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Complete List of Authors:	Lai, Shicong; Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China , ; Department of Urology, Beijing Hospital of the Ministry of Health, Beijing 100730, China, Peng, Panxin; Peking University China-Japan Friendship School of Clinical Medicine, Beijing 100029, China; China-Japan Friendship Hospital, Department of Urology Diao, Tongxiang; Beijing Hospital, National Center of Gerontology, China; Peking university fifth school of clinical medicine Hou, Huimin; Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China; Beijing Hospital, National Center of Gerontology, China Wang, Xuan; Beijing Hospital, National Center of Gerontology, China Zhang, Wei; Beijing Hospital, National Center of Gerontology, China; Peking university fifth school of clinical medicine Liu, Ming; Beijing Hospital, National Center of Gerontology, China Zhang, Yaoguang; Beijing Hospital, National Center of Gerontology, China Wang, Jianye; Beijing Hospital, National Center of Gerontology, China
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Photoselective Green-light Laser Vaporisation of the Prostate Versus Traditional Transurethral Resection of The Prostate for Benign Prostatic Hyperplasia: A Systematic Review and updated Meta-Analysis

Shi-Cong Lai[1,2], Pan-xin Peng[3,4], Tong-Xiang Diao[2,5], Hui-Min Hou[1,2], Xuan Wang[2], Wei Zhang[2,5], Ming Liu[2], Yao-Guang Zhang[2], Jian-Ye Wang[2]*

[1] Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China

[2] Beijing Hospital, National Center of Gerontology, China

[3] Peking University China-Japan Friendship School of Clinical Medicine, Beijing 100029, China

[4] Department of Urology, China-Japan Friendship Hospital, Beijing 100029, China

[5] Peking university fifth school of clinical medicine

 # Shi-Cong Lai and Pan-xin Peng contributed as the co-first author

*** Correspondence author: Jian-Ye Wang**

5. Address for correspondence:

Jian-Ye Wang, No.1 Da Hua Road, Dong Dan, Beijing 100730, P.R. China

Email: **wangjy@bjhmoh.cn**

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Abstract:

Objective To assess the overall efficacy and safety of green-light laser photoselective vaporisation of the prostate (PVP) compared with transurethral resection of the prostate (TURP) for the treatment of lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH). **Methods** A systematic search was performed from the biomedical databases including PubMed, EMBASE, and Cochrane Library. We followed the search strategy based on Preferred Reporting Items for Systematic Reviews and Meta-analysis statement when examining the literature. Outcomes reviewed including perioperative parameters, complications rates and functional outcomes. **Results** Twenty two publications involving 19 different prospective Clinical Trials with a total of 2665 patients were analyzed. Pooled analysis revealed that PVP was associated with less blood loss, transfusion, clot retention, TUR syndrome, capsular perforation, catheterization time and hospital stay, but with higher re-intervention rate and longer intervention duration (all $P<0.05$). In terms of the long-term functional outcomes, there were no significant difference in International Prostate Symptom Score (IPSS), maximum flow rate (Qmax), quality of life (QoL), postvoid residual (PVR) and International Index of Erectile Function (IIEF-5) between the two groups at the 3- ,24-,36- and 60-month follow-up. Although the Qmax at 6-month, the IPSS and QoL at 12-month follow-up reached a statistically significant difference, they were of no clinical significant difference. **Conclusion** The current analyses indicate that PVP is an effective alternative to TURP for BPH. When compared with TURP, it not only has a similar long-term efficacy in relation to IPSS, Qmax, QoL, PVR and IIEF, but also is

associated with less complications rates.

Keywords: Benign prostatic hyperplasia (BPH), Lower urinary tract symptoms (LUTS), Meta-analysis, Photoselective vaporisation of the prostate (PVP), Transurethral resection of the prostate (TURP)

Strengths and limitations of this study

It was the updated meta-analysis to systematically review the overall efficacy and safety of PVP and TURP for the treatment of LUTS secondary to BPH.

International Index of Erectile Function (IIEF-5) was first used as an outcome to compare the efficacy of these two surgical procedures in the study.

Due to the difference of surgical experience with laser technology, outcome definitions and measurement, heterogeneity among studies were found to be high in several parameters.

Despite a systematic search strategy, the inclusion criteria excluded non-English documents and had language bias.

These limitations notwithstanding, the research can guide the choice for the treatment of LUTS caused by BPH.

INTRODUCTION

Lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) are common medical complaint in aging males，which affects patients normal quality of life (Qol) a lot.[1] Surgical therapy was recommended for patient who were

failed previous medical treatments with 5-alpha-reductase inhibitors and alpha-blockers.[1-2] Since its introduction, Transurethral resection of the prostate (TURP) has been regarded as the "gold standard" surgical therapy for BPH due to its high success rate and low re-intervention rate on long-term follow-up.[3] Whereas more and more evidences indicate this procedure is also associated with high complications rate such as bleeding, urethral strictures, urinary incontinence and transurethral resection (TUR) syndrome.[4-6] Consequently, there is an urgent need to develop other minimally-invasive alternative therapies which might surpass TURP as the new reference standard.

Over last few decades, the laser therapies represented by photoselective vaporization of the prostate (PVP) had been using increasingly.[7-11] This technique is predominantly performed with 532-nm green laser generated by potassium-titanyl-phosphate (KTP) or lithium triborate crystal.[12] Unlike other types of lasers, the green laser is highly absorbed by haemoglobin in the soft tissue, but hardly at all by fluid medium, which leading to better coagulation and lower risk of deeper tissue injuries during vaporization.[13-14] To our knowledge， numerous studies have demonstrated that PVP had a noninferior mid-term clinical efficacy to TURP with respect to the functional results including International Prostate Symptom Score (IPSS), maximum flow rate (Qmax), postvoid residual volume (PVR) and QoL.[15-17] Nevertheless, none of them compared the sexual function and other long-term efficacy results after 24 months follow-up. Consequently, we sought to conduct an updated systematic review and meta-analysis gathering all the high quality information available in the literature to provide stronger evidence to clinicians.

MATERIALS AND METHODS

Literature Search and Article Selection

A comprehensive literature search was performed from the biomedical databases including PubMed, EMBASE, and Cochrane Library by July 2018. The following MeSH terms and free text words were used: benign prostatic hyperplasia, BPH, transurethral resection of the prostate, TURP, green-light laser， vaporization， photoselective vaporization of the prostate and PVP. These search terms were used singly and combination. In addition, hand searches of the references and citation lists of all relevant reviews were performed. The article language was restricted to English. For the literature selection, the search strategy was applied based upon the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement. Randomized controlled trials and methodologically sound prospective studies meeting the following criteria were included: (1) studies comparing the safety and efficacy of PVP versus TURP for surgical treatment of LUTS secondary to BPH; (2) The end points such as treatment-related adverse events and functional outcomes defined by IPSS, Qmax, PVR, Qol and IIEF were available; (3) full text of the study could be accessed.

Literature search, selection, and data extraction were undertaken by 2 reviewers (SL and PP) independently and then cross-checked. Any differences at this stage are resolved through discussion, if necessary, by a majority decision of the reviewers. A flowchart showed that the number of literatures selected or exclude at each stage was presented in **Fig. 1**. Ultimately, twenty two publications involving 19 different prospective Clinical Trials with a total of 2665 patients (1455 treated with PVP and

1210 in the TURP group) were selected for analysis.[2, 7-11, 18-33] The study design and detail patients' baseline characteristics were summarized in **Table 1**.

Assessment of Study Quality

We evaluated the level of evidence for each selected article based on the criteria recommended by the Oxford Center for Evidence Based Medicine.[34] As for methodological quality assessment, we use the Jadad scale [35] to assess the quality of RCTs and chose the Newcastle–Ottawa scale [36] to evaluate the Quality of prospective cohort studies. After a carefully review of the full text of all included studies, both of the RCTs and the non-randomized studies had a relatively high methodological quality (Jadad scale: 3 to 4 points and NOS: 8 to 9 points, respectively).

Data Extraction and Statistical Analysis

Preoperative parameters were extracted together with intraoperative data including operation time, changes in hemoglobin and transfusion rate. Postoperative data such as hospital stay, catheterization time and treatment-related complications were also analyzed. Functional results in terms of IPSS, Qmax, PVR, Qol and IIEF were assessed at 3, 6, 12, 24, 36 and 60 mouth. The mean difference or standardized mean difference (SMD) was used for assessing the continuous parameters. With respect to studies that expressed continuous data as median and range values, we contacted the authors or used the statistical formula elaborated by Hozo et al [37] or other methods recommended by the Cochrane Handbook for Systematic Reviews [38] to count the means and standard deviations. The results were expressed as risk ratio (RR) with a 95% confidence interval (CI) for dichotomous variables. The χ^2 and I^2 tests were used to assess the heterogeneity

of the study data. If χ^2 heterogeneity was reported as $p > 0.10$ and I^2 <50%, heterogeneity was considered to be low; a fixed effect was used for the calculations in the absence of any evidence of heterogeneity. Otherwise, a random effects model was applied. The pooled effects were determined by the z test and the p value <0.05 was considered statistically significant. In addition, due to different kinds of Greenlight™ lasers systems (80-, 120-, 160- and 180- W) were used in different studies, we performed subgroup analyses according to the device used. For several comparisons, sensitivity analyses were also used. All the data analysis was conducted with Review Manager 5.3 software.

RESULTS

1. Meta-analysis of functional outcomes

At baseline, the IPSS, *Q*max, PVR, QoL and IIEF of the participants in both the PVP and TURP groups were similar (**Table 2**).

1.1. IPSS at 3， 6, 12, and 24-month follow-up

The results of the pooled meta-analysis demonstrated that there was no significant difference in IPSS at the 3-month (MD = 0.01, 95%CI= -0.08 to 0.09; p = 0.85)**Fig. 2A**, the 6-month (MD = 0.30, 95%CI= -0.11 to 0.72; p = 0.15)**Fig. 2B** and the 24-month (MD = 0.02, 95%CI= -0.28 to 0.32; p = 0.92)**Fig. 3B** follow-up between PVP and TURP. However, the IPSS at the 12-month follow-up was comparable in both groups (MD = -0.10, 95%CI= -0.15 to -0.05; p < 0.0001)**Fig. 3A**.

1.2. Qmax at3, 6, 12, and 24-month follow-up

Pooled analysis revealed that there was no significant difference between the two

groups regarding Qmax at the 3-month (MD = -0.07, 95%CI= -1.22 to 1.08; p = 0.91)**Fig. 4A**, the 6-month (MD = -0.17, 95%CI= -0.98 to 0.63; p = 0.67)**Fig. 4B** and the 24-month (MD = 0.74, 95%CI= -0.80 to 2.29; p = 0.34)**Fig. 5B** follow-up. Due to the high heterogeneity, a sensitive analysis was conducted at the 24-month follow-up(MD = 0.03, 95%CI= -0.41 to 0.46; p = 0.91)**Fig. S1**. Nevertheless, the Qmax at the 12-month follow-up was slightly higher in the PVP group, reaching a statistically significant difference (MD = 0.62, 95%CI= 0.06 to 1.19; p = 0.03)**Fig. 5A**.

1.3. PVR at 3, 6, 12, and 24-month follow-up

When considering the PVR between the two groups, no significant difference were found at the 3-month (MD =6.65, 95%CI= -2.73 to 16.04; p = 0.16)**Fig. 6A**, the 6-month (MD = 2.07, 95%CI= -2.29 to 6.42; p = 0.35)**Fig. 6B**, the 12-month (MD = 0.85, 95%CI= -0.19 to 1.90; p = 0.11)**Fig. 7A** and the 24-month (MD = 1.58, 95%CI= -1.00 to 4.17; p = 0.23)**Fig. 7B** follow-up. Owing to the high heterogeneity, we conducted a sensitive analysis at the 3-month follow-up(MD = -0.15, 95%CI= -4.53 to 4.24; p = 0.95)**Fig. S2**.

1.4. Qol at 3, 6, 12, and 24-month follow-up

The overall results showed that the Qol of the 2 groups had no significant difference at the 3-month (MD = 0.02, 95%CI= -0.05 to 0.09; p = 0.59)**Fig. 8A**, the 12-month (MD = 0.01, 95%CI= -0.05 to 0.08; p = 0.75) **Fig. 9A** and the 24-month (MD = -0.07, 95%CI= -0.14 to 0.01; p = 0.10)**Fig. 9B** follow-up. However, this parameter at the 6-month follow-up was comparable in two groups (MD = -0.08, 95%CI= -0.13 to -0.02; p = 0.007)**Fig. 8B**.

1.5. IIEF at 6, 12, and 24-month follow-up

With respect to the sexual dysfunction of the two procedures, we performed a meta-analyze based on IIEF evaluation. Pooled analysis verified that the IIEF at the 24-month follow-up was slightly lower in the PVP group (MD = -0.68, 95%CI= -1.20 to -0.15; p = 0.01)**Fig. 11B**, whereas there was no significant difference between the two groups in terms of the IIEF at the 3-month (MD = -0.06, 95%CI= -0.47to -0.35; p = 0.76)**Fig. 10A**, the 6-month (MD = -0.07, 95%CI= -0.55 to 0.41; p = 0.78)**Fig. 10B** and the 12-month (MD = -0.06, 95%CI= -0.55 to 0.43; p = 0.82)**Fig. 11A** follow-up.

1.6. IPSS, Qmax, PVR, Qol and IIEF at 36- and 60-month follow-up

Three trails with a 3-years follow-up and two studies with a 5-years follow-up valuated that the two procedures had a similar efficacy. However, meta-analysis was not available because of the insufficient data reported in these studies.

2. Meta-analysis of perioperative parameters

2.1. Operation time

Fourteen studies reporting this outcome in comparing PVP against TURP were included in the meta-analysis. The overall operation time was about 6 min less for TURP (MD=15.24, 95% CI 8.91 to 21.54, P<0.01； **Table 3**). However, evidence of some statistical heterogeneity cannot be ignored (I^2=94). Therefore, a sensitivity analysis that excluded low-quality trials was conducted，whereas little alteration was found regarding this result (MD=10.83, 95% CI 7.52 to 14.14, P<0.01； **Table 3**).

2.2. Operative blood loss

Six studies including 724 participants (389 in the PVP group and 335 in the control

group) estimated the blood loss during operation. According to our analysis, heterogeneity was found among the trials (I^2 = 89), and thus, a random effects model was chosen. Pooled analysis showed that the decreased hemoglobin (Hb) in the PVP group was significantly lower than that in the TURP group (MD –1.33, 95% CI –0.25 to 0.61, *P<0.01*； **Table 3**).

2.3. Hospitalization time

For this outcome, a total of 11 studies including 1542 participants met the inclusion criteria. Due to different kinds of Greenlight™ lasers systems were used for different studies, a subgroup analysis was performed (MD=-1.98, 95% CI -2.56 to -1.39, P<0.01). However, evidence of some statistical heterogeneity cannot be ignored (I^2=98). Therefore, a sensitivity analysis was performed and little difference was found in the results (MD=-2.14, 95% CI -2.40 to -1.87, P<0.01； **Table 3**)

2.3. Catheterization time

14 available studies including 1655 participants (861 in thePVP group and 794 in control) were enrolled in the meta-analysis. Pooling data revealed that the PVP group had a significantly shorter catheter duration (MD=-1.25, 95% CI -1.58 to -0.92, P<0.01； **Table 3**).

3. Meta-analysis of Complications

3.1. Perioperative complications

The overall effect of the perioperative complications including bleeding-related transfusion, TUR syndrome, capsular perforation, clot retention, urinary tract infection and acute urinary retention were summarized in **Table 3**. According to our Meta-

analysis, PVP was found to have a significantly lower incidence rates of transfusion (RR=0.13, 95% CI 0.07 to 0.26, P<0.01), clot retention (RR=0.11, 95% CI 0.05 to 0.25, P<0.01), TUR syndrome (MD=0.19, 95% CI 0.06 to 0.61, P<0.01) and capsular perforations (MD=0.09, 95% CI 0.03 to 0.25, P<0.01). Furthermore, PVP had a higher risk of mild to moderate dysuria, whereas no obvious difference were noted regarding urinary tract infection (MD=1.16, 95% CI 0.83 to 1.62, P<0.01) and acute urinary retention rate (MD=1.20, 95% CI 0.79 to 1.84, P<0.01).

3.2. Long-term complications

In terms of the long-term complications of bladder neck contracture, retrograde ejaculation and urethral stricture, pooled analysis verified that there was no significant difference between PVP and TURP groups(**Table 3**).Nevertheless, the PVP was found to have a significant higher risk of re-intervention (MD=1.92, 95% CI 1.32 to 2.80, P<0.01； **Table 3**).

DISSCUSSION

Though TURP still represents the “gold standard” surgical method for symptomatic BPH in recent decades,[3] its treatment-related morbidity and complications rate is still up to 20%.[6, 11] In this case, urologists made many attempts to search for a safer technique but with noninferior clinical efficacy to TURP. With the rapid development of endoscopic technologies, PVP, as a promising minimally-invasive surgical procedure, was applied to practice and attracted a lot attention among urologists worldwide.[2, 10-11, 18-19, 21] The first generation laser system used for PVP performed with a high-powered KTP laser (60 W) at 532 nm was initially introduced

by Malek et al[39] in 1998, then the later generation including the KTP laser (80 W)，the Green-light high-performance system (HPS) laser (120 W) , the Green-light lithium triboride (LBO) laser (160 W) and the Green-light X-ray photoelectron spectroscopy (XPS) laser (180 W) systems were further developed.[2, 9-10, 22] To our best of knowledge, previous published studies comparing PVP and TURP have showed its identical medium term efficacy and safety for treating BPH. Nevertheless, the long-term efficacy between the two minimally invasive techniques remains controversial.

In current updated systematic review and meta-analysis, we reviewed 23 available comparative studies involving 2665 participants. Pooled analyses and sensitivity analysis indicated that both of the PVP and TURP groups had the similar long-term function results including subjective (IPSS, QoL) and objective variables (*Q*max, PVR). Although the IPSS at the 12-month follow-up，the Qmax at the 6-month follow-up and the QoL at the 12-month follow-up reached a statistically significant difference, it was of no clinical significant difference.

In terms of the sexual function evaluated by retrograde ejaculation rate, the conclusions were not consistent across studies.[7, 10, 19, 21, 32] Moreover, previously published meta-analyses did not evaluated IIEF due to an insufficient number of studies assessed this parameter. Under these circumstances, we performed a meta-analysis and the pooled analysis revealed that there was no significant difference in retrograde ejaculation rate between the two procedures. The result was also in line with the IIEF evaluation outcomes.

Currently, despite the longest RCT comparing PVP with TURP had a 60 month follow-

up and showed a similar improvement in IPSS, Qmax, PVR, Qol and IIEF, meta-analyses were not available due to the insufficient data reported in the two trails.[30, 33]

Regarding perioperative outcomes, our pooled analyses and sensitivity analyses identified that the operation time was significantly longer for PVP, whereas the duration of hospitalization and catheterization was shorter. After consulting relative literatures, the prolonged operative duration in PVP group may be associated with the following factors: Firstly, the laser power may exert a tremendous influence on this clinical outcome. According to the subgroup analyses classified by different device, the overall operation time was about 23 minutes longer for PVP in the 80W laser group while approximately 9 minutes and 7 minutes longer in the 120W- and 160W laser group. Furthermore, the surgeon's overall technical skills, learning curves of the different technologies and confidence may also play an important role in decreasing the mean operative time.

