Review Article

Optimising patient outcomes with photoselective vaporization of the prostate (PVP): a review

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Abstract: Benign prostatic hyperplasia (BPH) is a common pathology causing lower urinary tract symptoms (LUTS) and may significantly impact quality of life. While transurethral resection of the prostate (TURP) remains the gold standard treatment, there are many evolving technologies that are gaining popularity. Photoselective vaporization of the prostate (PVP) is one such therapy which has been shown to be non-inferior to TURP. We aimed to review the literature and discuss factors to optimise patient outcomes in the setting of PVP for BPH. A comprehensive search of the electronic databases, including MEDLINE, Embase, Web of Science and The Cochrane Library was performed on articles published after the year 2000. After exclusion, a total of 38 papers were included for review. The evolution of higher powered device has enabled men with larger prostates and those on oral anticoagulation to undergo safely and successfully PVP. Despite continued oral anticoagulation in patients undergoing PVP, the risk of bleeding may be minimised with 5-Alpha Reductase Inhibitor (5-ARI) therapy however further studies are required. Pre-treatment with 5-ARI's does not hinder the procedure however more studies are required to demonstrate a reliable benefit. Current data suggests that success and complication rate is largely influenced by the experience of the operator. Post-operative erectile dysfunction is reported in patients with previously normal function following PVP, however those with a degree of erectile dysfunction pre-operatively may see improvement with alleviation of LUTS.

Keywords: Benign prostatic hyperplasia (BPH); prostate; photoselective vaporization of the prostate (PVP); outcomes; urinary function; sexual function

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Introduction

Benign prostatic hyperplasia (BPH) and resulting lower urinary tract symptoms (LUTS) can have a significant impact on quality of life (1). BPH LUTS affects an estimated 70% of men aged 61–70 years and 90% of those aged 81–90 (2). Traditionally, transurethral resection of the prostate (TURP) has been the gold standard to relieve bladder outlet obstruction (BOO), however the risk of post-operative complications such as haematuria, compromise to sexual or urinary function and TUR syndrome have limited its wide spread use. Alternate surgical therapies have been developed including Photoselective vaporization of the prostate (PVP). PVP techniques have become increasingly popular amongst urologists and have been shown to be non-inferior to TURP with reduction in post-operative complications (3).

The GreenLight^{TM} Laser PVP (Boston Scientific, Malborough, MA, USA) is one such alternative method of surgical intervention of BPH. The GreenLight™ laser functions at a wavelength of 532 nm, which is within the green part of the visible spectrum (4). At this wavelength, the energy of the laser is absorbed strongly by highly vascularised tissue, that is, the prostate filled with haemoglobin rather than water which leads to vaporization of the prostatic tissue. Initially, PVP utilized a 60W potassium titanyl phosphate (KTP) laser (5). Subsequently, a higher-powered laser device was introduced in 2006 utilizing a lithium triborate (LBO) laser. This 120-W high-performance system (HPS) laser came with the objective to provide higher energy output and thus increasing prostate tissue vaporisation within a shorter period of time (6). More recently, a 180 W device was introduced with a subsequent upgrade of XPS-specific (Xcelerated Performance System), MoXy™ liquid-cooled, steel capped fibre. This upgrade allowed the XPS laser to perform vaporization at a faster rate by 50% as well as increasing the laser beam area from 0.28 to 0.44 mm^2 without affecting the actual depth of vaporization (7). With the XPS and MoXy fiber, PVP was reported to have shorter operating and photovaporization time in relation to prostate size (8).

No doubt, care should be used in patient selection. Optimizing patient selection may decrease the prevalence and severity of peri-operative complications and improve outcomes. Since the introduction of PVP technology in the management of BPH in 2002, there have been limited guidelines for optimal patient selection. We aimed to provide a contemporary review of the literature and highlight factors that may alter patient outcomes in the setting of PVP for BPH.

Methods

We performed a comprehensive literature search to review patient and surgical factors that may affect PVP outcomes. A search of the electronic databases, including MEDLINE, Embase, Web of Science and The Cochrane Library, as well as manual bibliography searches were performed during November 2016. An initial search using MESH terms included; photoselective vaporization of the prostate OR PVP, GreenLight laser, erectile function OR erectile dysfunction, BPH OR benign prostatic hyperplasia, outcome*, anti-coagula* was performed. From here our search strategy was as follows. "Photoselective vaporization of the prostate OR PVP" AND "GreenLight laser" was searched and then combined with "OR" with the remaining MESH terms. Search results were limited to those published in English, involving humans and published after the year 2000. Reviews, author replies, case studies, studies using ablation technique other than PVP in the green light spectrum, duplicates as well as others not relating to the topic were excluded. Where a study compared PVP to an alternate intervention, the paper was read and considered for inclusion if it commented on a predictor of PVP outcome such as prostate size. Article screening was performed by two authors (CP, DO) and discrepancies were resolved.

