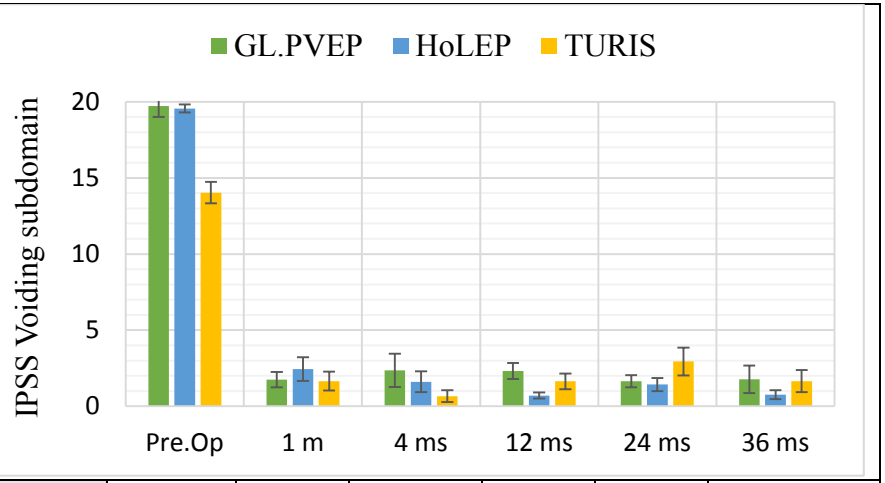
Figure 1: Study`s CONSORT flow chart





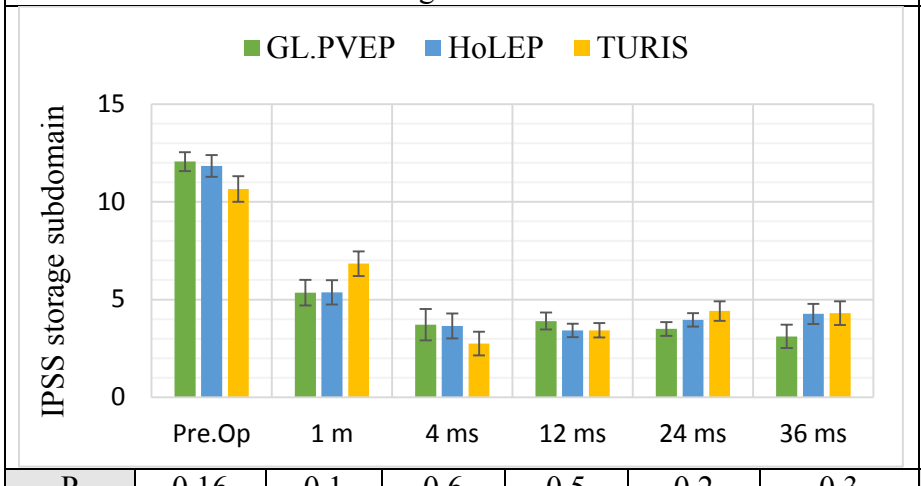
P	0.26	0.4	0.3	0.11	0.13	0.7

Figure 2.a.



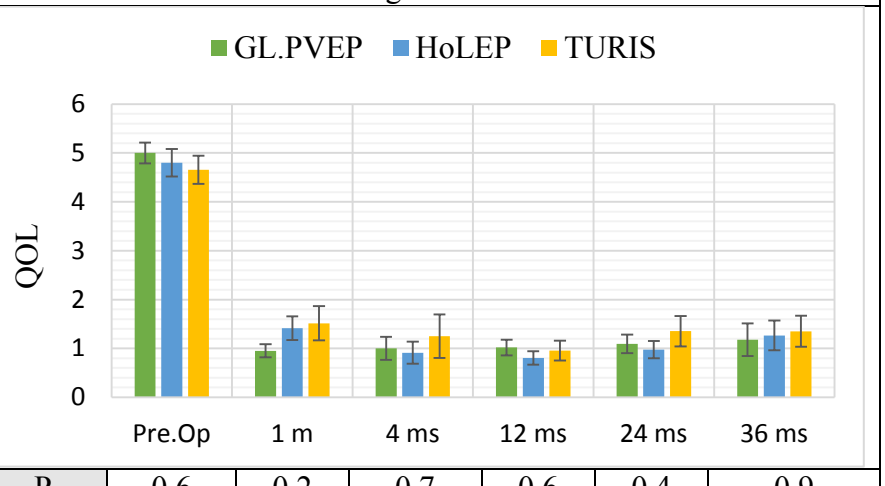
P	0.5	0.6	0.4	0.04	0.16	0.3

Figure 2.b.



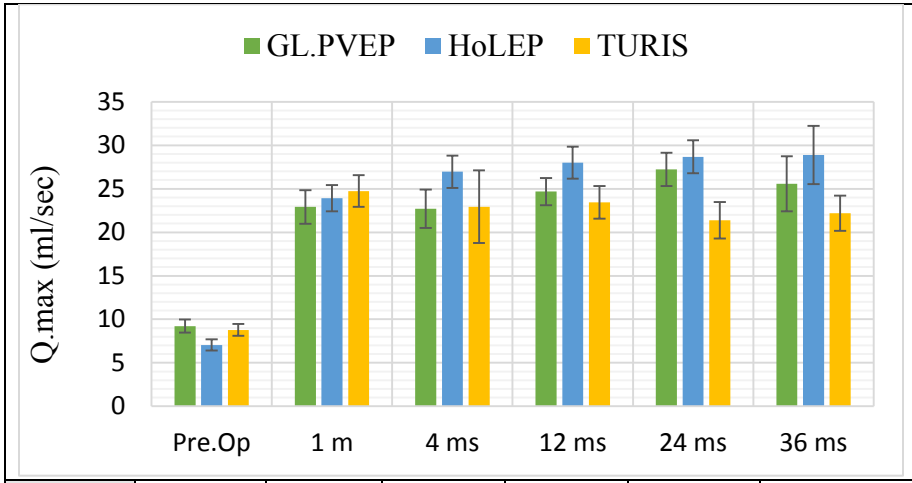
P	0.16	0.1	0.6	0.5	0.2	0.3

Figure 2.c.