With respect to the safety of the two procedures, it is well known that the most serious complications of TURP, such as bleeding and TUR syndrome were closely associated with prostate size and longer operative times.[6, 40] However, the pooled analysis indicated that the incidence rates of perioperative complications including bleeding, blood transfusion, the clot retention, capsule perforation and TUR syndrome were significantly lower in PVP group. This could be explained by the characteristics of the green light laser. Firstly, the 532-nm wavelength is highly absorbed by hemoglobin in prostatic tissues but not by water.[13] In vaporization, the high-power laser energy was instantly absorbed by the blood, which then resulted in quickly vaporizing the tissue

and creating a prostate cavity with minimal blood loss.[41] In this case, other bleeding-related complications occurred less frequently in PVP group. Secondly, The KTP laser energy penetrates only 1 to 2 mm of tissue. The high-power laser energy could be concentrated into the surface coat of prostatic tissue, which then resulted in rapidly vaporization and leaving a 0.2-cm rim of coagulated tissue behind.[13]

Due to the fluid medium used for PVP procedure was glycine instead of saline, TUR syndrome did not occur in PVP.

Regarding other postoperative complications such as acute urinary retention, UTIs, bladder neck contracture and urethral stricture, no significant differences were noted between the groups.

Though PVP had these advantages, it was associated with higher risk of dysuria and re-intervention.

In the literature, the dysuria rate after PVP was reported to be between 6% and 30%.[27, 42] It most likely caused by the thermal damage and edema in urethral tissue. Additionally, the shorter catheterization time could be another reason for such irritable symptom. Despite the higher dysuria rate in PVP cohort, this symptom in all patients were classified as mild to moderate degree, which could be resolved spontaneously within 2 months of follow-up.[21, 27] Thus suggesting that transient dysuria is not a serious problem after PVP.

But why did the PVP have such a higher risk of re-intervention? Inadequate energy delivery, which may lead to incomplete tissue removal, might play an important role regarding the outcome of the procedure.[32, 43] According to our subgroup analysis, the

80-W PVP laser group had a significant higher risk of re-intervention than TURP. However, the difference between other higher power PVP laser groups (120-W, 160W and 180W) and TURP cohort were not statistically significant. Additionally, the GOLIATH study identified that the 180-W XPS laser system was superior to TURP with respect to this parameter. Hence, such kind of adverse event would markedly decrease with the advent of higher power laser systems.

Another important drawback of PVP is the absence of tissue for histologic examination, which might preclude the identification of incidental prostate cancer. Therefore, if there is a rapidly increasing and high value of PSA, it would be much more worthwhile to use TURP rather than laser evaporation. In addition, an intensive examination including prostate-specific antigen measurements, digital rectal examinations and ultrasonography guide prostate biopsies must be performed if cancer is suspected.[12, 44]

As LUTS secondary to BPH were chronic health conditions, its managements pose a large economic burden on patients and the healthcare system caring for them.[2, 45] It is vital to evaluate the cost effectiveness of the two surgical therapies in clinical practice. Basing on a cost-effectiveness analysis, Armstrong et al hold that the PVP procedure was unlikely to be cost effective because of the relatively expensive consumables.[46] However, Patel argued against that their conclusions were limited by the absence of high-quality and long-term data (only two RCTs with limited follow-up).[47]Although the initial investment of the equipment and surgeon's training were significant, the overall cost may be partially compensated by the shorter hospitalization and lower incidence of post-operative complications for PVP compared to TURP.[31] Considering

the high number of cases per annum, PVP can save a large amount of medical resources. However, the conclusion should be interpreted cautiously.

Our meta-analysis, which was undertaken using the currently available comparative studies, also has some limitations. First of all, despite a systematic search strategy, the inclusion criteria excluded non-English documents and had language bias. Secondly, due to no adequate LE 1 evidence with long-term follow-up to date comparing the clinical outcomes of the two therapies, 5 high quality prospective cohort studies were included into our analysis. In addition, several included RCTs did not describe the detailed randomization concealment and blinding methods. Thirdly, due to the difference of surgical experience with laser technology, outcome definitions and measurement, heterogeneity among studies were found to be high in several parameters. However, despite of these limitations, our study provided the most up-to-date information concerning the comparison of PVP and TURP in surgical management of BPH.

CONCLUSION

Taken together, our meta-analytical findings indicate that PVP not only has a non-inferior long-term efficacy to TURP regarding IPSS, *Q*max, QoL, PVR and IIEF, but also is associated with less complications rates. We can safely conclude that PVP can be offered as a first-line alternative to the traditional TURP for treating LUTS secondary to BPH. However, the findings of this study should be further confirmed by more large-sample, well-designed and long-term RCTs. 、

AUTHOR CONTRIBUTIONS

SCL and PXP designed the study, conducted a systematic literature search to identify all relevant studies, assessed the eligibility and quality of each selected study, and performed data extraction and statistical analysis. TXD and HMH coordinated the study and performed data acquisition. XW, WZ and YGZ participated in collecting and interpreting the data, drafed and revised the paper. ML and JYW participated in critical reviewed the paper. All authors read and approved the final manuscript.

COMPETING FINANCIAL INTERESTS

All authors declare no competing financial interests

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Legend

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow chart.

Fig. 2 Forest plots illustrating the meta-analysis of IPSS at 3-month (A) and 6-month follow-up (B).

Fig. 3 Forest plots illustrating the meta-analysis IPSS at 12-month (A) and 24-month follow-up (B).

Fig. 4 Forest plots illustrating the meta-analysis of Qmax at 3-month (A) and 6-month follow-up(B).

Fig. 5 Forest plots illustrating the meta-analysis of Qmax at 12-month (A) and 24-month follow-up(B).

Fig. 6 Forest plots illustrating the meta-analysis of PVR at 3-month (A) and 6-month follow-up(B).

Fig. 7 Forest plots illustrating the meta-analysis of PVR at 12-month (A) and 24-month follow-up(B).

Fig. 8 Forest plots illustrating the meta-analysis of Qol at 3-month (A) and 6-month follow-up(B).

Fig. 9 Forest plots illustrating the meta-analysis of Qol at 12-month (A) and 24-month follow-up(B).

Fig. 10 Forest plots illustrating the meta-analysis of IIEF at 3-month (A) and 6-month follow-up(B).

Fig. 11 Forest plots illustrating the meta-analysis of IIEF at 12-month (A) and 24-month follow-up(B).

Table 1 Baseline characteristics of comparative studies included in Meta-analysis

Table 2 Pooled estimates of baseline IPSS, Qmax, PVR, QoL and IIEF between the two groups.

Table 3 Meta-analysis results regarding the safety of PVP compared with TURP

Supplementary files

Fig. S1 Sensitivity analysis result of Qmax at 24-month follow-up.

Fig. S2 Sensitivity analysis result of PVR at 3-month follow-up

Table 1 Baseline characteristics of comparative studies included in Meta-analysis

Authors and year	design	Techniques	No. of patients	Laser power	follow-up, (months)	Intervention Sample size	Age (years)	Prostate size (ml)	IPSS	*Q*max (mL/s)	PVR (mL)	QoL	IIEF	LE	Study quality
Kumar et al 2013	RCT	PVP	58	120W	12		64.58±6.64	52.79±16.13	20.05±2.75	6.68±2.00	143.35±52.67	3.60±1.01	16.65±2.80	2a	3*
		TURP	60				63.68±6.57	52.20±15.93	20.71±2.68	7.00±1.97	139.25±54.28	3.73±0.97	16.95±2.86		
Lukacs et al 2012	RCT	PVP	68	120W	12		66.9±7.8	50.54±16.53	22 (17–26)	7.79±2.75	89.5 (30-158)	70 (68–80)	N/A	2a	3*
		TURP	68				67.6±7.6	50.11±14.73	20 (15–23)	7.76±2.64	75 (28–126)	75 (65–85)	N/A		
Pereira-Correia et al 2012	RCT	PVP	10	120W	24		66.4（52 – 76）	43.4(30– 58）	22 (9 – 33)	10（3 – 18）	150（25 – 250）	N/A	23（22 – 24）	2a	4*
		TURP	10				63.5（56 – 78）	47（30– 60）	25(15 – 31）	6.4（4 – 11）	177（50 – 300）	N/A	23（22 – 25）		
Capitan et al 2011	RCT	PVP	50	120W	12		69.8±8.44	51.29±14.72	23.74±5.24	8.03±3.14	N/A	4.52±0.27	N/A	2a	3*
		TURP	50				67.7±6.7	53.10±13.75	23.52±4.38	3.88±2.71	N/A	4.14±1.06	N/A		
Al-Ansari et al 2010	RCT	PVP	60	120W	36		66.3±9.4	61.8±22	27.2±2.3	6.9±2.2	53.2±25	N/A	N/A	2a	3*
		TURP	60				67.1±8	60.3±20	27.9±2.7	6.4±2	57±21	N/A	N/A		
Xue et al 2013	RCT	PVP	100	120W	36		72.1±11.3	65.8 ± 23.6	23.0 ± 5.1	8.0 ± 3.6	148.3 ± 101.6	4.2 ± 0.9	N/A	2a	3*
		TURP	100				71.0±10.8	67.3 ± 24.7	23.2 ± 5.0	8.2 ± 3.8	151.1 ± 105.2	4.3 ± 0.8	N/A		
Horasanli et al 2008	RCT	PVP	39	80W	6		69.2±7.1	86.1±8.8	18.9±5.1	8.6±5.2	183±50.1	N/A	19.9±5.1	2a	3*
		TURP	37				68.3±6.7	88±9.2	20.2±6.8	9.2±5.6	176.9±45.3	N/A	20.1±5.5		
Mohanty et al 2012	RCT	PVP	60	80W	12		66.68±8.62	44.77±14.09	19.98±3.27	7.41±2.07	145.8±70.33	3.97±0.82	17.98±3.55	2a	3*
		TURP	57				65.74±9.09	49.02±15.93	20.88±3.87	6.75±1.63	143.23±65.96	3.91±0.78	17.40±4.76		
Bouchier-Hayes et al 2009	RCT	PVP	60	80W	12		**>50**	N/A	25.28±5.93	8.81±2.55	129.2±155.7	4.74±1.23	N/A	2a	3*
		TURP	59					N/A	25.41±5.72	8.86±2.99	111.3±113.7	5.08±0.94	N/A		
Bachmann et al 2014	RCT	PVP	136	180W	6		65.9±6.8	48.6±19.2	21.2±5.9	9.5±3.0	110.1±88.5	4.6±1.1	13.2±7.6	2a	3*
		TURP	133				65.4±6.6	46.2±19.1	21.7±6.4	9.9±3.5	109.8±103.9	4.5±1.4	13.7±7.5		
Bachmann et al 2015	RCT	PVP	136	180W	12		65.9±6.8	48.6±19.2	21.2±5.9	9.5±3.0	110.1±88.5	4.6±1.1	13.2±7.6	2a	3*
		TURP	133				65.4±6.6	46.2±19.1	21.7±6.4	9.9±3.5	109.8±103.9	4.5±1.4	13.7±7.5		

Thomas et al 2016	RCT	PVP	136	180W	24	65.9±6.8	48.6±19.2	21.2±5.9	9.5±3.0	110.1±88.5	4.6±1.1	13.2±7.6	2a	3*
		TURP	133			65.4±6.6	46.2±19.1	21.7±6.4	9.9±3.5	109.8±103.9	4.5±1.4	13.7±7.5		
Telli et al 2015	RCT	PVP	39	120W	24	67 (51–87)	60 (41–75)	20 (12–30)	10.6 (5–17)	60 (20–220)	N/A	N/A	2a	3*
		TURP	62			69 (56–87)	55 (40–72)	19 (10–31)	12.5 (3–21)	65 (10–220)	N/A	N/A		
Kumar et al 2016	RCT	PVP	58	120W	36	64.58±6.64	52.79±16.13	20.05±2.75	6.68±2.00	143.35±52.67	3.60±1.01	16.65±2.80	2a	3*
		TURP	60			63.68±6.57	52.20±15.93	20.71±2.68	7.00±1.97	139.25±54.28	3.73±0.97	16.95±2.86		
Mordasini et al 2018	RCT	PVP	112	80W	60	68.4±8.7	36.1±11.5	20.3±7.0	8.9±4.1	91.1±88.3	4.2±1.1	N/A	2a	3*
		TURP	126			67.6±8.4	37.9±14.3	20.4±7.5	8.5±4.6	114.5±136.4	4.3±14	N/A		
Chen et al 2011	PCS	PVP	57	160	6	69.5±7.4	60.2±27.8	19.7±6.0	6.9±4.0	93.7±79.7	N/A	N/A	2b	9#
		TURP	51			67.1±6.9	58.3±26.2	21.8±7.3	6.8±2.3	102.2±70.1	N/A	N/A		
Bachmann et al 2005	PCS	PVP	37	N/A	6	71.0±9.3	65.1±36.9	18.1±5.9	6.9±2.2	146.1±106.9	3.3±1.7	N/A	2b	9#
		TURP	64			68.7±7.9	48.9±21.2	17.3±6.3	6.9±2.2	120.7±49.0	3.4±1.6	N/A		
Ruszat et al 2008	PCS	PVP	113	80W	24	62.3±5.0	56.3±27.4	20±6.4	8.5±4.1	203±226	N/A	N/A	2b	9#
		TURP	75			61.7±5.5	45.3±21.0	19±6.9	9.8±5.0	104±108	N/A	N/A		
		PVP	91			75.0±2.8	64.8±26.8	18.6±5.8	7.3±2.7	215±247				
		TURP	40			74.0±2.6	54.2±21.2	16.0±7.1	9.2±5.4	124±141				
		PVP	65			84.3±3.1	69.3±32.7	14.1±7.4	7.1±4.2	200±219				
		TURP	12			82.4±2.8	44.9±22.1	15.5±6.7	7.6±3.9	231±350				
Tasci et al 2008	PCS	PVP	40	N/A	24	71.8±5.9	108.4±15.8	22.3±5.6	6.2±2.2	116.5±60.5	3.6±0.7	N/A	2b	9#
		TURP	41			70.1±5.4	104.2±12.5	22.6±3.9	6.5±1.8	110.7±59.8	3.5±0.6	N/A		
Tugcu et al 2008	PCS	PVP	112	N/A	24	67.5±7.4	49.1±11.9	17.9±4.9	6.9±1.9	107.9±63.0	3.4±0.6	N/A	2b	9#
		TURP	98			66.3±7.9	47.7±8.4	17.7±3.5	7.2±1.7	100.3±57.1	3.4±0.5	N/A		
Nomura et al 2009	PCS	PVP	78	80	12	72.0(67.0,78.0)	50.5(38.6,70.3)	23 (17, 27)	6.8 (5.2, 9.5)	69 (31, 139)	5 (5, 6)	N/A	2b	9#
		TURP	51			70.5 (66.5, 76.0)	42.8 (34.6, 54.0)	22 (16, 27)	7.3 (5.3, 10.2)	60 (31, 140)	5 (4, 5)	N/A		
Guo et al 2015	PCS	PVP	257	**80W**	60	**69.7±8.9**	**52.3±19.3**	**19.4±6.3**	**8.3±6.0**	119.5±83.8	3.7±1.7	N/A	2b	9#
		TURP	104			**66.4±8.4**	**44.2±19.1**	**18.4±6.3**	**10.0±5.2**	95.6±98.4	3.7±1.3	N/A		

LE = level of evidence;# Using Newcastle-Ottawa Scale (score from 0 to 9)； * Using Jadad scale (score from 0 to 5); RCT= randomized controlled trial; IPSS = International Prostate Symptom Score; QoL = quality of life; Qmax = maximum flow rate; PVR = postvoid residual volume; N/A = not available; TURP = transurethral resection of the prostate; PVP=Photoselective vaporization of the prostate; IIEF=international index of erectile function; PCS=prospective cohort study.

Table 2. Meta-analysis results regarding the baseline parameters of PVP compared with TURP

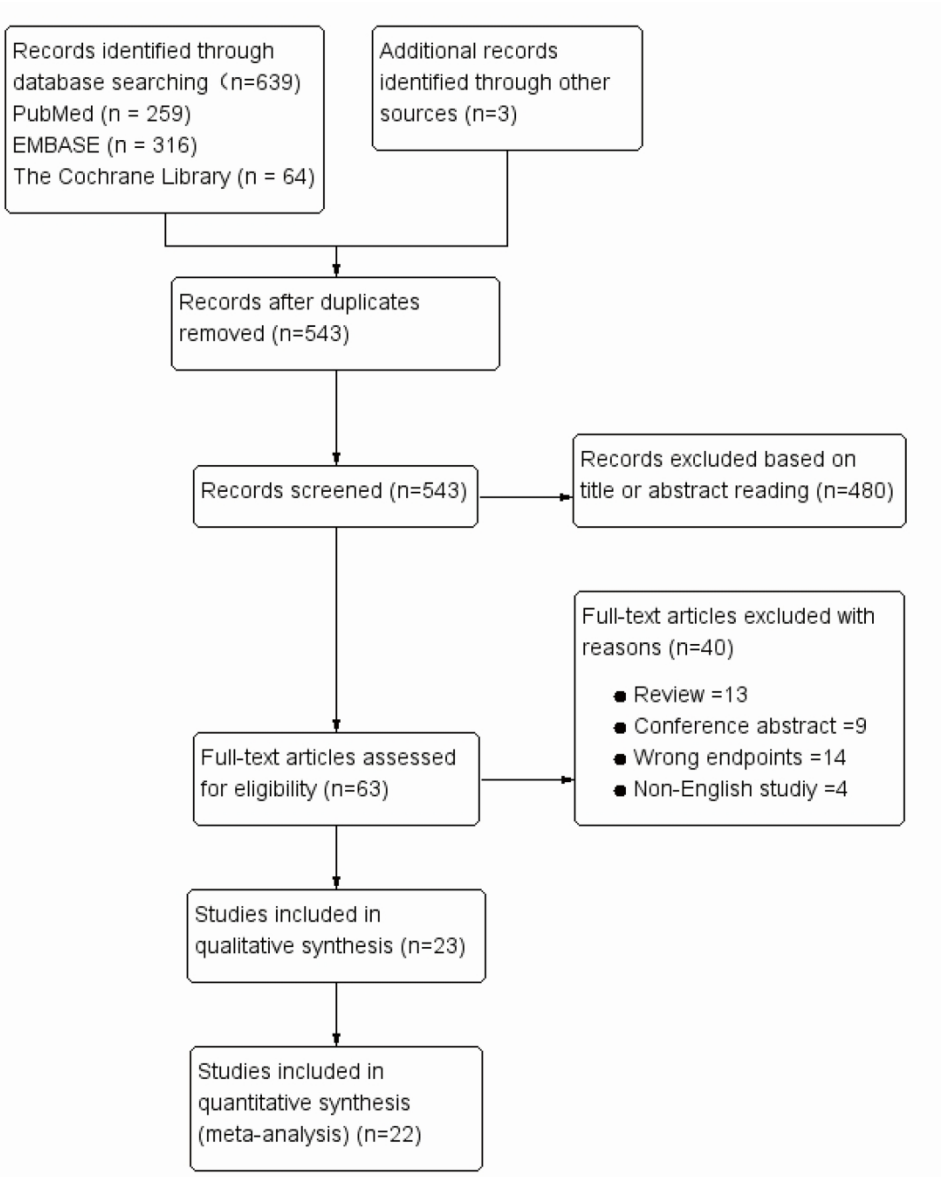
Outcomes	No.of studies	Sample size		Heterogeneity(Total)				MD or RR(95%CI)	Test for overall effect	
		PVP	TURP	chi^2	df	I^2%	P value			
IPSS										
Baseline	14	1179	989	11.32	13	0	0.58	-0.29 [-0.68, 0.10]	Z=1.47	p=0.14
Qmax										
Baseline	14	1179	989	70.23	13	81	<0.00001	0.05[-0.51, 0.61]	Z=0.17	p=0.87
PVR										
Baseline	12	1016	864	9.24	11	0	0.6	2.19[-3.22,7.61]	Z=0.79	p=0.43
Qol										
Baseline	10	910	766	11.15	9	19	0.27	0.01 [-0.07,0.10]	Z=0.33	P=0.74
IIEF										
Baseline	4	1.10	293	287	3	0	0.78	-0.12 [-0.85,0.61]	Z=0.33	P=0.74