The initial search strategy yielded 340 results, of these 310 were not relevant or suitable for inclusion. In total, 30 papers were reviewed and deemed suitable for inclusion in the current review. Bibliographies were searched for relevant articles with the same exclusion criteria as above and yielded a further 8 papers. The outline of the review is to focus on patient factors and surgical factors considering pre-operative, operative and postoperative perspectives.

Pre-operative factors

5α-reductase inhibitors (5-ARI)

The use of 5α-reductase inhibitors (5-ARI) has been reported to reduce peri-operative haemorrhage in the setting of TURP (9), however whether this benefit translates to PVP is contentious. It is postulated that the mechanism by which 5 ARIs reduced peri-operative haemorrhage is by preventing the conversion of testosterone to dihydrotestosterone (DHT). The reduced DHT suppresses angiogenesis through the downregulation of vascular endothelial growth factor (VEGF). This lowers the mean microvascular vessel density in the sub urethral region and thus decreases bleeding tendency (10-12).

Dutasteride is one such 5-ARI that blocks both type I and type II receptors. Bepple *et al.* performed a double blind, randomised-controlled trial using the 80 W KTP laser. This group demonstrated that patients randomized to dutasteride experienced a trend toward decreased operative time, joules used and blood loss during surgery (13). In this study, subjects receiving 5-ARI commenced the therapy three months preoperatively and continued it for 12 months post-PVP. Additionally, patient perceived level of postoperative haematuria was significantly reduced in the group receiving dutasteride (1 *vs.* 2, P=0.02). These improved peri-operative outcomes on patients administered preoperative dutasteride have been corroborated by recent series. Lee *et al.* identified that preoperative dutasteride therapy is associated with a reduced rate of conversion to

TURP from PVP (3.5% *vs.* 22.5%) (14).

The vaporization effect of PVP is dependent on the vascularity of the target prostatic tissue. Accordingly, the negative impact of 5-ARI therapy prior to PVP must be considered due to decreased angiogenesis and circulating haemoglobin circulating for green light uptake and vaporization. Indeed, Kuntzman *et al.* demonstrated that bloodless cadaver tissue to be less responsive to KTP laser vaporization than living canine tissue (15). Intra-operatively, Strom *et al.* reported that six months of 5-ARI therapy prior to PVP had no effect on operative duration (31±19 *vs.* 32±25 mins), lasering time (13±9.2 *vs.* 13.4±10.3 mins) or energy used (87.1±62.4 *vs.* 91.8±69.7 kJ) (16). Similarly, post-operative functional data appears independent of the presence of 5-ARI therapy. Specifically, Bepple *et al.* reported equivocal BPH QoL (quality of life) score, PSA, PVR, prostate volume and AUA symptom scores were comparable between groups (13). Similar results were reported in a prospective study by Akari *et al.* who demonstrated no significant difference between IPSS scores, PVR and Qmax between patients on or off 5-ARI therapy following 80 W PVP (17). Similar results were reported by Strom *et al.* in patients undergoing 120 W PVP (16).

Accordingly, the current data suggests that 5-ARI therapy may reduce intra-operative bleeding without compromise on laser energy administration and long-term functional outcomes. Despite this, the most recent AUA guidelines concluded that there is insufficient evidence to make a strong recommendation for prescribing 5ARIs prior to all PVP or TURP procedures (18).

Vardenafil

The use of phosphodiesterase inhibitors (PDE5-I) through inhibition of PDE5, increases blood flow to the prostate tissue. It has been postulated that increased blood flow may improve vaporization outcomes through greater uptake of the 532 nm wavelength (19). Buse *et al.* assessed Vardenafil 10 mg the night before the procedure and a further 20 mg one hour before vaporization. This group reported no impact on peri-operative outcomes. Indeed, more robust data is required to identify the role of PDE5-I in PVP and TURP procedures.

Oral anti-coagulants

With the introduction of effective combination medical therapies time to surgery has been significantly delayed (20), and the age of patients requiring surgical management is likely to increase along with comorbidities and subsequent requirement for long term anticoagulation (21) . Traditionally, ongoing anticoagulation is a contraindication to TURP and despite technical developments it is still associated with a blood transfusion rate of 2.0–7.1% (22). PVP is proposed to be safer in the context of active anticoagulation as this creates a thin layer of coagulation in the area of tissue removal, through oxyhaemoglobin uptake of the 532 nm wavelength (23). Although in theory it should be safe to continue anticoagulation, urologists remain cautious of continuing therapy in the perioperative period. To date, many studies have assessed the use of peri-operative anti-coagulation therapy during PVP procedures. Despite this, most studies do not discriminate between those taking antiplatelet agents and anticoagulation agents. Most do not regard these two groups as one and the same, as they are two separate pharmacologic classes.