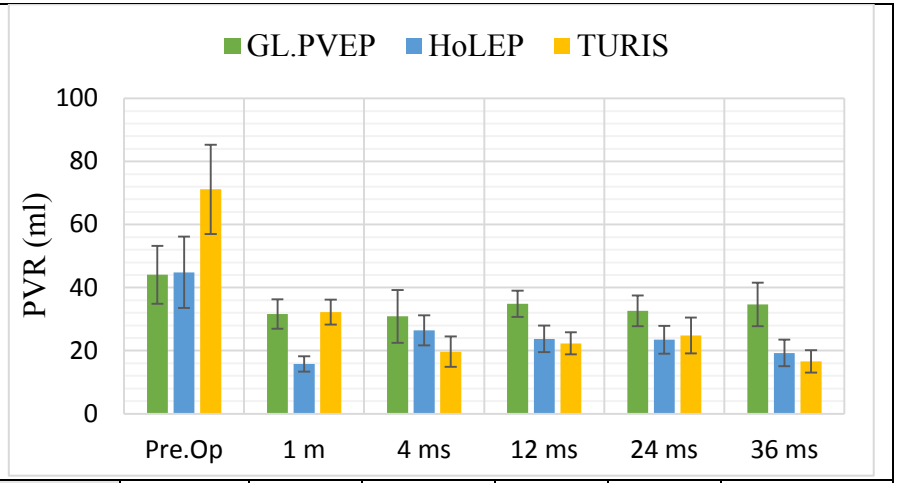
P	0.6	0.2	0.7	0.6	0.4	0.9

Figure 2.d.



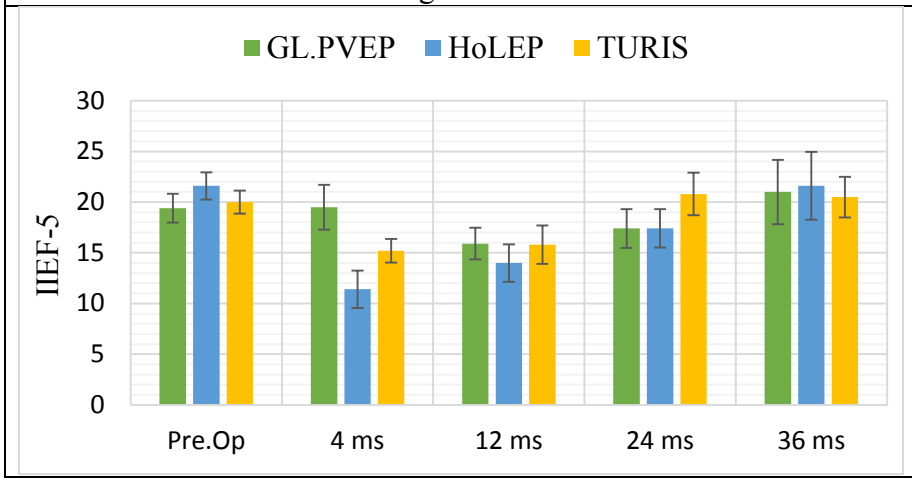
P	0.09	0.7	0.4	0.17	0.03	0.29

Figure 2.e.



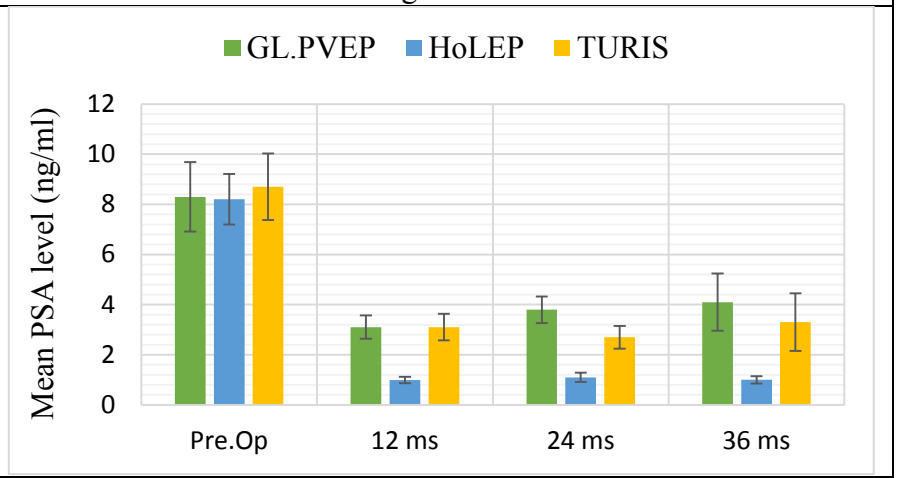
P	0.17	0.05	0.5	0.06	0.35	0.07

Figure 2.f.



P	0.7	0.5	0.9	0.4	0.7

Figure 2.g.



P	0.9	<0.001	0.003	<0.001

Figure 2.i.

Figure 2.a to f; urinary functional outcome measures, **Figure 2.g;** erectile function changes, **Figure 2.i;** PSA level changes over time. **Error bars;** standard errors of the mean. **P;** significance level (P value)