* Using sensitive analyze; CI=confidence interval, MD=mean difference, RR=risk ratio; IPSS = International Prostate Symptom Score; PVP=Photoselective vaporization of the prostate; PVR = postvoid residual volume; QoL = quality of life; Qmax = maximum flow rate; IIEF=International Index of Erectile Function; TURP = transurethral resection of the prostate;

Table 3 Meta-analysis results regarding the safety of PVP compared with TURP

Outcomes	No.of studies	Sample size		Heterogeneity(Total)				MD or RR(95%CI)	Test for overall effect	
		PVP	TURP	chi^2	df	I^2%	P value			
Operation time	14	979	870	216.27	13	94	<0.00001	15.24 [8.91,21.54]	Z=4.72	P<0.00001
	12*	900*	792*	42.98*	11*	74*	<0.0001*	10.83 [7.52, 14.14]*	Z=6.41*	P<0.00001*
Hospitalization time	11	819	723	600.62	10	98	<0.00001	-1.98 [-2.56, -1.39]	Z=6.59	P<0.00001
	10*	707*	625*	41.10*	9*	78*	<0.00001*	-2.14 [-2.40, -1.87]*	Z=16.02*	P<0.00001*
Catheterization time	14	861	794	964.75	13	99	<0.00001	-1.25 [-1.58, -0.92]	Z=7.48	P<0.00001
Blood loss	6	389	335	46.05	5	89	<0.00001	-1.33 [-2.05, -0.61]	Z=3.62	P=0.0003
Transfusion	14	1110	946	11.18	13	0	0.60	0.13 [0.07, 0.26]	Z=6.08	P<0.00001
TUR syndrome	7	590	435	0.73	6	0	0.99	0.19 [0.06, 0.61]	Z=2.81	P=0.005
Capsular perforation	7	641	451	1.95	6	0	0.92	0.09 [0.03, 0.25]	Z=4.57	P<0.00001
Clot retention	8	699	504	2.00	7	0	0.96	0.11 [0.05, 0.25]	Z=5.48	P<0.00001
Urinary tract infection	13	1049	860	9.09	12	0	0.70	1.16 [0.83, 1.62]	Z=0.88	P=0.38
Acute urinary retention	10	694	653	5.75	9	0	0.76	1.20 [0.79, 1.84]	Z=0.86	p=0.39
Bladder neck contracture	8	523	520	4.35	7	0	0.74	1.06 [0.55, 2.04]	Z=0.16	P=0.87
Urethral stricture	15	1172	980	9.56	14	0	0.79	0.80 [0.55, 1.17]	Z=1.15	p=0.25
Retrograde ejaculation	4	320	314	10.59	3	72	0.01	0.56 [0.29, 1.06]	Z=1.78	p=0.07
Dysuria	12	1079	854	37.70	11	71	<0.0001	2.16 [1.18, 3.98]	Z=2.48	p=0.01
Re-intervention	12	980	809	14.46	11	24	0.21	1.92 [1.32, 2.80]	Z=3.38	P=0.0007

* Using sensitive analyze; CI=confidence interval; MD=mean difference; PVP=Photoselective vaporization of the prostate; RR=risk ratio; TURP = transurethral resection of the prostate; TUR syndrome= transurethral resection syndrome



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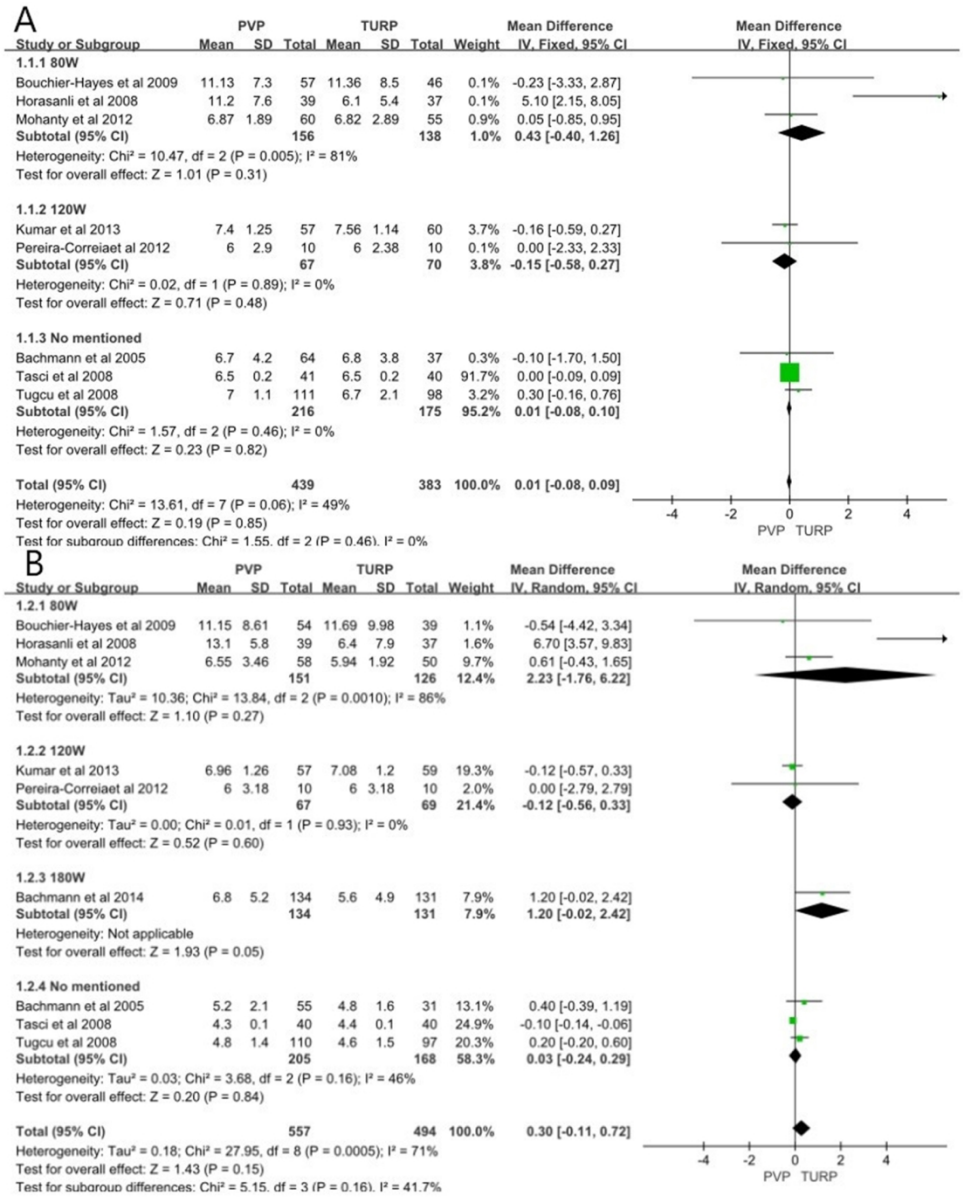

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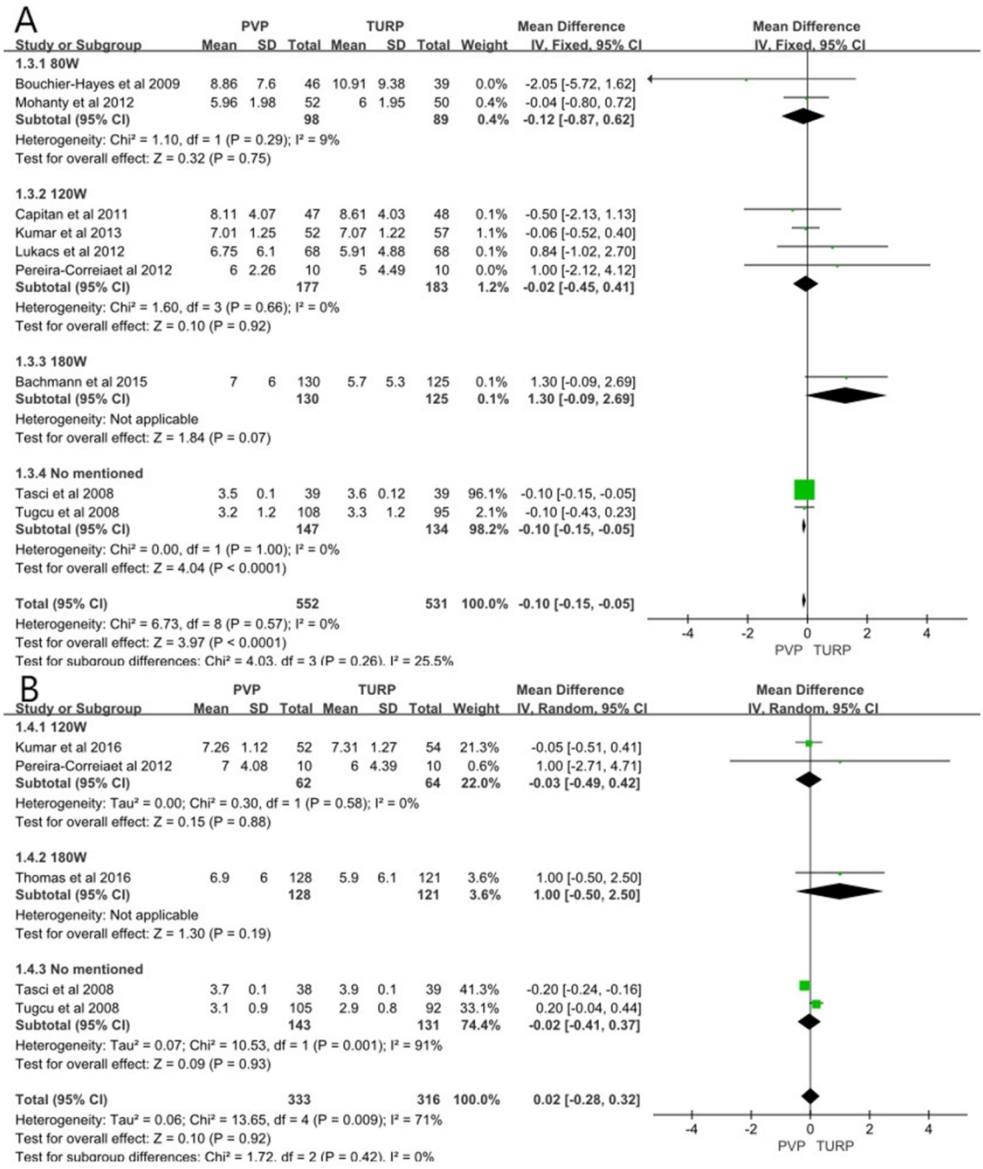

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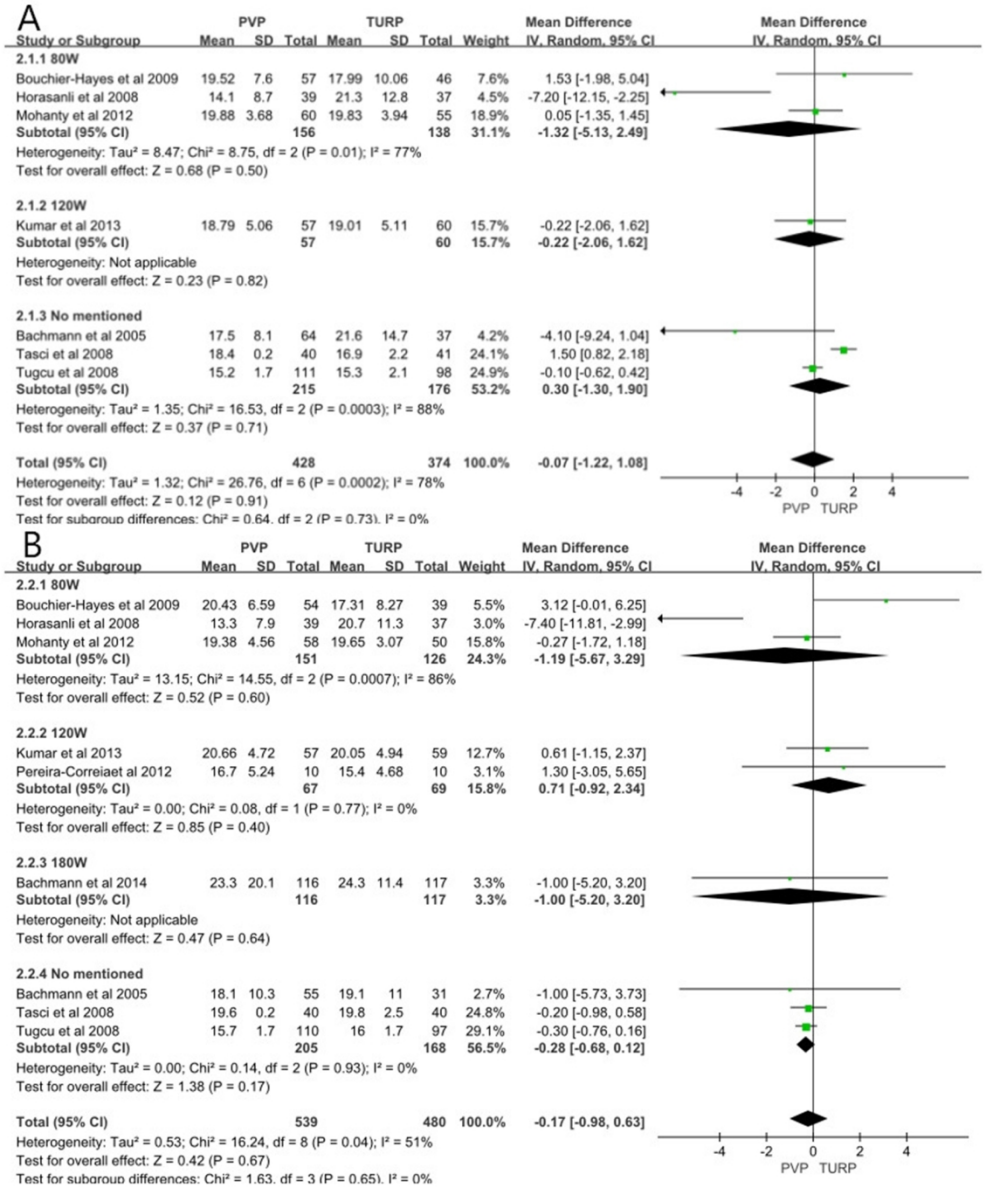

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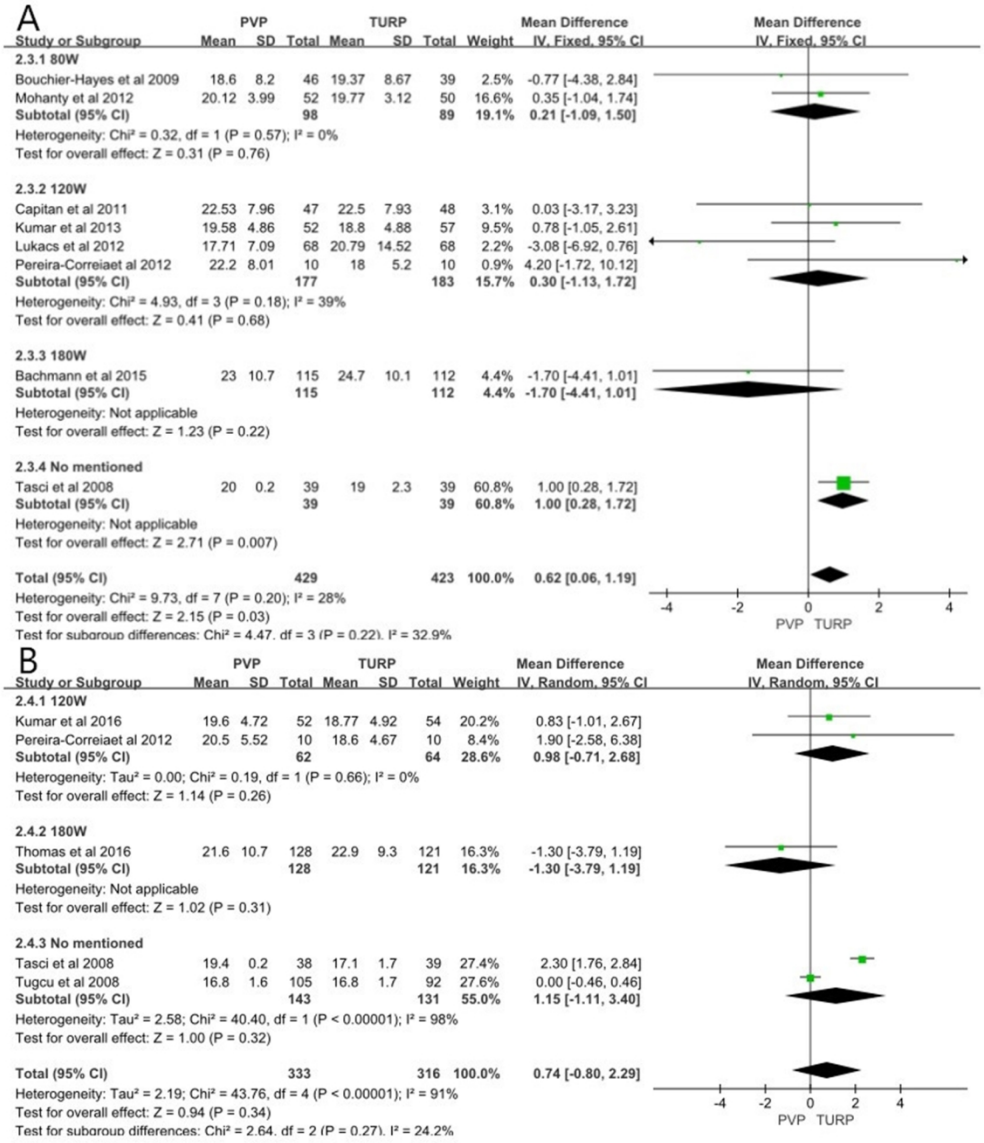