Tam *et al.* prospectively investigated 48 patients receiving either anti-platelet or anti-coagulation therapy prior to PVP with a 120 W HPS side firing laser (24). Platelet-aggregating inhibitors were continued throughout the perioperative period, while warfarin was stopped for several days before the operation and a heparin infusion was titrated. Of the 48 patients, one case was converted to TURP for intraoperative bleeding and one patient required a post-operative blood transfusion for secondary haematuria and clot retention. Similarly, Ruszat *et al.* compared patients on anti-platelet or anticoagulation therapy to those not on anticoagulation (25). Compared with the control group, overall combined patients on oral anticoagulation had a significantly longer hospital length of stay (3.8±2.7 *vs.* 2.8±1.9 days), were older (74±9 *vs.* 68±9 years) and had a higher ASA score (2.6±0.6 *vs.* 1.8±1.4) (25). This is likely to be expected given comorbidities requiring long term anticoagulation or antiplatelet therapy. Findings of longer hospital length of stay has been corroborated by Lee *et al.* who performed a retrospective review of 384 patients. This group however did identify that there was a significantly higher rate of conversion to TURP in men on anticoagulation compared with those not on anticoagulation (13.5% *vs.* 6.1%) (14). Finally, Woo *et al.* (23) focused on a single agent, investigating the impact of continuing warfarin on patients undergoing PVP using the 120 W Lithium Triborate laser (LBO). Of the 43 included patients, none required conversion to TURP for bleeding. Although two men, with preoperative prostate volumes >100 mL, required prolonged catheterisation for haematuria (96 and 36 hours), no patients required a blood transfusion. Mean postoperative hospital length of stay was 32±38 hours.

Accordingly, current data suggests that it may be safe to continue anticoagulation in patients undergoing PVP for BPH, providing a previously unavailable surgical option for patients who are unable to cease antiplatelet or anti coagulation therapy.

Patient factors

Prostate size

Patients with large prostates present at least two main issues for the clinician offering PVP treatment. The first issue relates to the gross tissue mass that is required to be photovaporized to achieve a satisfactory outcome. Secondly, large prostates have a higher tendency to bleed secondary to highly vascularised prostate with shear stress of larger vessels associated with haemoglobin uptake, bubbling and vaporization (26). Therefore, there are still a number of surgeons who prefer to perform TURP or other treatments for men with larger prostates. Nevertheless, technological advances resulting in higher powered lasers and reduction in operative time, have enabled treatment of men with prostates greater than 220 g with PVP (5).

While a vast majority of recent literature report outcomes of PVP on moderate sized prostate only, there have been an increasing number of series on patients with larger prostate volumes. Emara *et al.* reported that the average PVP performed on 33 patients with prostate volume of at least 80cc with an average operating time of 44 minutes (22–73 minutes) and average of 420 kJ (204–750 kJ). Woo *et al.* (27) published a paper on patients with large prostate glands (>120 cc) treated with mean operating time of 109 minutes (70–162 minutes), average laser time was 86 minutes (56–139 minutes), average energy was 582 kJ (394–825 kJ) with 2–3 fibre replacements. Hueber *et al.* performed a series of 250 cases using 120W HPS and stratified patients' characteristics according to prostate volumes of <60, 60–100 and >100 cc. This study achieved considerable results in treating LUTS regardless of prostate size. However, the outcomes showed longer operating time as well as higher energy usage for larger prostates (>100 cc) and had a 9% rate of retreatment (28). Although the complication rate does not appear to be greater following PVP for larger prostates, it should be noted that the re treatment rate for inadequate removal of tissue is greater for prostates greater than 60 cc (29).

Prostate configuration and respective outcomes following PVP were assessed by Gu *et al.* This group identified that although there was a significant difference in prostate volume between those with tri-lobar and bi-lobar prostates, there was no significant difference in outcomes between the two groups (30).

There is a growing body of literature to support the notion of performing PVP in patients with larger prostates. At present, there are no guidelines that suggest an upper prostate size limit for performing PVP, however it should be noted that these cases may be technically demanding and is not recommended during the learning curve of PVP.