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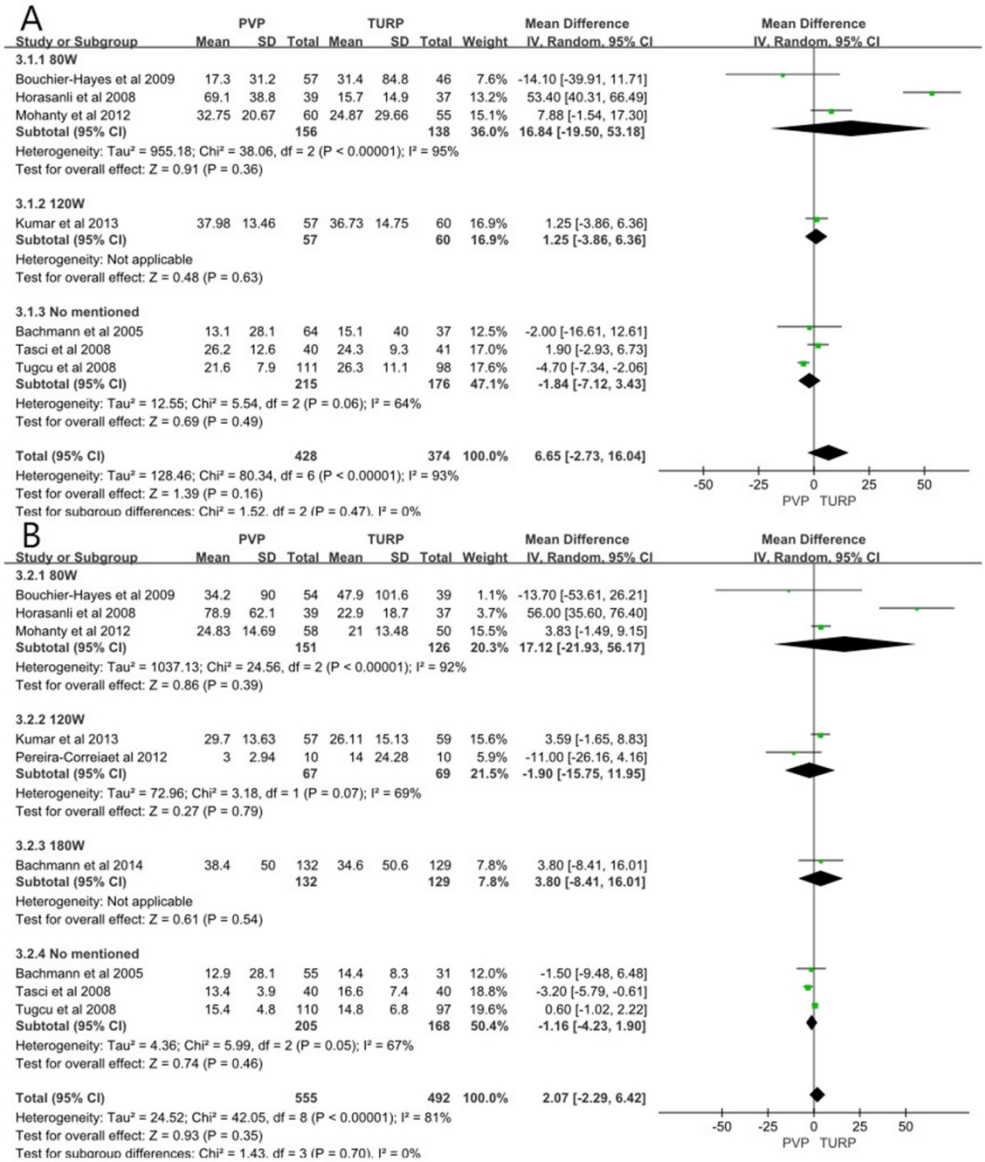

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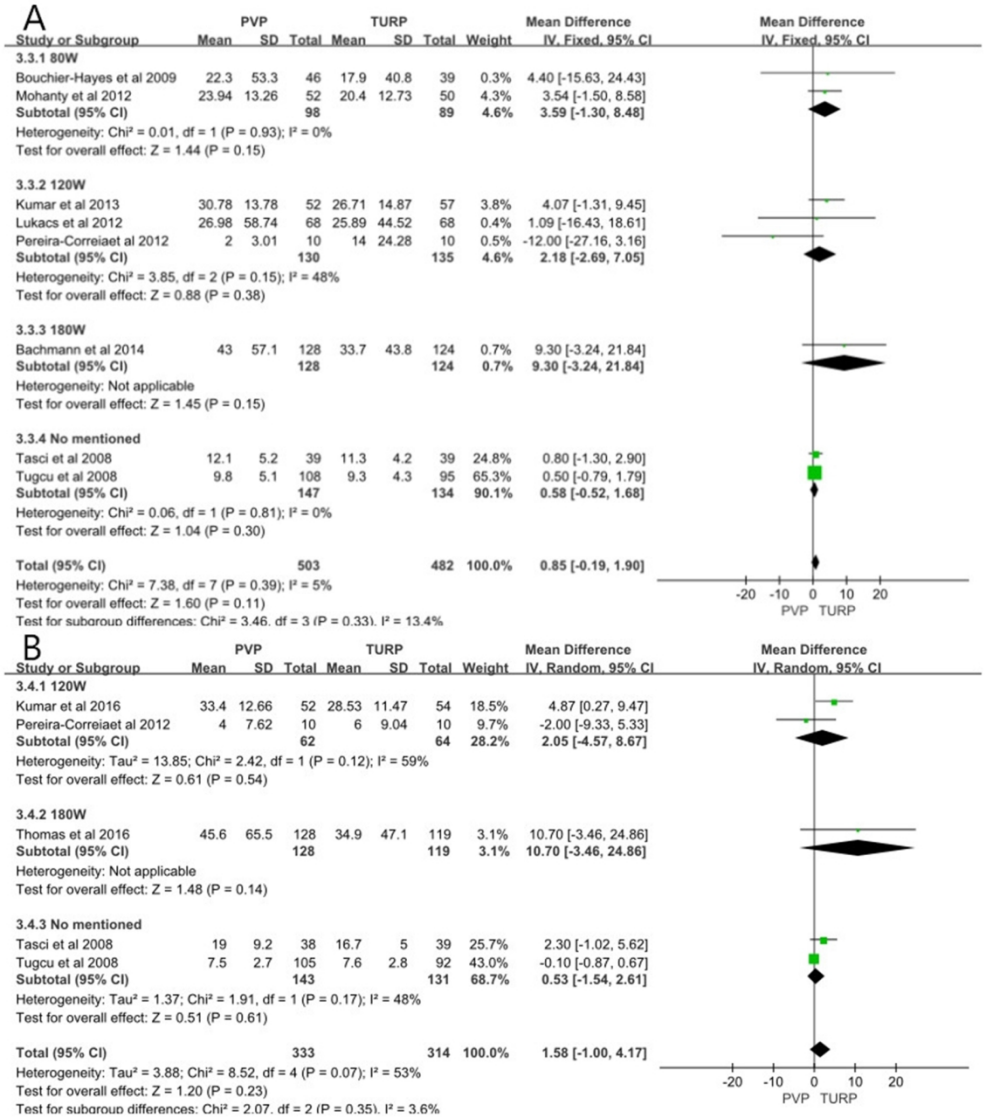

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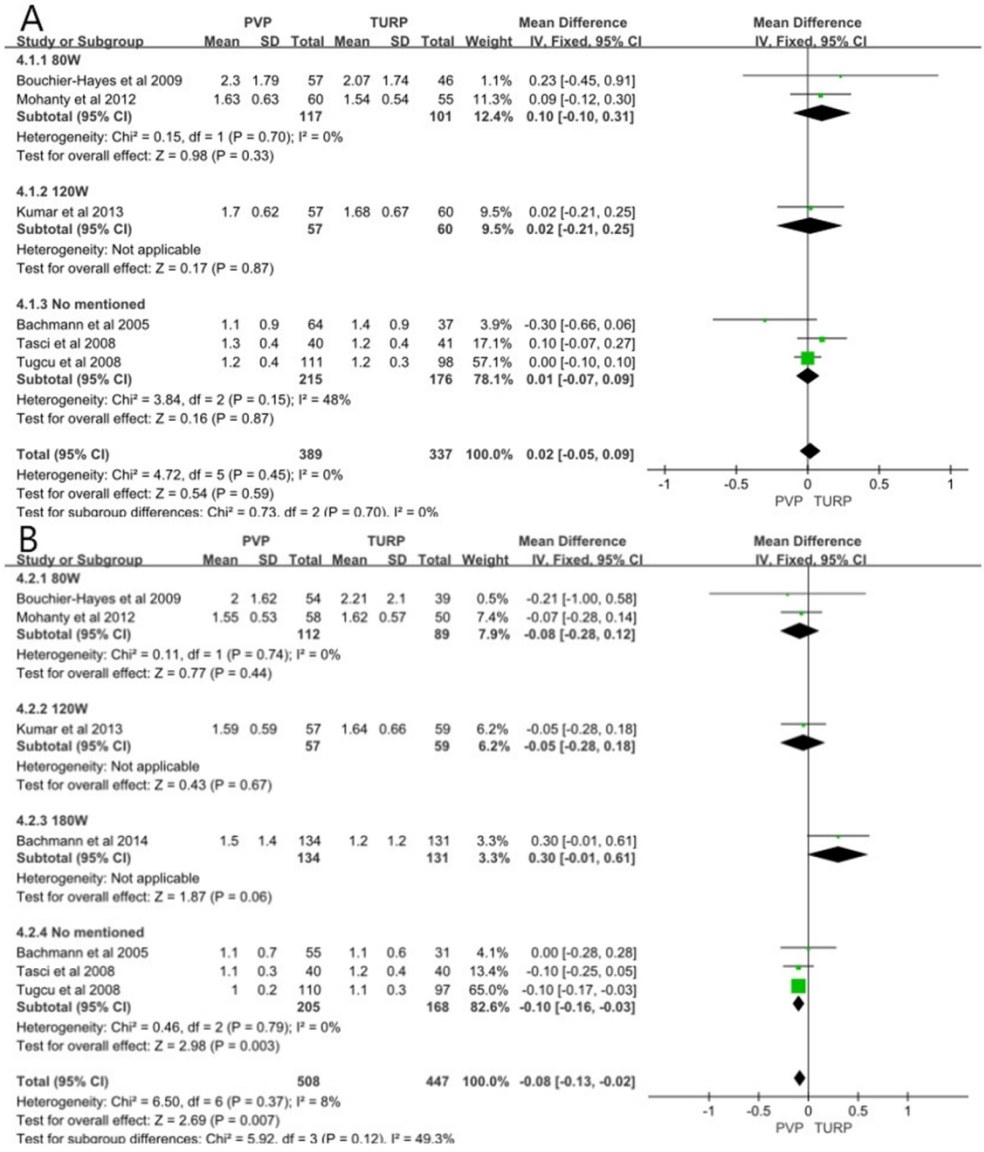

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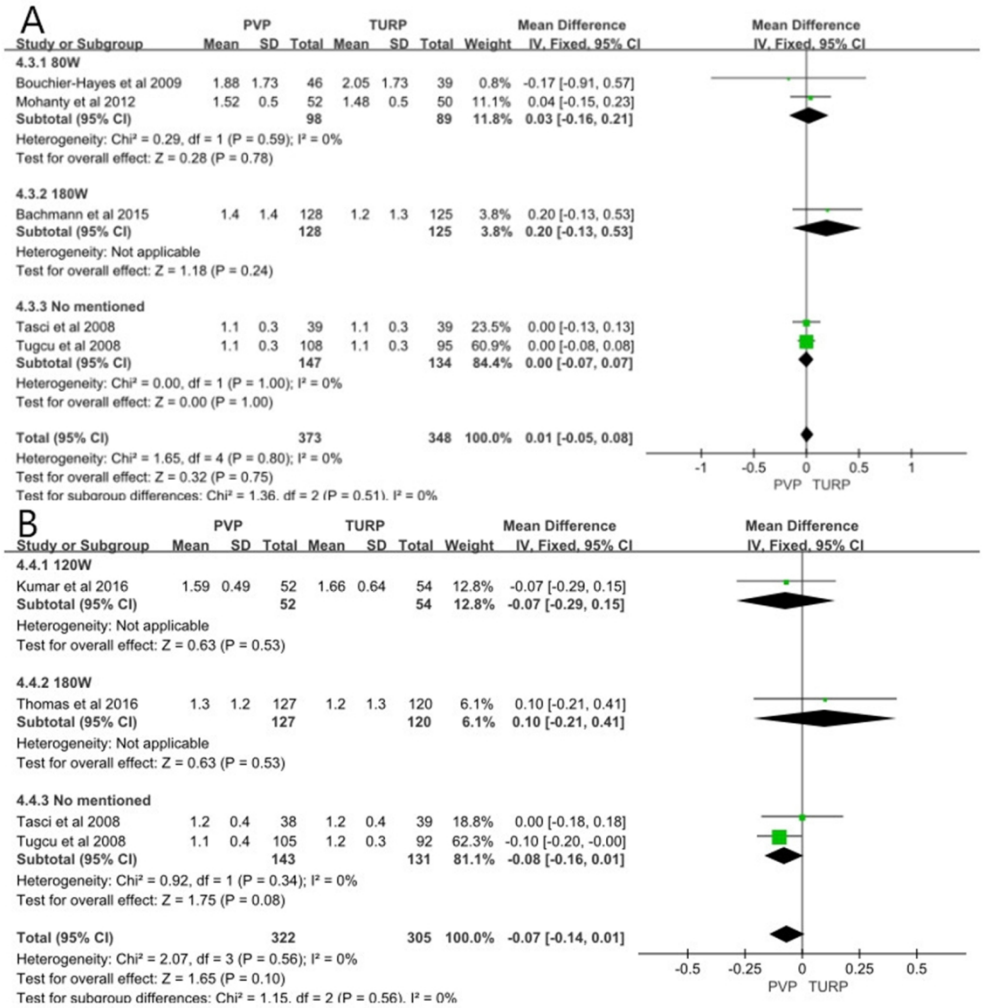

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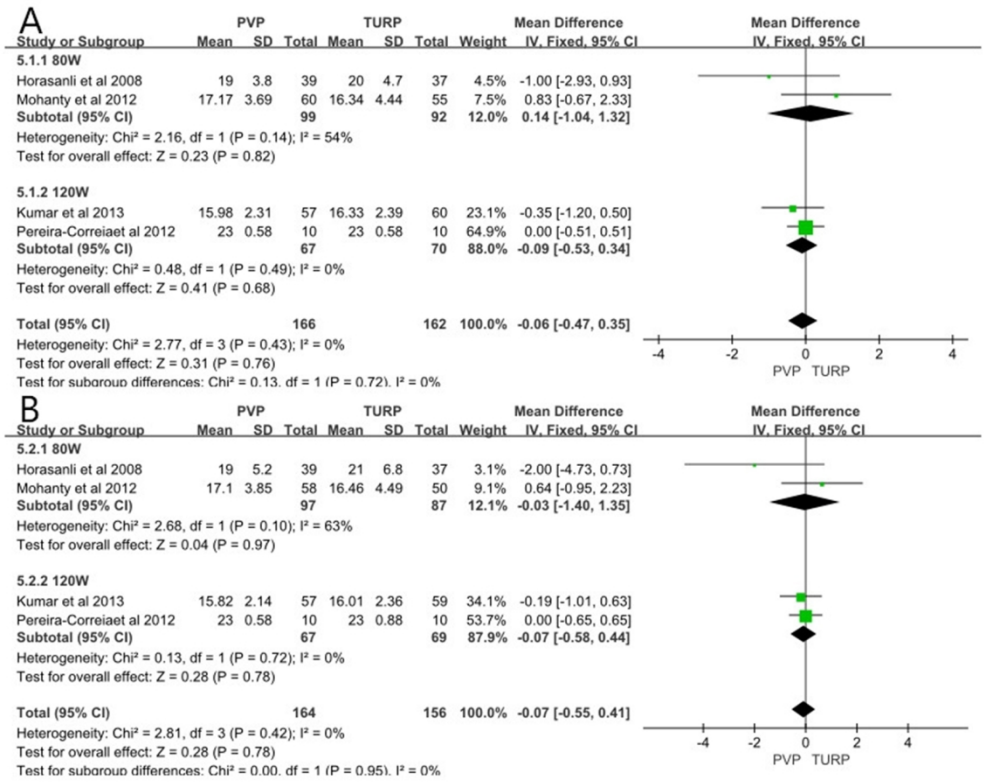

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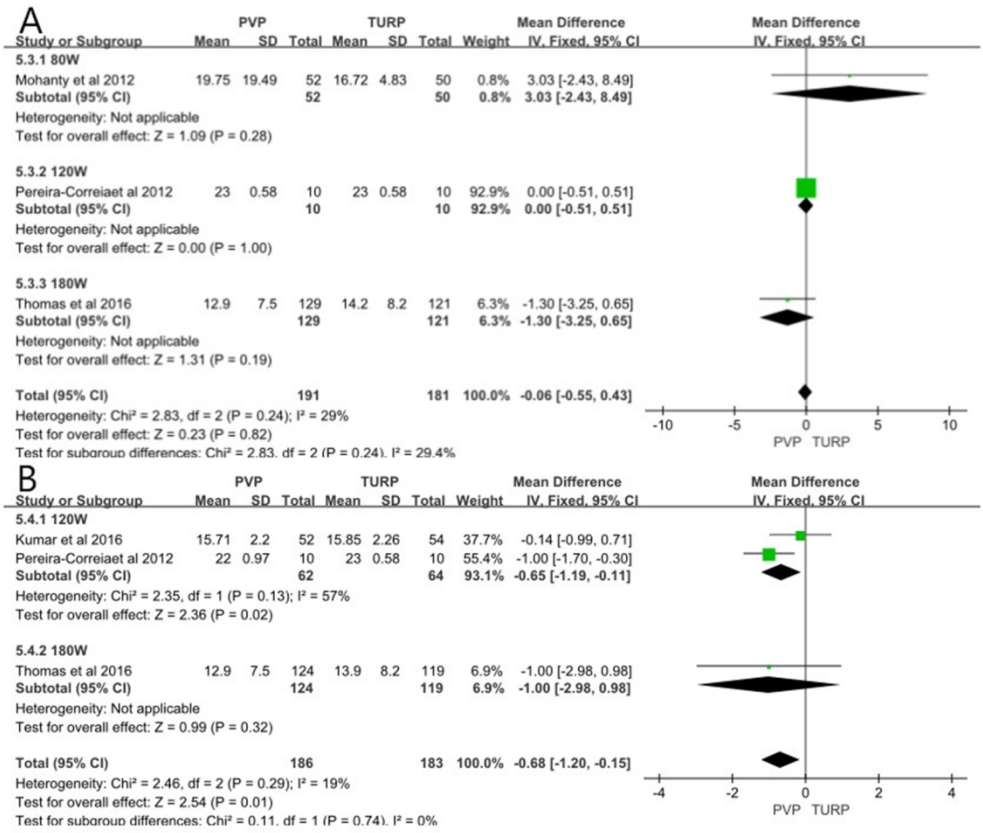

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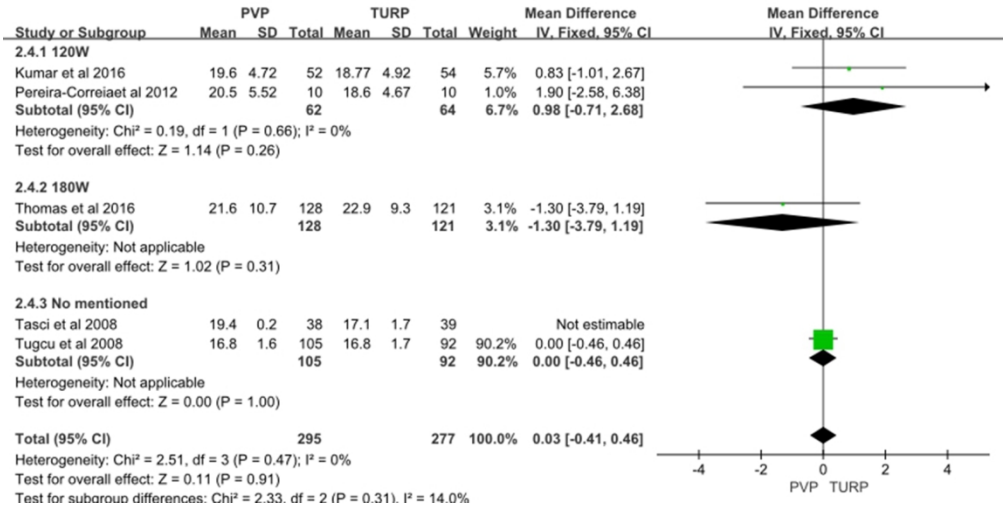

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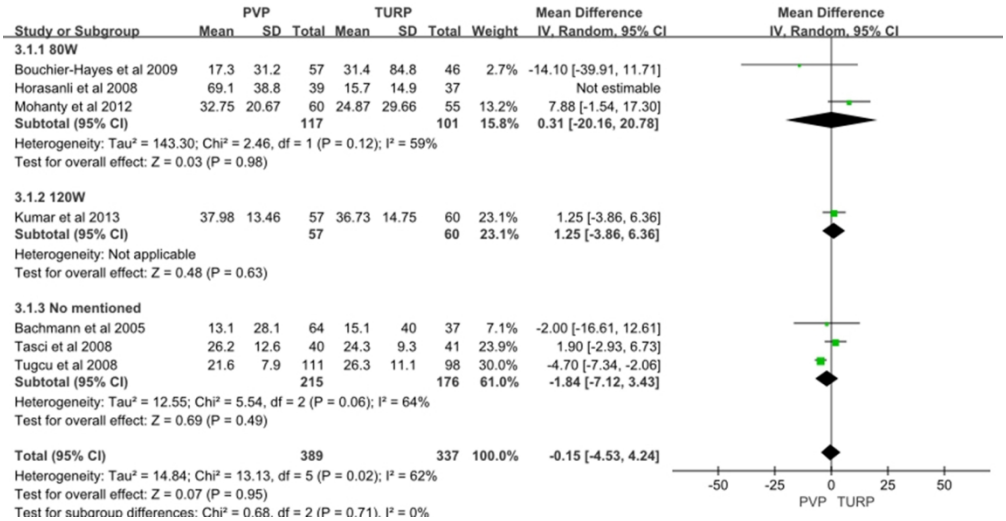

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	None
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7-8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7-8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6-7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6-7
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8-12
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8-12
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	8-12
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8-12
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-17
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	18

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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BMJ Open

Comparison of photoselective green light laser vaporization versus traditional transurethral resection for benign prostate hyperplasia: an up-to-date systematic review and meta-analysis of randomized control trials and prospective studies

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Complete List of Authors:	Lai, Shicong; Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China , ; Department of Urology, Beijing Hospital of the Ministry of Health, Beijing 100730, China, Peng, Panxin; Peking University China-Japan Friendship School of Clinical Medicine, Beijing 100029, China; China-Japan Friendship Hospital, Department of Urology Diao, Tongxiang; Beijing Hospital, National Center of Gerontology, China; Peking university fifth school of clinical medicine Hou, Huimin; Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China; Beijing Hospital, National Center of Gerontology, China Wang, Xuan; Beijing Hospital, National Center of Gerontology, China Zhang, Wei; Beijing Hospital, National Center of Gerontology, China; Peking university fifth school of clinical medicine Liu, Ming; Beijing Hospital, National Center of Gerontology, China Zhang, Yaoguang; Beijing Hospital, National Center of Gerontology, China Seery, Samuel; Chinese Academy of Medical Sciences and Peking Union Medical College, School of Humanities and Social Sciences Wang, Jianye; Beijing Hospital, National Center of Gerontology, China
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Keywords:	Prostate disease < UROLOGY, UROLOGY, Adult urology < UROLOGY

Comparison of photoselective green light laser vaporization versus traditional transurethral resection for benign prostate hyperplasia: an up-to-date systematic review and meta-analysis of randomized control trials and prospective studies

Shi-Cong Lai[1,2#], Pan-xin Peng[3,4#], Tong-Xiang Diao[2,5], Hui-Min Hou[1,2], Xuan Wang[2], Wei Zhang[2,5], Ming Liu[2], Yao-Guang Zhang[2], Samuel Seery[6], Jian-Ye Wang[2]*

[1] Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China

[2] Department of Urology, Beijing Hospital, National Center of Gerontology, Beijing 100730, China

[3] Peking University China-Japan Friendship School of Clinical Medicine, Beijing 100029, China

[4] Department of Urology, China-Japan Friendship Hospital, Beijing 100029, China

[5] Peking university fifth school of clinical medicine

[6] School of Humanities and Social Sciences, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100730, China

 # Shi-Cong Lai and Pan-xin Peng contributed as the co-first author

*** Correspondence author: Jian-Ye Wang**

5. Address for correspondence:

Jian-Ye Wang, No.1 Da Hua Road, Dong Dan, Beijing 100730, P.R. China

Email: **wangjy@bjhmoh.cn**

Word count

Title: 28

Abstract: 300

Article: 3907

References: 48

Number of tables, figures, supplementary files: 3, 3, 1

Abstract

Objective: To assess the efficacy and safety of green-light laser photoselective vaporisation of the prostate (PVP) compared with transurethral resection of the prostate (TURP) for the treatment of lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH).

Design: Systematic review and meta-analysis conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement.

Data sources: PubMed, EMBASE, The Cochrane Library until October 2018

Eligibility criteria: Randomized controlled trials and prospective studies comparing the safety and efficacy of PVP versus TURP for treating LUTS manifesting through BPH.

Data extraction and synthesis: Perioperative parameters, complications rates and functional outcomes including treatment-related adverse events such as International Prostate Symptom Score (IPSS), maximum flow rate (Qmax), postvoid residual (PVR), Qquality of Life (Qol) and International Index of Erectile Function (IIEF).

Results: Twenty two publications about 19 different clinical studies with a total of 2665 patients were analyzed. Pooled analysis revealed PVP is associated with reduced blood loss, transfusion, clot retention, TUR syndrome, capsular perforation, catheterization time and hospitalization, but also with higher re-intervention rate and longer intervention duration (all $p < 0.05$). No significant difference in IPSS, *Q*max, QoL, PVR

or IIEF at 3, 24, 36 or 60 months was identified. There was a significant difference in Qmax at 6 months, and IPSS and QoL at 12 months although these differences were not clinically significant.

Conclusion: PVP is an effective alternative with additional safety benefits compared with TURP for BPH. PVP not only has an equivalent long-term efficacy in relation to IPSS, *Q*max, QoL, PVR and IIEF, but is associated with fewer complications. The main drawbacks are dysuria and re-intervention although both can be managed effectively, and with noninvasive techniques. The additional drawback is that PVP can't acquire histological tissue examination which removes an opportunity to identify prostate cancer.

Keywords: Benign prostatic hyperplasia (BPH), Lower urinary tract symptoms (LUTS), Meta-analysis, Photoselective vaporisation of the prostate (PVP), Transurethral resection of the prostate (TURP)

Strengths and limitations of this study

- This up-to-date meta-analysis included a larger number of studies involving more participants which adds precision to previous findings
- This study analyzed both safety and efficacy, focusing on sexual functioning and quality of life measures because LUTS treatment related adverse events have a hugely detrimental impact on ones' psychological well-being
- Quality assessment methods used did not highlight substantial differences between studies because blinding is not possible given the characteristics of the two interventions under investigation
- Due to the limited number of studies in this field we were unable to conduct subgroup analysis around laser power (i.e., 80W, 120W, 180W etc.) which is necessary to identify the most effective/efficient standard
- Surgical experience with laser technology, drop outs and withdrawals as well as other important factors are seldom reported in any detail which inhibits further analysis

INTRODUCTION

Lower urinary tract symptoms (LUTS) commonly occur in the aging male population, affecting more than 1 in 4 of those above 50 years of age. LUTS manifest through benign prostatic hyperplasia (BPH) and often have a hugely negative impact on quality of life (Qol) [1]. Treatments for BPH range from medicinal interventions to surgery, where transurethral resection of the prostate (TURP) remains the surgical gold standard. Surgical therapy is recommended for patients whom have not benefitted from medical interventions such as, 5-alpha-reductase inhibitors and alpha-blockers [1, 2]. TURP has been been found to have a high success rate and low re-intervention rate at long-term follow-up[3], however, increasingly evidence indicates this invasive procedure is also associated with serious complications such as bleeding, urethral strictures, urinary incontinence and transurethral resection (TUR) syndrome[4-6]. Consequently, there is an urgent need to develop minimally-invasive therapies which do not have such a negative impact on patients' lives.

Laser therapies offer a new direction in BPH therapies and photoselective vaporization of the prostate (PVP) is increasingly being studied for its potential as a new first line treatment [7-11]. This technique is generally performed with a 532-nm green laser generated using potassium-titanyl-phosphate (KTP) or lithium triborate crystals [12]. Unlike other types of laser, the green laser is easily absorbed by soft tissue haemoglobin, while hardly at all by other fluid mediums, which leads to improved coagulation and lowers the risk of deeper tissue injuries during vaporization [13, 14]. Numerous

studies provide supporting evidence of increased benefit, demonstrating that PVP has superior mid-term clinical efficacy compared with TURP across functional outcomes including International Prostate Symptom Score (IPSS), maximum flow rate (Qmax), postvoid residual volume (PVR), International Index of Erectile Function (IIEF) and QoL[15, 16].

In a previous meta-analysis published in 2013, Teng et al [17] found that PVP and TURP have similar treatment efficacies although due to the minimally invasive nature, PVP offers several potential benefits. While this early research provided some optimism, studies have yet to compare sexual function outcomes or efficacy results at 24 months, and across all available RCTs and prospective studies. Consequently, we sought to conduct an up-to-date systematic review and meta-analysis of high quality studies to support clinical decision-makers treating BPH.

MATERIALS AND METHODS

Patient and Public Involvement

This study was a systematic review and meta-analysis. Ethics committee approval was unnecessary because all data were extracted from existing literature, and this report did not involve individual patient data. In addition, neither patients nor the public were involved in the design and planning of the study.

Literature Search and Article Selection

A comprehensive literature search was performed using biomedical databases

including PubMed, EMBASE, and the Cochrane Library up until October 2018. The following MeSH terms and free text words were used: benign prostatic hyperplasia, BPH, transurethral resection of the prostate, TURP, green-light laser, vaporization, photoselective vaporization of the prostate and PVP. These terms were used singly and in combination (For further details please see supplement file 1). Additionally, manual searches were commenced for references and citations included within pertinent reviews. Language was restricted to English and the search and selection strategy was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement [18]. Randomized controlled trials and prospective studies meeting the following criteria were included: (1) studies comparing the safety and efficacy of PVP versus TURP for surgical treatment of LUTS secondary to manifesting BPH, (2) endpoints such as treatment-related adverse events and functional outcomes such as IPSS, Qmax, PVR, Qol and IIEF when available (3) providing the full text of the study could be accessed.

Literature searching, selection, and data extraction was undertaken independently by two reviewers (SL and PP) which was then cross-checked. Any discrepancies were resolved through discussion. A flowchart representing the search and selection process is presented in **Fig. 1**.

Assessment of Study Quality

Levels of evidence for each selected report was undertaken based upon the criteria recommended by the Oxford Centre for Evidence Based Medicine[19]

Methodological reporting quality of RCTs was assessed using Jadad[20] and the Newcastle–Ottawa scale[21] was used to evaluate the quality of the prospective cohort studies included.

Data Extraction and Statistical Analysis

Preoperative parameters were extracted together with intraoperative data including operation times, changes in hemoglobin and transfusion rates. Postoperative data including length of hospitalization, duration of catheterization and treatment-related complications were also analyzed. Functional results including IPSS, Qmax, PVR, Qol and IIEF were assessed at 3, 6, 12, 24, 36 and 60 months.

Mean difference (MD) was used to assess continuous parameters. Authors were contacted when data were expressed as medians with corresponding range values. Otherwise, the statistical formula elaborated by Hozo et al[22] was implemented to back-calculate means and standard deviation in accordance with the recommended methods described in the Cochrane Handbook for Systematic Reviews[23].

Results were expressed as risk ratios (RR) with corresponding 95% confidence interval (CI) for dichotomous variables. I^2 was utilized to assess heterogeneity across studies. An I^2 <50% is generally considered an acceptable level of heterogeneity therefore a fixed effect was applied. In instances where the I^2 >50% a random effects model was applied as is the standard procedure for higher levels of heterogeneity. Pooled effects were synthesized using Z test and a p value <0.05 was set at the threshold for statistical significance.

Sensitivity analysis

Sensitivity analysis was conducted to assess the systematicity of this study and in an effort to reduce random errors which may affect pooled estimate representativeness. As such, Qmax at 24 months, PVR at 3-months, operation times, and period of hospitalization analyses were adjusted by removing non RCTs or trials assessed to be lower quality. All the data analysis was conducted with Review Manager 5.3 software.

RESULTS

The predetermined search and selection criteria yielded 22 publications [2, 7-11, 24-39], reporting 19 separate clinical studies. Three studies (i.e., Bachman et al., 2014[10], 2015[29] and Thomas et al. 2016[30]) refer to an identical study, and two studies (Kumar et al. 2013[24] and 2016[31]) were from the same trials in different period. In total, there were 2,665 patients involved, 1,455 of whom had been treated with PVP and 1,210 with TURP. Patient characteristics and study characteristics are summarized in **Table 1**. Overall, RCTs included in this meta-analysis can be consider of reasonably high quality with 8 studies achieving 3 scores, while 7 slightly lower achieving a Jadad score of 2. All prospective studies included can be considered high quality having been awarded 9 using the Newcastle-Ottowa Scale.

1. Meta-analysis of functional outcomes

Baseline data including IPSS, *Q*max, PVR, QoL and IIEF for all participants in both the PVP and TURP groups were similar (**Table 2**).

1.1. IPSS at 3, 6, 12, and 24 month follow-up

Pooled analysis suggests there is no significant difference in IPSS at the 3, 6, or 24 month follow-up points. At 3 months the MD = 0.01 ($p = 0.85$) please see **Fig. 2 a1.** At 6 months the MD = 0.30 ($p = 0.15$), see **Fig. 2 a2. A**t the 12 month follow-up stage there was a statistically significant difference with a MD = -0.10 ($p < 0.01$), see **Fig. 2 a3**, however; at 24 months there was no significant difference (MD = 0.02, $p = 0.92$), see **Fig. 2 a4**.

1.2. Qmax at 3, 6, 12, and 24 month follow-up

Pooled analysis suggests there is no significant difference between the PVP and TURP groups regarding Qmax at the 3 month follow-up stage with an MD = -0.07 ($p = 0.91$), see **Fig. 2 b1.** At the 6 month juncture the MD = -0.17, although this was also not statistically significant ($p = 0.67$), see **Fig. 2 b2**. At 12 months Qmax measures were slightly higher in the PVP group (MD = 0.62), which can be considered a statistically significant difference ($p = 0.03$), although only *borderline* when considering confidence intervals (95%CI= 0.06 to 1.19), see **Fig. 2 b3** for details. At 24 months the MD = 0.74 ($p = 0.34$) which was again non significant (see **Fig. 2 b4** for details**)**. High levels of heterogeneity were observed ($I^2 = 91\%$) hence sensitivity analysis was conducted at the 24-month follow-up point which yielded an MD = 0.26, although this was not a significant finding ($p = 0.72$), see **Fig. 3a**.

1.3. PVR at 3, 6, 12, and 24 month follow-up

PVR between the two groups, yielded no significant difference at 3 months (MD

=6.65, $p = 0.16$), see **Fig. 2 c1**, at 6 months (MD = 2.07, $p = 0.35$), see **Fig. 2 c2**, at 12 months (MD = 0.85, $p = 0.11$), see **Fig. 2 c3,** or at the 24 month follow-up point (MD = 1.58, $p = 0.23$), see **Fig. 2 c4**. Again, high levels of heterogeneity ($I^2 = 93\%$) was observed and so further sensitivity analysis was conducted at the 3 month follow-up juncture although this did not yield a significant interaction with an MD = 1.90 ($p = 0.38$), see **Fig. 3b** for details.

1.4. Qol at 3, 6, 12, and 24-month follow-up

There was no significant difference in QoL across data points analyzed. At the 3-month point there was an MD = 0.02, ($p = 0.59$) see **Fig. 2 d1**. At the 6 month follow-up point this appears to be a statistically significant difference (MD = -0.08), although again this can not be clinically relevant and can only be considered of borderline significance (95%CI= -0.13 to -0.02), despite the low p value ($p = 0.007$), see **Fig. 2 d2**. At 12 months (MD = 0.01, $p = 0.75$), see **Fig. 2 d3** and at 24 months (MD = -0.07, $p = 0.10$), see **Fig. 2 d4**, there was no significant difference.

1.5. IIEF at 6, 12, and 24 month follow-up

An analysis of sexual functioning, was performed using IIEF. There was no significant difference between the two groups in terms of the IIEF at the 3 month point (MD = -0.06, $p = 0.76$) see **Fig. 2 e1**, at the 6-month (MD = -0.07, $p = 0.78$) see **Fig. 2 e2** or at the 12 month point (MD = -0.06, $p = 0.82$) see **Fig. 2 e3**. Pooled analysis does suggest IIEF at the 24 month follow-up was lower in the PVP group compared to the TURP group with a MD = -0.68, which can be statistically significant but again must

be presented with caution due to the upper confidence interval being so close to the null (95%CI= -1.20 to -0.15, p = 0.01), see **Fig. 2 e4.**

2. Meta-analysis of perioperative parameters

2.1. Operation time

Fourteen studies comparing PVP against TURP reported operation times. Overall, TURP takes less time than PVP with a MD=15.24 minutes, and this was a significant finding (p <0.01) see **Table 3**. However, there was extreme heterogeneity across this sample (I^2 = 94%). As such, sensitivity analysis was conducted by removing low-quality trials (**Fig. 3c**) which lowered the level of heterogeneity (I^2 = 17%) and lowered the mean difference to 10.60 minutes (95%CI 8.39 to 12.81, p <0.01), see **Table 3**.

2.2. Operative blood loss

Six studies involving 724 participants (PVP group = 389, TURP = 335) provided blood loss estimates during operations. Across this study cohort heterogeneity was extreme (I^2 = 89%), and thus, a random effects model was implemented. The pooled statistic suggested that blood loss in the PVP group was significantly lower than in the TURP group with a MD of –1.33g/dl (p <0.01*),* see **Table 3** for details.

2.3. Periods of hospitalization

Eleven studies involving 1,542 participants met our inclusion criteria for the analysis of periods of hospitalization. Pooled statistics highlighted a significant reduction in hospitalization times with a MD = -1.98 days (p <0.01) for PVP compared

with TURP. However, again the level of heterogeneity across this sample was extreme (I^2 = 98%) therefore sensitivity analysis (**Fig.3d**) was again performed although this had a negligible impact on the results (MD = -1.83 days, 95% CI -2.25 to -1.40, p <0.01). See **Table 3** for further details.

2.3. Catheterization time

Fourteen available studies including 1,655 participants (861 in the PVP group and 794 in the TURP group) were involved in this meta-analysis. Pooled data revealed that the PVP group had a significantly shorter catheterization times with an MD = -1.25 days, (p <0.01) see **Table 3**.