PSA and prostate configuration

PSA has been considered as a predictor of success of PVP. Te *et al.* suggested that there is a significant difference in efficacy in patients with a PSA of ≤6.0 or ≥6.1 ng/mL before PVP (31). Although those with PSA of ≤6.0 ng/mL had significantly superior postoperative urinary flow rate and post void residual, those with total Prostate Specific Antigen (tPSA) ≥6.1 ng/mL still had acceptable outcomes. It is probable that these results reflect larger prostate volumes in the group with the higher tPSA value. Te *et al.* used the 80 W laser and it is possible that greater de-bulking of the larger prostates would be possible with the higher powered 180 W laser now available.

Operative factors

Adequate training and learning curve

The introduction of PVP was accompanied by the requirement of surgeons to develop new skills sets. Accordingly, a significant learning curve has been associated with PVP. Several groups have reported the use of a GreenLight simulator as a training tool to optimise the quality of utilising PVP equipment (32). The training simulation included a 30-minute tutorial by an experienced operator and was subsequently followed by ten sessions of five training modules. The use of a training simulator resulted in improvements in operating times, error rates and instrument costs. Clinically, Misrai *et al.* performed a single surgeon series and reported that 120 consecutive cases were required to optimize operating time (33). In this series, following the learning curve, total energy to prostate tissue efficiency increased over time.

PVP method

To date few studies have compared techniques for PVP. However, for patients with larger prostates, Zorn *et al.* recommended making two initial incision lines to serve as a depth and limit guide (7). This group also recommended using sweep angles of 0, 15, or 30 degrees and sweep speed of 0.5 to 1.0 sweeps/second as this has been shown in bovine models to remove significantly more tissue than faster sweep speeds and angles of 45, 60, and 90 degrees (7,34). Tam *et al.* noted a decrease in urethral stricture rate when the 26 F laser cystoscope was exchanged for a 22.5 F laser cystoscope (24).

Photoselective vaporesection technique was reported by Gong *et al.* using the LBO laser system (Aurora 120 W laser, Realton Corp., Beijing, China) with a front-firing laser rather than side firing (35). This technique is performed with an incision at the distal portion towards the prostate capsule and subsequently expanded transversely and in a retrograde fashion towards the bladder neck in order to remove the median lobe. The operating planes are then resected at 3- and 9-o'clock positions with the aim removing the prostate tissue using similar fashion as resecting the median lobe. For medium sized prostates, this technique is divided in two parts—first by removing the proximal of the prostate, followed by distal portion of the prostate. Limited functional data supporting the use of vaporesection is available.

Photoselective vapor-incision technique (VIT) was reported Azizi introduced using the XPS 180 W system (36). In this method, the description of this surgical approach is similar in fashion to the vaporesection technique, but utilised different types of instruments. This study concluded that the VIT method had a larger amount of adenoma removed in comparison to standard PVP methods. The VIT method had superior functional outcomes in terms of IPSS score, uroflow parameters and greater PSA reduction. However, it had longer laser and operating times and greater energy use.

There are no recent publications regarding anterior prostatic tissue at this stage as the main prostatic tissue causing bladder outlet obstruction are lateral lobes and median lobe of the prostate. However, in the authors' experience, some surgeons tend to avoid anterior prostatic tissue resection due to the possibility of capsular perforation.

Post-operative

Sexual function

The impact of surgical intervention for LUTS on erectile function has been well-documented. TURP has had varying reports ranging from those showing a deterioration in erectile function of up to an overall improvement of 14% (37). As PVP matures, so has the literature surrounding post-PVP erectile function. Advances in laser technologies and power impairs the comparison between series.

Kumar *et al.* assessed the short term effect of PVP on erectile function using the 80 W Laser (38). It was found that those with normal erectile function preoperatively had a significant decrease in erectile function postoperatively, up to one year follow up. Those who had erectile dysfunction pre-operatively however did not have an increased level of dysfunction post operatively. This same group however have since published further data showing no significant impact on erectile function at one year follow up (39). It is possible the results from the newer study reflects greater operator experience and adjustment in technique.

Hossack *et al.* conducted a prospective analysis of the effect of the 120 W LBO laser on erectile function (37). Interestingly they found 30% of men claimed to be sexually inactive at the beginning of the study. These men were significantly older (mean, 75 years) than those who were sexually active (mean, 65 years) and were not included in the erectile dysfunction analysis. Of the men who claimed to be sexually active pre-operatively it was found that the 120 W LBO laser is associated with a major decline in erectile function in 12.4% of men at 3 months and 24% of men at 1 year. Major decline was defined as a change of >5 points in the IIEF 5 (international index of erectile function) score. This being said 8.3% and 6% of men, with pre existing erectile dysfunction, reported significant improvement at 3 and 12 months respectively.