3. Meta-analysis of Complications

3.1. Perioperative complications

The overall effect of perioperative complications including bleeding-related transfusion, TUR syndrome, capsular perforation, clot retention, urinary tract infection and acute urinary retention are summarized in **Table 3**. According to this meta-analysis, PVP was found to have significantly lower incidence of transfusion with an RR=0.14 (p <0.01), and clot retention (RR=0.14, p <0.01). There was also a small, but significant difference in the occurrence of TUR syndrome (RR=0.19, p <0.01) and capsular perforations (RR=0.09, p <0.01). Furthermore, PVP appears to have a higher risk of mild to moderate dysuria, although there was no substantial difference regarding urinary tract infection (RR=1.15, 95% CI 0.85 to 1.55, p = 0.38) and acute urinary retention rate (RR=1.19, 95% CI 0.80 to 1.75, p = 0.39).

3.2. Long-term complications

Analysis of long-term complications such as bladder neck contracture, retrograde ejaculation and urethral stricture, suggests there is no significant difference between PVP and TURP. Bladder neck contracture (RR=1.05, $p = 0.87$), retrograde ejaculation (RR = 0.72, $p = 0.11$) and urethral stricture (RR=0.81, $p = 0.25$), see **Table 3** for further details. However, PVP was found to have a significant higher risk of re-intervention (RR=1.81, $p < 0.01$) see **Table 3** for details.

DISCUSSION

Over the past two decades TURP has remained the gold standard surgical intervention for symptomatic BPH despite the high rate of treatment-related morbidities and complications which have a hugely negative impact on approximately 20% of those treated [3, 6, 11]. Uurologists continue to search for safer techniques without diminishing clinical efficacy compared to TURP. Endoscopic technologies are being developed, and PVP emerged as a promising intervention which attracted our attention because this is a minimally-invasive surgical procedure. The first generation PVP laser system utilized high-powered KTP lasers (60W) at 532 nm and was initially introduced in 1998[40]. More advanced generations including the KTP laser (80W)，the Green-light high-performance system (HPS) laser (120W) , the Green-light lithium triboride (LBO) laser (160W) and the Green-light X-ray photoelectron spectroscopy (XPS) laser (180W) systems were then sequentially introduced up until 2018, raising hopes of treating symptomatic BPH, effectively and safely.

Previous research comparing PVP and TURP has demonstrated that there is no significant difference in medium term efficacy or safety when treating BPH, however; the long-term efficacy between these two techniques remains controversial. In this up-to-date systematic review and meta-analysis, we reviewed all available RCTs and prospective studies (n = 22) up until October 2018 which involved a total of 2,665 participants. Pooled analyses and sensitivity analysis suggest both PVP and TURP have similar long-term function outcomes, which were analyzed using both subjective (IPSS, QoL) and objective (*Q*max, PVR) measures. IPSS at 12 month follow-up，*Q*max at 6 months and QoL at 12 months highlighted a statistically significant difference, although the differences was not substantial.

This study adds to the current evidence base in terms of understanding sexual functioning post-intervention. Previous clinical studies have evaluated retrograde ejaculation rates although conclusions could not be provided with any authority because findings were generally consistent and gathered over relatively short periods of time.[7, 10, 25, 27, 38] The longest running RCT which compared PVP with TURP had a 60 month follow-up, and suggested there is similar improvement in IPSS, Qmax, PVR, Qol and IIEF.[36, 39] Previously conducted meta-analyses have also not had the opportunity to evaluate IIEF due to an insufficient number of studies collecting and reporting this particular outcome. Fortunately, IIEF is increasingly being used to analyze sexual functioning which enabled us to design and perform this meta-analysis given the increased availability of evidence in this area. Pooled analysis however suggests there is no significant difference in retrograde ejaculation rate nor is there a

significant difference in IIEF outcomes between PVP and TURP.

There were substantial differences in perioperative factors analyzed across this sample of studies. Pooled analyses and sensitivity analyses highlighted that operation times are significantly longer for PVP, whereas the duration of hospitalization and catheterization are significantly shorter. Prolonged operative duration involved in PVP interventions appears to be associated with laser power and individual surgeon's experience and related skills. Laser power is classified according different devices, and overall operation times are prolonged by approximately 23 minutes for PVP with an 80W laser, approximately 9 minutes with 120W and 7 minutes with 120W and 160W lasers. Furthermore, a surgeon's overall technical skills and confidence place him/her at a point on a learning curve for new technologies which is likely to be an important factor in the length of operations.

Safety is another key issue because the most serious TURP complications, such as bleeding and TUR syndrome are known to correlate with prostate size and longer operative times[6, 41]. This analysis highlighted additional benefits, in that the incidence of perioperative complications including bleeding, blood transfusion, clot retention, capsule perforation and TUR syndrome are significantly lower for those receiving the PVP intervention. This can be explained by the characteristics of the green light laser, where the 532-nm wavelength is easily absorbed by hemoglobin in prostatic tissues but not by water[13]. Likewise in vaporization, high-power laser energy is instantly absorbed by the blood, ensuring quicker vaporization into the tissue which

creates a prostate cavity with minimal blood loss[42]. In this case, other bleeding-related complications occur less frequently for those receiving PVP. Another possible explanation could be that KTP laser energy penetrates only 1 to 2 mm of tissue. Therefore, high-power laser energy might be concentrated into the surface coat of prostatic tissue, which then ensures rapid vaporization, leaving a 0.2cm rim of coagulated tissue behind[13]. It may also be the case that the fluid medium used for PVP procedures is saline solution rather than glycine, therefore TUR syndrome does not occur in PVP although further research is necessary.

Additional postoperative complications such as acute urinary retention, UTIs, bladder neck contracture and urethral stricture were analyzed although no significant differences between TURP and PVP interventions was identified. However, PVP had two distinct disadvantages when compared with TURP. PVP appears to be associated with a higher risk of developing dysuria and for re-intervention. Dysuria rates after PVP have reported to be between 6% and 30%[33, 43]. There may be several reasons for this although most likely postoperative dysuria is caused by thermal damage and edema in urethral tissue. Also, shorter catheterization times could be another cause of this irritable symptom. That said, this symptom in all patients was classified as mild to moderate, and therefore can be effectively managed, if not resolved altogether within 2 months of follow-up[27, 33]. This suggests that transient dysuria is not a serious complication of PVP, the more serious complication is re-intervention.

There may be a number of reasons post-PVP patients are at a higher risk of re-

intervention. There may be inadequate energy delivery, leading to incomplete tissue removal which might play an important role regarding the outcome of the procedure [38, 44]. According to our further analysis, those who received an 80W PVP intervention were at significantly higher risk of re-intervention compared with TURP. However, the difference between other higher power PVP laser groups (i.e., 120W, 160W and 180W) and TURP cohort were not statistically significant. Additionally, the GOLIATH study suggests that the 180W XPS laser system is superior to TURP when considering this particular parameter. Logically, this type of adverse event would markedly decrease with the advent of higher power laser systems.

As well as having a higher risk of dysuria and re-intervention, PVP is administered in the absence of histologic tissue examination, which might limit opportunities to incidentally identify prostate cancer. In order to address this clinicians might want to consider whether there is a rapidly increasing or high value prostate-specific antigen (PSA), it might be more beneficial to use TURP rather than laser evaporation techniques. In addition, an extensive examination including PSA measures, digital rectal examinations and ultrasonography which guide prostate biopsies ought to be performed if cancer is suspected[12, 45]. Prostate cancer is often diagnosed in the late stages which is nearly always too late and therefore *opportunities* to diagnose this insidious disease must not be disregarded.

LUTS manifests secondarily through BPH and is a chronic health condition. The management of these symptoms create additional economic burden for patients and

healthcare systems, generally[2, 46]. It is vital to evaluate the cost effectiveness of the two surgical therapies in clinical practice. Based upon a cost-effectiveness analysis, Armstrong et al suggest that the PVP procedure is unlikely to be cost effective because of the relatively expensive consumables[47]. However, Patel argues that there is an absence of high-quality and long-term data, in fact only two RCTs with short term follow-ups were available at the time[48]. This study suggests that any initial investment in equipment and surgeon's training may be at least partially offset by shorter lengths of hospitalization and lower incidence of post-operative complications for PVP compared to TURP. Considering high number of cases each year, PVP may actually lower the demand for medical resources in this field although this also requires further research.

This meta-analysis was undertaken using all currently available comparative clinical studies, however; there are some limitations. First of all, despite designing a systematic search strategy, our inclusion criteria meant that non-English documents were omitted, therefore there must be some language bias. Secondly, there are very few RCTs with long-term follow-up endpoints in this field of interest which must be addressed. To overcome this, we designed this study to incorporate five prospective cohort studies which added a layer of sophistication to this analysis.

None of the RCTs included described blinding methods which is considered a distinct quality deficit but this is to be expected given the nature of the interventions explored. Actually, this perhaps highlights the need to use the CONSORT quality

appraisal method or the Delphi method in further studies. A more substantial concern however is that several studies did not report withdrawal or drop outs. This was the main determining factor in our quality assessment and this must be addressed in further research. Thirdly, there was consistently, substantial to extreme heterogeneity across this study sample. Sensitivity analysis only partially accounted for such high levels of heterogeneity therefore further controls should be embedded across trials in this field. Increased sample sizes, or multi-centre trials involving large numbers of participants as well as age stratification may elaborate on our present understanding. Despite these limitations, this study provides the most up-to-date information concerning the comparison of PVP and TURP in surgical management of BPH.

CONCLUSION

These findings confirm previous studies which suggested that PVP may be superior in long-term efficacy to TURP. PVP has increased IPSS, *Q*max, QoL, PVR and IIEF benefit, and is associated with fewer complications. As such, we recommend PVP is offered as the first-line treatment for LUTS secondary to BPH rather than the traditional TURP method. The only addendum is that PVP can't acquire histological tissue examination which removes an opportunity to identify prostate cancer. Withdrawals and drop outs are not always reported in full and there is a need to use a more comprehensive quality assessment tool to appraise studies in this field because blinding is not possible. Further research is of course necessary, and should be conducted with larger samples, over longer periods.

AUTHOR CONTRIBUTIONS

SCL and PXP designed and conducted the systematic search to identify all relevant studies. SCL and PXP then assessed eligibility and the quality of each study, before extracting data and conducting statistical analysis. TXD and HMH coordinated the study and performed data acquisition. XW, WZ and YGZ participated in data interpretation and drafting this article. SS, ML and JYW reviewed and revised this report for critical content and scientific rigour. All authors read and approved the final manuscript

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DATA AVAILABLITY STATEMENT

No additional unpublished data were available.

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Legend

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow chart

Figure 2. Forest plot of IPSS at 3 months (a1), 6 months (a2), 12 months (a3) and 24 months (a4); Forest plot of Qmax at 3 months (b1), 6 months (b2), 12 months (b3) and 24 months (b4); Forest plot of PVR at 3 months (c1), 6 months (c2), 12 months (c3) and 24 months (c4); Forest plot of Qol at 3 months (d1), 6 months (d2), 12 months (d3) and 24 months (d4); Forest plot of IIEF at 3 months (e1), 6 months (e2), 12 months (e3) and 24 months (e4). (IPSS = International Prostate Symptom Score; QoL = quality of life; Qmax = maximum flow rate; PVR = postvoid residual volume; IIEF=international index of erectile function)

Figure 3. Sensitivity analysis of the Qmax at 24-month follow-up (a); PVR at 3-month follow-up (b); operation times (c); and period of hospitalization (d). (Qmax = maximum flow rate; PVR = postvoid residual volume).

Table 1 Baseline characteristics of comparative studies.

Table 2 Meta-analytical outputs summarizing baseline parameters of PVP compared with TURP.

Table 3 Meta-analytical outputs for the safety of PVP compared with TURP.

Supplementary file

Supplement file 1 Electronic search strategy in PUBMED.

Table 1. Baseline characteristics of comparative studies

Authors and year	Design	Group	Laser power (W)	No. of patients	Age (years)	Prostate size (ml)	IPSS	*Q*max (mL/s)	PVR (mL)	QoL	IIEF	Follow-up, (months)	LE	Study quality
Kumar et al 2013	RCT	PVP	120	58	64.58±6.64	52.79±16.13	20.05±2.75	6.68±2.00	143.35±52.67	3.60±1.01	16.65±2.80	12	2a	3*
		TURP		60	63.68±6.57	52.20±15.93	20.71±2.68	7.00±1.97	139.25±54.28	3.73±0.97	16.95±2.86			
Lukacs et al 2012	RCT	PVP	120	68	66.9±7.8	50.54±16.53	22 (17–26)	7.79±2.75	89.5 (30-158)	70 (68–80)	N/A	12	2a	3*
		TURP		68	67.6±7.6	50.11±14.73	20 (15–23)	7.76±2.64	75 (28–126)	75 (65–85)	N/A			
Pereira-Correia	RCT	PVP	120	10	66.4（52 – 76）	43.4(30– 58）	22 (9 – 33)	10（3 – 18）	150（25 – 250）		23（22 – 24）	24	2a	2*
et al 2012		TURP		10	63.5（56 – 78）	47（30– 60）	25(15 – 31）	6.4（4 – 11）	177（50 – 300）		23（22 – 25）			
Capitan et al 2011	RCT	PVP	120	50	69.8±8.44	51.29±14.72	23.74±5.24	8.03±3.14		4.52±0.27		12	2a	3*
		TURP		50	67.7±6.7	53.10±13.75	23.52±4.38	3.88±2.71		4.14±1.06				
Al-Ansari et al 2010	RCT	PVP	120	60	66.3±9.4	61.8±22	27.2±2.3	6.9±2.2	53.2±25			36	2a	3*
		TURP		60	67.1±8	60.3±20	27.9±2.7	6.4±2	57±21					
Xue et al 2013	RCT	PVP	120	100	72.1±11.3	65.8 ± 23.6	23.0 ± 5.1	8.0 ± 3.6	148.3 ± 101.6	4.2 ± 0.9		36	2a	2*

		TURP		100	71.0±10.8	67.3 ± 24.7	23.2 ± 5.0	8.2 ± 3.8	151.1 ± 105.2	4.3 ± 0.8				
Horasanli et al 2008	RCT	PVP	80	39	69.2±7.1	86.1±8.8	18.9±5.1	8.6±5.2	183±50.1		19.9±5.1	6	2a	2*
		TURP		37	68.3±6.7	88±9.2	20.2±6.8	9.2±5.6	176.9±45.3		20.1±5.5			
Mohanty et al 2012	RCT	PVP	80	60	66.68±8.62	44.77±14.09	19.98±3.27	7.41±2.07	145.8±70.33	3.97±0.82	17.98±3.55	12	2a	3*
		TURP		57	65.74±9.09	49.02±15.93	20.88±3.87	6.75±1.63	143.23±65.96	3.91±0.78	17.40±4.76			
Bouchier-Hayes et al 2009	RCT	PVP	80	60	>50		25.28±5.93	8.81±2.55	129.2±155.7	4.74±1.23		12	2a	3*
		TURP		59			25.41±5.72	8.86±2.99	111.3±113.7	5.08±0.94				
Bachmann et al 2014	RCT	PVP	180	136	65.9±6.8	48.6±19.2	21.2±5.9	9.5±3.0	110.1±88.5	4.6±1.1	13.2±7.6	6	2a	3*
		TURP		133	65.4±6.6	46.2±19.1	21.7±6.4	9.9±3.5	109.8±103.9	4.5±1.4	13.7±7.5			
Bachmann et al 2015	RCT	PVP	180	136	65.9±6.8	48.6±19.2	21.2±5.9	9.5±3.0	110.1±88.5	4.6±1.1	13.2±7.6	12	2a	2*
		TURP		133	65.4±6.6	46.2±19.1	21.7±6.4	9.9±3.5	109.8±103.9	4.5±1.4	13.7±7.5			
Thomas et al 2016	RCT	PVP	180	136	65.9±6.8	48.6±19.2	21.2±5.9	9.5±3.0	110.1±88.5	4.6±1.1	13.2±7.6	24	2a	3*
		TURP		133	65.4±6.6	46.2±19.1	21.7±6.4	9.9±3.5	109.8±103.9	4.5±1.4	13.7±7.5			
Telli et al 2015	RCT	PVP	120	39	67 (51–87)	60 (41–75)	20 (12–30)	10.6 (5–17)	60 (20–220)			24	2a	2*

		TURP		62	69 (56–87)	55 (40–72)	19 (10–31)	12.5 (3–21)	65 (10–220)					
Kumar et al 2016	RCT	PVP	120	58	64.58±6.64	52.79±16.13	20.05±2.75	6.68±2.00	143.35±52.67	3.60±1.01	16.65±2.80	36	2a	2*
		TURP		60	63.68±6.57	52.20±15.93	20.71±2.68	7.00±1.97	139.25±54.28	3.73±0.97	16.95±2.86			
Mordasini et al 2018	RCT	PVP	80	112	68.4±8.7	36.1±11.5	20.3±7.0	8.9±4.1	91.1±88.3	4.2±1.1		60	2a	2*
		TURP		126	67.6±8.4	37.9±14.3	20.4±7.5	8.5±4.6	114.5±136.4	4.3±14				
Chen et al 2011	PCS	PVP	160	57	69.5±7.4	60.2±27.8	19.7±6.0	6.9±4.0	93.7±79.7			6	2b	9#
		TURP		51	67.1±6.9	58.3±26.2	21.8±7.3	6.8±2.3	102.2±70.1					
Bachmann et al 2005	PCS	PVP		37	71.0±9.3	65.1±36.9	18.1±5.9	6.9±2.2	146.1±106.9	3.3±1.7		6	2b	9#
		TURP		64	68.7±7.9	48.9±21.2	17.3±6.3	6.9±2.2	120.7±49.0	3.4±1.6				
Ruszat et al 2008	PCS	PVP	80	113	62.3±5.0	56.3±27.4	20±6.4	8.5±4.1	203±226			24	2b	9#
		TURP		75	61.7±5.5	45.3±21.0	19±6.9	9.8±5.0	104±108					
		PVP		91	75.0±2.8	64.8±26.8	18.6±5.8	7.3±2.7	215±247					
		TURP		40	74.0±2.6	54.2±21.2	16.0±7.1	9.2±5.4	124±141					
		PVP		65	84.3±3.1	69.3±32.7	14.1±7.4	7.1±4.2	200±219					

		TURP		12	82.4±2.8	44.9±22.1	15.5±6.7	7.6±3.9	231±350				
Tasci et al 2008	PCS	PVP		40	71.8±5.9	108.4±15.8	22.3±5.6	6.2±2.2	116.5±60.5	3.6±0.7	24	2b	9#
		TURP		41	70.1±5.4	104.2±12.5	22.6±3.9	6.5±1.8	110.7±59.8	3.5±0.6			
Tugcu et al 2008	PCS	PVP		112	67.5±7.4	49.1±11.9	17.9±4.9	6.9±1.9	107.9±63.0	3.4±0.6	24	2b	9#
		TURP		98	66.3±7.9	47.7±8.4	17.7±3.5	7.2±1.7	100.3±57.1	3.4±0.5			
Nomura et al 2009	PCS	PVP	80	78	72.0(67.0,78.0)	50.5(38.6,70.3)	23 (17, 27)	6.8 (5.2, 9.5)	69 (31, 139)	5 (5, 6)	12	2b	9#
		TURP		51	70.5 (66.5, 76.0)	42.8 (34.6, 54.0)	22 (16, 27)	7.3 (5.3, 10.2)	60 (31, 140)	5 (4, 5)			
Guo et al 2015	PCS	PVP	80	257	69.7±8.9	52.3±19.3	19.4±6.3	8.3±6.0	119.5±83.8	3.7±1.7	60	2b	9#
		TURP		104	66.4±8.4	44.2±19.1	18.4±6.3	10.0±5.2	95.6±98.4	3.7±1.3			

LE = level of evidence;# Using Newcastle-Ottawa Scale (score from 0 to 9)； * Using Jadad scale (score from 0 to 5); RCT= randomized controlled trial; IPSS = International Prostate Symptom Score; QoL = quality of life; Qmax = maximum flow rate; PVR = postvoid residual volume; TURP = transurethral resection of the prostate; PVP=Photoselective vaporization of the prostate; IIEF=international index of erectile function; PCS=prospective cohort study.