In more recent times, Kumar *et al.* have studied the 120 W LBO laser also. Again they concluded that there was no significant impact on erectile function at 1 year follow up (39). It was not documented whether participants were sexually active pre-operatively. Men were divided into groups A and B, group A being those with an IIEF 5 score >19 and group B <19. This division means that there will be some men with a degree of erectile dysfunction included in group A, which may obscure a real decline in erectile function in men without pre existing dysfunction. Further sub analysis of these men to determine whether those with no reported erectile dysfunction pre-operatively do in fact not have a significant decline post operatively.

Spaliviero *et al.* have reported that the 180W KTP laser did not have a detrimental effect on erectile function (40). This group used the SHIM (Sexual Health Inventory for Men) and was limited by the small sample size. It again was difficult to determine whether those with no erectile dysfunction preoperatively remained that way post operatively from presentation of the data set.

A recent meta-analysis performed by Li *et al.* (41) showed that in direct comparisons, all surgical treatments did not decrease postoperative International Index of Erectile Function (IIEF)-5 score except for PVP. Moreover, patients who underwent Holmium Laser Enucleation of the prostate (HoLEP), Plasmakinetic Enucleation of the Prostate (PKEP), Thulium laser, and TURP had their postoperative erectile function significantly increased.

There is no consensus on the impact of PVP on erectile function. It appears that men who report significant erectile dysfunction pre-operatively, likely secondary to LUTS, may achieve a degree of improvement in erectile function with alleviation of the symptoms. However, men without pre existing erectile dysfunction may experience major dysfunction post operatively. Further investigation into the mechanism underlying erectile dysfunction post PVP for management of LUTS is required.

Post-operative LUTS

It has been documented that between 18% and 50% of patients experience postoperative LUTS post-TURP (42,43). The GOLIATH study investigated 281 patients with benign prostatic obstruction and found the most common Clavian grade 1 adverse events to be storage symptoms, urinary incontinence and bleeding in both patients who had undergone TURP or PVP. Irritative symptoms, pain or discomfort occurred in 16.2% of patients who underwent PVP and 18% of patients who underwent TURP. There was no statistically significant difference between the two groups (P=0.747) (3).

Post-operative storage symptoms are common after PVP or HoLEP (44), however they are typically transient and resolve by one year follow up. Inflammation is thought to be linked to the development of BPH with intra-prostatic inflammatory infiltration found in 43–98% of resected tissue (45,46). Activated T cells contribute to prostatic growth via cytokines. Interleukin-17 (IL-17) augments the production of IL-6 and IL-8 as well as stimulating the expression of COX-2, which is up regulated in macrophages and epithelial cells in BPH (47). It has been postulated that by blocking the pro-inflammatory pathways with non-steroidal anti-inflammatories (NSAIDs), the LUTS associated with BPH may be alleviated. A meta-analysis of NSAIDs for LUTS in the setting of BPH revealed an improvement in urinary symptoms and flow measures but the long-term efficacy is not known (47). At present there are no studies investigating the application of this principle to post PVP LUTS, however a study by Kara *et al.* found NSAIDs to be safe and effective for pain management post TURP (48). There is likely to be a similar role post PVP.

Rare complications

Although PVP has been shown to be a safe and effective procedure for the management of BPH, there have been reports of rare but serious complications. The 180 W laser is more powerful than the preceding 80 and 120 W lasers raising concerns regarding safety, however the depth of ablation remains 1-2mm suggesting this is a function of wavelength rather than power (49).

Complications documented following PVP include capsular perforation, damage to the bladder or ureteral orifices and even more rare but serious is the development of a prostatosymphyseal fistula (PSF) leading to urinoma and osteitis pubis (50). This difficult to manage complication is not limited to PVP and has also been documented to occur following TURP (51,52). PSF is rare and as such was not reported in any of the reviewed literature.

Although PVP is a safe and effective procedure for the management of BPH, as is the case for any operation, serious complications can occur. As such it is imperative the operator has undertaken adequate training prior to performing the procedure solo.

Conclusions

Although TURP remains the gold standard for BPH, the introduction of PVP appears to represent an efficacious alternative. The evolution of the higher powered devices has reduced operative time and aided the treatment of patients with larger prostates. Additionally, continuing anti-platelet and anticoagulation therapy appears safe in patients undergoing PVP. Treatment prior to PVP with 5-ARI's reduces the risk of peri-operative haemorrhage without compromise to operative ease. Although not yet instigated for post PVP storage symptoms, NSAIDs are likely to provide relief in the setting of inflammation. PVP continues to evolve as a promising technology for BPH and with the right patient selection and optimisation may improve patient outcomes.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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