Bachmann et al 2014， Bachmann et al 2015 and Thomas et al 2016 are from the same trials in different period; Kumar et al 2013 and Kumar et al 2016 are from the same trials in different period.

Table 2. Meta-analytical outputs summarizing baseline parameters of PVP compared with TURP

Parameter	No.of studies	Sample size		Heterogeneity(Total)				MD (95%CI)	Test for overall effect	
		PVP	TURP	chi^2	df	I^2%	P value			
IPSS										
Baseline	14	1179	989	11.32	13	0	0.58	-0.29 [-0.68, 0.10]	Z=1.47	p=0.14
Qmax										
Baseline	14	1179	989	70.23	13	81	<0.01	0.05[-0.51, 0.61]	Z=0.17	p=0.87
PVR										
Baseline	12	1016	864	9.24	11	0	0.6	2.19[-3.22,7.61]	Z=0.79	p=0.43
Qol										
Baseline	10	910	766	11.15	9	19	0.27	0.01 [-0.07,0.10]	Z=0.33	P=0.74
IIEF										
Baseline	5	351	297	1.58	4	0	0.81	-0.13 [-0.86,0.60]	Z=0.34	P=0.73

CI=confidence interval, MD=mean difference, RR=risk ratio; IPSS = International Prostate Symptom Score; PVP=Photoselective vaporization of the prostate; QoL = quality of life;

PVR = postvoid residual volume; Qmax = maximum flow rate; IIEF=International Index of Erectile Function; TURP = transurethral resection of the prostate

Table 3. Meta-analytical outputs for the safety of PVP compared with TURP

Outcomes	No.of studies	Sample size		Heterogeneity(Total)				MD or RR(95%CI)	Test for overall effect	
		PVP	TURP	chi^2	df	I^2 (%)	*P*		Z	*P*
Operation time	14	979	870	216.27	13	94	<0.01	15.24 [8.91,21.54]	4.72	<0.01
	6*	429*	428*	6.01*	5*	17*	0.31*	10.60 [8.39, 12.81]*	9.40*	<0.01*
Hospitalization time	11	819	723	600.62	10	98	<0.01	-1.98 [-2.56, -1.39]	6.59	<0.01
	3*	240*	229*	6.29*	2*	68*	<0.01*	-1.83 [-2.25, -1.40]*	8.42*	<0.01*
Catheterization time	14	861	794	964.75	13	99	<0.01	-1.25 [-1.58, -0.92]	7.48	<0.01
Blood loss	6	389	335	46.05	5	89	<0.01	-1.33 [-2.05, -0.61]	3.62	<0.01
Transfusion	14	1110	946	10.87	13	0	0.62	0.14 [0.08, 0.26]	6.10	<0.01

TUR syndrome	7	590	435	0.73	6	0	0.99	0.19 [0.06, 0.61]	2.82	<0.01
Capsular perforation	7	641	451	1.84	6	0	0.93	0.09 [0.03, 0.26]	4.51	<0.01
Clot retention	8	699	504	1.72	7	0	0.97	0.14 [0.07, 0.29]	5.32	<0.01
Urinary tract infection	13	1049	860	8.79	12	0	0.72	1.15 [0.85, 1.55]	0.89	0.38
Acute urinary retention	10	694	653	5.55	9	0	0.78	1.19[0.80, 1.75]	0.86	0.39
Urinary incontinence	4	296	263	4.28	3	30	0.23	1.45[0.74, 2.86]	1.08	0.28
Bladder neck contracture	8	523	520	4.32	7	0	0.74	1.05 [0.57, 1.94]	0.16	0.87
Urethral stricture	15	1172	980	9.37	14	0	0.81	0.81 [0.57, 1.16]	1.14	0.25
Retrograde ejaculation	4	320	314	15.06	3	80	<0.01	0.72 [0.49, 1.07]	1.62	0.11
Dysuria	12	1079	854	24.80	11	58	0.01	1.76 [1.17, 2.65]	2.71	<0.01
Re-intervention	12	980	809	14.58	11	25	0.20	1.81 [1.28, 2.56]	3.35	<0.01

* Using sensitivity analysis; CI=confidence interval; MD=mean difference; PVP=Photoselective vaporization of the prostate; RR=risk ratio; TURP = transurethral resection of the prostate; TUR syndrome= transurethral resection syndrome

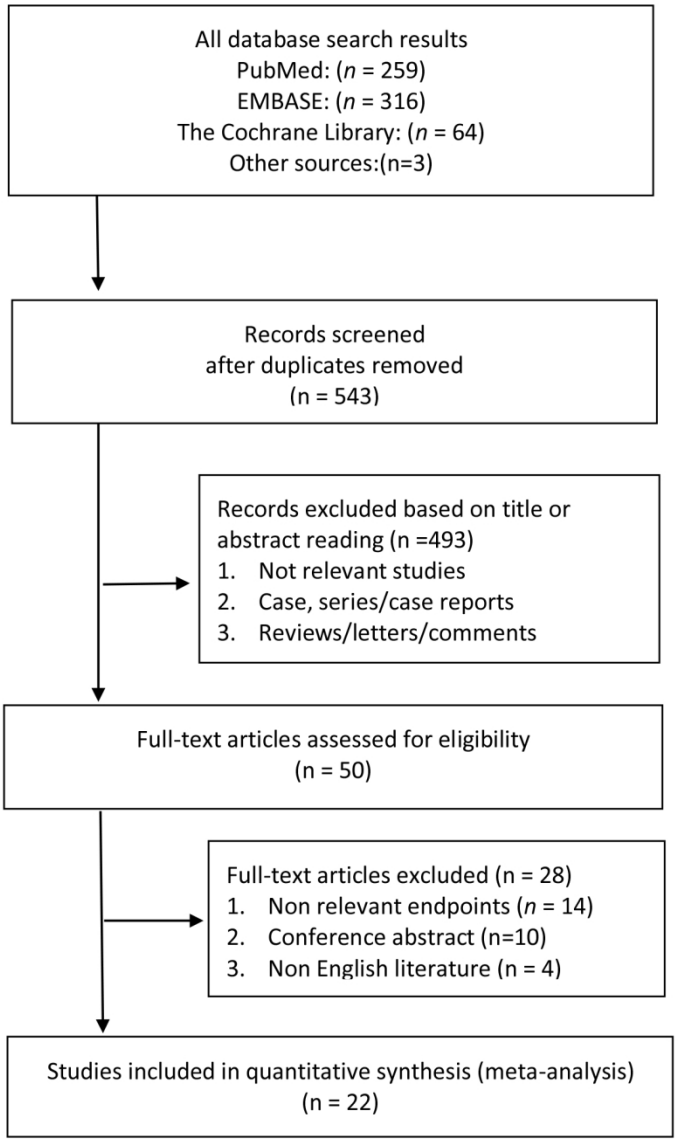

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow chart

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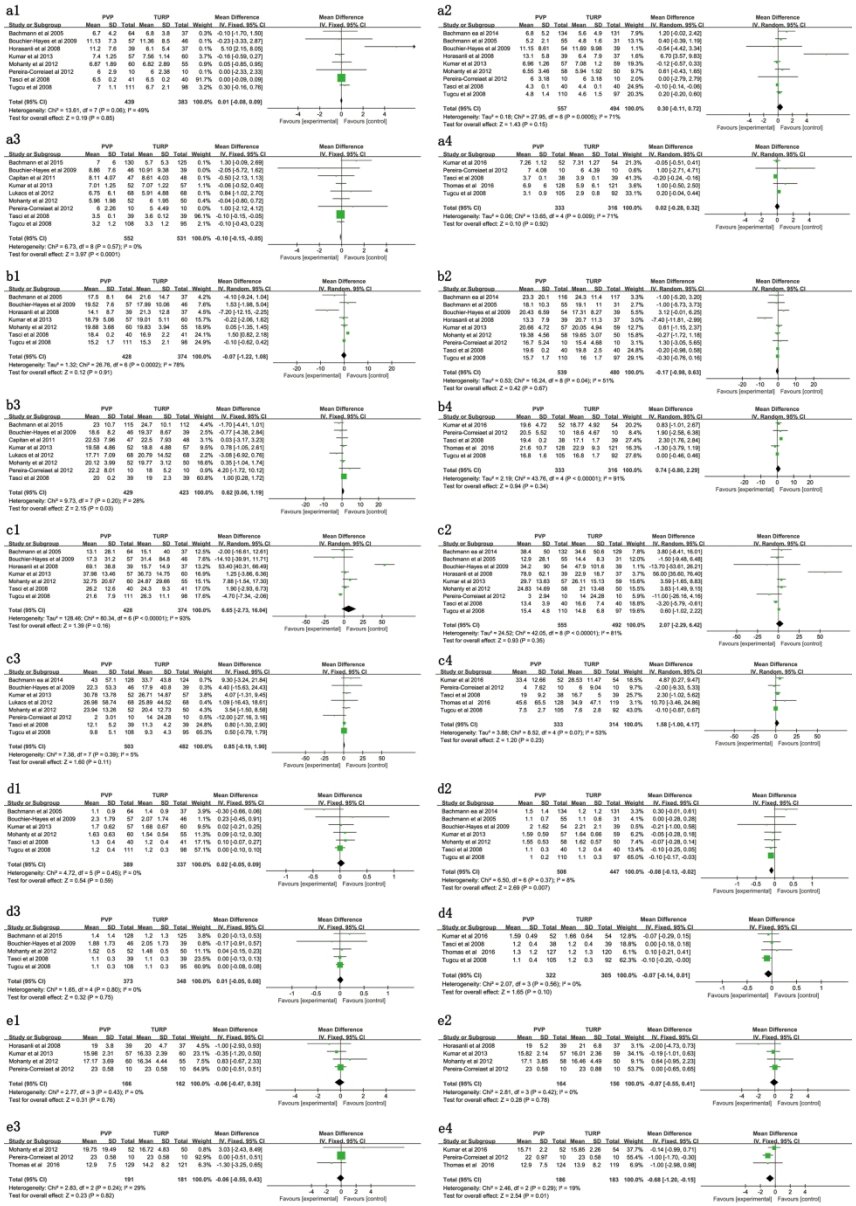

Figure 2. Forest plot of IPSS at 3 months (a1), 6 months (a2), 12 months (a3) and 24 months (a4); Forest plot of Qmax at 3 months (b1), 6 months (b2), 12 months (b3) and 24 months (b4); Forest plot of PVR at 3 months (c1), 6 months (c2), 12 months (c3) and 24 months (c4); Forest plot of QoI at 3 months (d1), 6 months (d2), 12 months (d3) and 24 months (d4); Forest plot of IIEF at 3 months (e1), 6 months (e2), 12 months (e3) and 24 months (e4). (IPSS = International Prostate Symptom Score; QoL = quality of life; Qmax = maximum flow rate; PVR = postvoid residual volume; IIEF=international index of erectile function)

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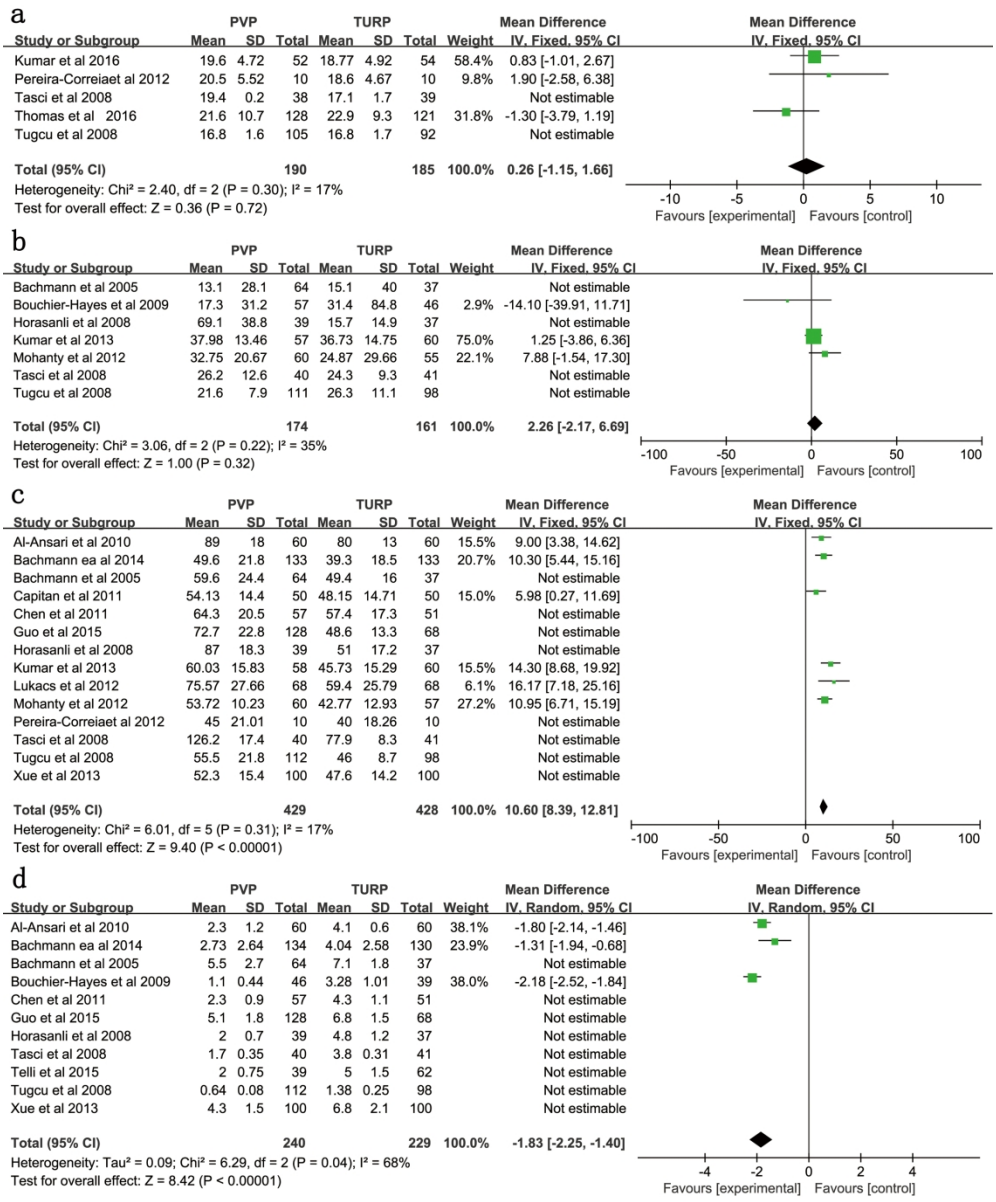

Figure 3. Sensitivity analysis of the Qmax at 24-month follow-up (a); PVR at 3-month follow-up (b); operation times (c); and period of hospitalization (d). (Qmax = maximum flow rate; PVR = postvoid residual volume).

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	6-7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	None
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7-8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7-8
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8-9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-14
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-14
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10-14
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11-13
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	14-19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	19-20
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	20
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	21

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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Comparison of photoselective green light laser vaporization versus traditional transurethral resection for benign prostate hyperplasia: an up-to-date systematic review and meta-analysis of randomized control trials and prospective studies

Search strategy in PUBMED

((((((((((((Hyperplasia, Prostatic) OR Prostatic Hypertrophy) OR Adenoma, Prostatic) OR Adenomas, Prostatic) OR Prostatic Adenomas) OR Prostatic Adenoma) OR Benign Prostatic Hyperplasia) OR Prostatic Hyperplasia, Benign) OR Prostatic Hypertrophy, Benign) OR Benign Prostatic Hypertrophy) OR Hypertrophy, Benign Prostatic)) AND ((((((((((((Prostate Transurethral Resection) OR Prostate Transurethral Resections) OR Transurethral Prostate Resection) OR Prostate Resection, Transurethral) OR Prostate Resections, Transurethral) OR Resection, Transurethral Prostate) OR Resections, Transurethral Prostate) OR Transurethral Prostate Resections) OR TURP) OR TURPs) OR Prostatectomy, Transurethral) OR Prostatectomies, Transurethral) OR Transurethral Prostatectomies) OR Transurethral Prostatectomy)) AND (((PVP) OR photoselective vaporisation) OR green-light laser)

The last quest was updated on December 20, 2018

BMJ Open

Comparison of photoselective green light laser vaporization versus traditional transurethral resection for benign prostate hyperplasia: an updated systematic review and meta-analysis of randomized controlled trials and prospective studies

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Complete List of Authors:	Lai, Shicong; Department of Urology, Beijing Hospital of the Ministry of Health, Beijing 100730, China, ; Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China Peng, Panxin; Peking University China-Japan Friendship School of Clinical Medicine, Beijing 100029, China; China-Japan Friendship Hospital, Department of Urology Diao, Tongxiang; Beijing Hospital, National Center of Gerontology, China; Peking university fifth school of clinical medicine Hou, Huimin; Beijing Hospital, National Center of Gerontology, China; Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China Wang, Xuan; Beijing Hospital, National Center of Gerontology, China Zhang, Wei; Beijing Hospital, National Center of Gerontology, China; Peking university fifth school of clinical medicine Liu, Ming; Beijing Hospital, National Center of Gerontology, China Zhang, Yaoguang; Beijing Hospital, National Center of Gerontology, China Seery, Samuel; Chinese Academy of Medical Sciences and Peking Union Medical College, School of Humanities and Social Sciences Wang, Jianye; Beijing Hospital, National Center of Gerontology, China
Primary Subject Heading:	Urology
Secondary Subject Heading:	Urology, Surgery
Keywords:	Prostate disease < UROLOGY, UROLOGY, Adult urology < UROLOGY

Comparison of photoselective green light laser vaporization versus traditional transurethral resection for benign prostate hyperplasia: an updated systematic review and meta-analysis of randomized controlled trials and prospective studies

Shi-Cong Lai[1,2#], Pan-Xin Peng[3,4#], Tong-Xiang Diao[1,5], Hui-Min Hou[1,2], Xuan Wang[1], Wei Zhang[1,5], Ming Liu[1], Yao-Guang Zhang[1], Samuel Seery[6]， Jian-Ye Wang[1]*

[1] Department of Urology, Beijing Hospital, National Center of Gerontology, Beijing 100730, China

[2] Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China

[3] Peking University China-Japan Friendship School of Clinical Medicine, Beijing 100029, China

[4] Department of Urology, China-Japan Friendship Hospital, Beijing 100029, China

[5] Peking university fifth school of clinical medicine

[6] School of Humanities and Social Sciences, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100730, China

 # Shi-Cong Lai and Pan-xin Peng contributed as the co-first author

*** Correspondence author: Jian-Ye Wang**

5. Address for correspondence:

Jian-Ye Wang, No.1 Da Hua Road, Dong Dan, Beijing 100730, P.R. China

Email: **wangjy@bjhmoh.cn**

Word count

Title: 28

Abstract: 300

Article: 3938

References: 49

Number of tables, figures, supplementary files: 3, 3, 1

Abstract

Objective: To assess the efficacy and safety of green-light laser photoselective vaporisation of the prostate (PVP) compared with transurethral resection of the prostate (TURP) for lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH).

Design: Systematic review and meta-analysis, conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement.

Data sources: PubMed, EMBASE, The Cochrane Library until October 2018

Eligibility criteria: Randomized controlled trials and prospective studies comparing the safety and efficacy of PVP versus TURP for LUTS manifesting through BPH.

Data extraction and synthesis: Perioperative parameters, complications rates and functional outcomes including treatment-related adverse events such as International Prostate Symptom Score (IPSS), maximum flow rate (Qmax), postvoid residual (PVR), Quality of Life (Qol) and International Index of Erectile Function (IIEF).

Results: 22 publications consisting of 2665 patients were analyzed. Pooled analysis revealed PVP is associated with reduced blood loss, transfusion, clot retention, TUR syndrome, capsular perforation, catheterization time and hospitalization, but also with a higher re-intervention rate and longer intervention duration (all $p < 0.05$). No significant difference in IPSS, *Q*max, QoL, PVR or IIEF at 3, 24, 36 or 60 months was identified. There was a significant difference in Qol at 6 months (MD = -0.08; 95%CI -0.13 to -0.02; $p = 0.007$), and IPSS (MD = −0.10; 95%CI −0.15 to −0.05; p<0.0001) and *Q*max (MD = 0.62; 95% CI 0.06 to 1.19; p=0.03) at 12 months although these

differences were not clinically relevant.

Conclusion: PVP is an effective alternative, holding additional safety benefits. PVP has equivalent long-term IPSS, *Q*max, QoL, PVR, IIEF efficacy, and fewer complications. The main drawbacks are dysuria and re-intervention although both can be managed with non-invasive techniques. The additional shortcoming is that PVP does not acquire histological tissue examination which removes an opportunity to identify prostate cancer.

Keywords: Benign prostatic hyperplasia (BPH), Lower urinary tract symptoms (LUTS), Meta-analysis, Photoselective vaporisation of the prostate (PVP), Transurethral resection of the prostate (TURP)

Strengths and limitations of this study

- This updated meta-analysis included a larger number of studies involving more participants which adds precision to previous findings
- This study analyzed both safety and efficacy, focusing on sexual functioning and quality of life measures because LUTS treatment related adverse events have a hugely detrimental impact on ones' psychological well-being
- Quality assessment methods used did not highlight substantial differences between studies because blinding is not possible given the characteristics of the two interventions under investigation
- Due to the limited number of studies in this field, we were unable to conduct subgroup analysis around laser power (i.e., 80W, 120W, 180W etc.) which is necessary to identify the most effective/efficient standard
- Surgical experience with laser technology, drop outs and withdrawals as well as other important factors were seldom reported in any detail which inhibits further analysis

INTRODUCTION

Lower urinary tract symptoms (LUTS) commonly occur in the aging male population, affecting more than 1 in 4 of those above 50 years of age. LUTS manifest through benign prostatic hyperplasia (BPH) and often have a hugely negative impact on quality of life (Qol) [1]. Treatments for BPH range from medicinal interventions to surgery, where transurethral resection of the prostate (TURP) remains the surgical gold standard. Surgical therapy is recommended for patients whom have not benefitted from medical interventions such as, 5-alpha-reductase inhibitors and alpha-blockers [1, 2]. TURP has been found to have a high success rate and low re-intervention rate at long-term follow-up [3], however; increasingly evidence indicates this invasive procedure is also associated with serious complications such as bleeding, urethral strictures, urinary incontinence and transurethral resection (TUR) syndrome [4-6]. Consequently, there is an urgent need to develop minimally-invasive therapies which do not have such a negative impact on patients' lives.

Laser therapies offer a new direction in BPH therapies and photoselective vaporization of the prostate (PVP) is increasingly being studied as a potential new first line treatment [7-11]. This technique is generally performed with a 532-nm green laser generated using potassium-titanyl-phosphate (KTP) or lithium triborate crystals [12]. Unlike other types of laser, the green laser is easily absorbed by soft tissue haemoglobin, while hardly at all by other fluid mediums, which leads to improved coagulation and lowers the risk of deeper tissue injuries during vaporization [13, 14]. Numerous studies provide supporting evidence of increased benefit, demonstrating that PVP has superior

mid-term clinical efficacy compared with TURP across functional outcomes including International Prostate Symptom Score (IPSS), maximum flow rate (Qmax), postvoid residual volume (PVR), International Index of Erectile Function (IIEF) and QoL [15, 16].

In a previous meta-analysis published in 2013, Teng et al [17] found that PVP and TURP have similar treatment efficacies although due to the minimally invasive nature, PVP offers several potential benefits. While this early research provided some optimism, studies have yet to compare sexual function outcomes or efficacy results at 24 months, and across all available RCTs and prospective studies. Consequently, we sought to conduct an updated systematic review and meta-analysis of high quality studies to support clinical decision-makers treating BPH.

MATERIALS AND METHODS

Patient and Public Involvement

Neither patients nor the public were involved in the design and planning of the study.

Literature Search and Article Selection

A comprehensive literature search was performed using biomedical databases including PubMed, EMBASE, and the Cochrane Library up until October 2018. The following MeSH terms and free text words were used: benign prostatic hyperplasia, BPH, transurethral resection of the prostate, TURP, green-light laser, vaporization, photoselective vaporization of the prostate and PVP. These terms were used singly and in combination (for further details please see supplement file 1). Additionally, manual

searches were commenced for references and citations included within pertinent reviews. Language was restricted to English and the search and selection strategy was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement [18]. Randomized controlled trials and prospective studies meeting the following criteria were included: (1) studies comparing the safety and efficacy of PVP versus TURP for surgical treatment of LUTS secondary to manifesting BPH, (2) endpoints such as treatment-related adverse events and functional outcomes such as IPSS, Qmax, PVR, Qol and IIEF when available, and (3) providing the full text of the study could be accessed.

Literature searching, selection, and data extraction was undertaken independently by two reviewers (SL and PP) which was then cross-checked. Any discrepancies were resolved through discussion. A flowchart representing the search and selection process is presented in **Fig. 1**.

Assessment of Study Quality

Study quality was assessed in accordance with criteria recommended by the Oxford Centre for Evidence Based Medicine [19] Methodological reporting quality of RCTs was assessed using Jadad [20] and the Newcastle–Ottawa scale [21] was used to evaluate the quality of the prospective cohort studies included.

Data Extraction and Statistical Analysis

Preoperative parameters were extracted together with intraoperative data including operation times, changes in hemoglobin and transfusion rates. Postoperative data including length of hospitalization, duration of catheterization and treatment-related

complications were also analyzed. Functional results including IPSS, Qmax, PVR, Qol and IIEF were assessed at 3, 6, 12, 24, 36 and 60 months after surgery.

Mean difference (MD) was used to assess continuous parameters. Authors were contacted when data were expressed as medians with corresponding range values. Otherwise, the statistical formula elaborated by Hozo et al [22] was implemented to back-calculate means and standard deviation in accordance with the recommended methods described in the Cochrane Handbook for Systematic Reviews [23].

Results were expressed as risk ratios (RR) with corresponding 95% confidence interval (CI) for dichotomous variables. I^2 was utilized to assess heterogeneity across studies. An I^2 <50% is generally considered an acceptable level of heterogeneity therefore a fixed effect model was applied. In instances where the I^2 >50% a random effects model was applied as is the standard procedure for higher levels of heterogeneity. Pooled effects were synthesized using Z test and a p value <0.05 was set at the threshold for statistical significance.

Sensitivity analysis

Sensitivity analysis was conducted to assess the reliability of the findings of this study. As such, Qmax at 24 months, PVR at 3-months, operation times, and period of hospitalization were further analysed by removing non-RCTs. All data analyses were conducted with Review Manager 5.3 software.

RESULTS

The predetermined search and selection criteria yielded 22 publications [2, 7-11, 24-

39], reporting 19 separate clinical studies. Three studies (i.e., Bachman et al., 2014 [10], 2015 [29] and Thomas et al. 2016 [30]) refer to an identical study, and two studies (Kumar et al. 2013 [24] and 2016 [31]) were from the same trials over different periods of time. In total, there were 2,665 patients involved, 1,455 of whom had been treated with PVP and 1,210 with TURP. Patient characteristics and study characteristics are summarized in **Table 1**. Overall, RCTs included in this meta-analysis can be considered of reasonably high quality with 8 studies achieving a score of 3, while 7 slightly lower quality achieved Jadad scores of 2. All prospective studies included can be considered high quality having been awarded 9 using the Newcastle-Ottowa Scale.

1. Meta-analysis of functional outcomes

Baseline data including IPSS, *Q*max, PVR, QoL and IIEF for all participants in both the PVP and TURP groups were similar (**Table 2**).

1.1. IPSS at 3, 6, 12, and 24 month follow-up

Pooled analysis suggests there is no significant difference in IPSS at the 3, 6, or 24 month follow-up points. At 3 months the MD = 0.01 ($p = 0.85$) please see **Fig. 2 a1.** At 6 months the MD = 0.30 ($p = 0.15$), see **Fig. 2 a2. A**t the 12 month follow-up stage there was a statistically significant difference with a MD = -0.10 ($p < 0.01$), see **Fig. 2 a3**, however; at 24 months there was no significant difference (MD = 0.02, $p = 0.92$), see **Fig. 2 a4**.

1.2. Qmax at 3, 6, 12, and 24 month follow-up

Pooled analysis suggests there is no significant difference between PVP and TURP regarding Qmax at the 3 month follow-up stage with an MD = -0.07 ($p = 0.91$), see **Fig.**

2 b1. At the 6 month juncture the MD = -0.17 (p = 0.67), see **Fig. 2 b2**. At 12 months Qmax measures were slightly higher in the PVP group (MD = 0.62), which may be considered a statistically significant difference (p = 0.03), although only *borderline* when considering confidence intervals (95%CI= 0.06 to 1.19), see **Fig. 2 b3** for details. At 24 months the MD = 0.74 although was again non significant (p = 0.34), see **Fig. 2 b4** for details. However, an extreme level of heterogeneity were observed (I^2 = 91%) hence sensitivity analysis was conducted at the 24-month follow-up point which yielded an MD = 0.26, although this was not a significant finding (p = 0.72), see **Fig. 3a**.

1.3. PVR at 3, 6, 12, and 24 month follow-up

PVR between the two groups, yielded no significant difference at 3 months (MD =6.65, p = 0.16), see **Fig. 2 c1**, at 6 months (MD = 2.07, p = 0.35), see **Fig. 2 c2**, at 12 months (MD = 0.85, p = 0.11), see **Fig. 2 c3,** or at the 24 month follow-up point (MD = 1.58, p = 0.23), see **Fig. 2 c4**. Again, a high level of heterogeneity (I^2 = 93%) was observed and so sensitivity analysis was conducted at the 3 month follow-up juncture. This did not highlight a significant difference between groups (p = 0.38), see **Fig. 3b** for details.

1.4. Qol at 3, 6, 12, and 24-month follow-up

There was no clinical relevant difference in QoL across the time points analyzed, however; at six months there appears to be a statistically significant difference. At the 3-month point there was an MD = 0.02, (p = 0.59) see **Fig. 2 d1**. At the 6 month follow-up point this appears to be a statistically significant difference (MD = -0.08), although

again this may not be clinically relevant and can only be considered of borderline significance (95%CI = -0.13 to -0.02), despite the low p value (p = 0.007), see **Fig. 2 d2**. At 12 months (MD = 0.01, p = 0.75), see **Fig. 2 d3** and at 24 months (MD = -0.07, p = 0.10), see **Fig. 2 d4**, there was no significant difference.

1.5. IIEF at 6, 12, and 24 month follow-up

An analysis of sexual functioning was performed using IIEF. There was no significant difference between the two groups in terms of the IIEF at the 3 month point (MD = -0.06, p = 0.76) see **Fig. 2 e1**, at the 6-month (MD = -0.07, p = 0.78) see **Fig. 2 e2** or at the 12 month point (MD = -0.06, p = 0.82) see **Fig. 2 e3**. Pooled analysis does highlight a lower IIEF at the 24 month follow-up in the PVP group compared to the TURP group with a MD = -0.68, which may be statistically significant but again must be interpreted with caution because to the upper confidence interval is so close to zero (95%CI= -1.20 to -0.15, p = 0.01), see **Fig. 2 e4.**

2. Meta-analysis of perioperative parameters

2.1. Operation time

Fourteen studies comparing PVP against TURP reported operation times. Overall, TURP takes less time than PVP with a MD=15.24 minutes, and this was a significant finding (p <0.01) see **Table 3**. However, there was extreme heterogeneity across this sample (I^2 = 94%). As such, sensitivity analysis was conducted by removing low-quality trials (**Fig. 3c**) which lowered the level of heterogeneity (I^2 = 17%) and lowered the mean difference to 10.60 minutes (95%CI 8.39 to 12.81, p <0.01), see **Table 3**.

2.2. Operative blood loss

Six studies involving 724 participants (PVP n = 389, TURP n = 335) provided blood loss estimates during operations. The pooled statistic suggested that the drop in hemoglobin levels in the PVP group was significantly lower than in the TURP group with a MD of –1.33g/dl (p <0.01*),* see **Table 3** for details.

2.3. Periods of hospitalization

Eleven studies involving 1,542 participants met our inclusion criteria for the analysis of periods of hospitalization. Pooled statistics highlighted a significant reduction in hospitalization times with a MD = -1.98 days (p <0.01) for PVP compared with TURP. However, again the level of heterogeneity across this sample was extreme (I^2 = 98%) therefore sensitivity analysis (**Fig.3d**) was again performed although this had a negligible impact on the results (MD = -1.83 days, 95% CI -2.25 to -1.40, p <0.01). See **Table 3** for further details.

2.3. Catheterization time

Fourteen available studies including 1,655 participants (861 in the PVP group and 794 in the TURP group) were involved in this meta-analysis. Pooled data revealed that the PVP group had a significantly shorter catheterization time with an MD = -1.25 days, (p <0.01) see **Table 3**.

3. Meta-analysis of Complications

3.1. Perioperative complications

The overall effect of perioperative complications including bleeding-related transfusion, TUR syndrome, capsular perforation, clot retention, urinary tract infection and acute urinary retention are summarized in **Table 3**. According to this meta-analysis,

PVP was found to have significantly lower incidence of transfusion with an RR=0.14 (p <0.01), and clot retention (RR=0.14, p <0.01). There was also a substantial and significant difference in the occurrence of TUR syndrome (RR=0.19, p <0.01) and capsular perforations (RR=0.09, p <0.01). Furthermore, PVP appears to have a higher risk of mild to moderate dysuria (RR=1.76, 95%CI 1.17 to 2.65, p <0.01), although there was no substantial or significant difference regarding urinary tract infection (RR=1.15, 95% CI 0.85 to 1.55, p = 0.38) or acute urinary retention rate (RR=1.19, 95%CI 0.80 to 1.75, p = 0.39).

3.2. Long-term complications

Analysis of long-term complications such as bladder neck contracture, retrograde ejaculation and urethral stricture, suggests there is no significant difference between PVP and TURP. Bladder neck contracture (RR=1.05, p = 0.87), retrograde ejaculation (RR = 0.72, p = 0.11) and urethral stricture (RR=0.81, p = 0.25), see **Table 3** for further details. However, PVP was found to have a significantly higher risk of re-intervention (RR=1.81, p <0.01) see **Table 3** for details.

DISCUSSION

Over the past two decades TURP has remained the gold standard surgical intervention for symptomatic BPH despite having high rates of treatment-related morbidities and complications which have a hugely negative impact on approximately 20% of those receiving this intervention [3, 6, 11]. Urologists continue to search for safer techniques without diminishing clinical efficacy compared to TURP.

Endoscopic technologies are being developed, and PVP emerged as a promising

intervention which attracted our attention because this is a minimally-invasive surgical procedure. The first generation PVP laser system utilized high-powered KTP lasers (60W) at 532 nm and was initially introduced in 1998 [40]. More advanced generations including the KTP laser (80W)， the Green-light high-performance system (HPS) laser (120W) , the Green-light lithium triboride (LBO) laser (160W) and the Green-light X-ray photoelectron spectroscopy (XPS) laser (180W) systems were then sequentially introduced up until 2018, raising hopes of treating symptomatic BPH, effectively and safely.

Previous research comparing PVP and TURP has demonstrated that there is no significant difference in medium term efficacy or safety when treating BPH, however; the long-term efficacy between these two techniques remains controversial. In this updated systematic review and meta-analysis, we reviewed all available RCTs and prospective studies (n = 22) up until October 2018 which involved a total of 2,665 participants. Pooled analyses and sensitivity analysis suggests both PVP and TURP have similar long-term function outcomes, which were analyzed using both subjective (IPSS, QoL) and objective (*Q*max, PVR) measures. IPSS at 12 month follow-up， *Q*max at 6 months and QoL at 12 months highlighted a statistically significant difference, although the differences were only small.

This study adds to the current evidence base in terms of understanding sexual functioning post-intervention. Previous clinical studies have evaluated retrograde ejaculation rates although conclusions could not be provided with any authority because findings were generally inconsistent and gathered over relatively short periods of time

[7, 10, 25, 27, 38]. The longest running RCT which compared PVP with TURP had a 60 month follow-up, and suggested there is similar improvement in IPSS, Qmax, PVR, Qol and IIEF [36, 39].

Previously conducted meta-analyses have not had the opportunity to evaluate IIEF due to the relatively small number of studies collecting and reporting this particular outcome. Fortunately, IIEF is increasingly being used to analyze sexual functioning which enabled us to design and perform this meta-analysis given the increased availability of evidence in this area. Pooled analysis however suggests there is no significant difference in the retrograde ejaculation rate nor is there a significant difference in IIEF outcomes between PVP and TURP.

This meta-analysis did highlight substantial differences in perioperative factors analyzed across this sample of studies. Pooled analyses and sensitivity analyses show that operation times are significantly longer for PVP, whereas the duration of hospitalization and catheterization are significantly shorter. Prolonged operative duration involved in PVP interventions appears to be associated with laser power and individual surgeon's experience and related skills. Laser power is determined for each individual device, and evidence from previous studies suggest that overall operation times are prolonged by approximately 23 minutes for PVP with an 80W laser, approximately 9 minutes with 120W and 7 minutes with 120W and 160W lasers. Furthermore, literature shows a surgeon's overall technical skills and confidence place him/her at a point on a learning curve for new technologies which is likely to be an important factor in the length of operations.

Safety is another key issue because the most serious TURP complications, such as bleeding and TUR syndrome are known to correlate with prostate size and longer operative times [6, 41]. This analysis highlighted additional benefits, in that the incidence of perioperative complications including bleeding, blood transfusion, clot retention, capsule perforation and TUR syndrome are significantly lower for those receiving the PVP intervention. Although, this can be explained by the characteristics of the green light laser, where the 532-nm wavelength is easily absorbed by hemoglobin in prostatic tissues but not by water [13]. Likewise in vaporization, high-power laser energy is instantly absorbed by the blood, ensuring quicker vaporization into the tissue which creates a prostate cavity with minimal blood loss [42].

Other bleeding-related complications occur less frequently for those receiving PVP. However, another possible explanation could be that KTP laser energy penetrates only 1 to 2 mm of tissue. Therefore, high-power laser energy might be concentrated into the surface coat of prostatic tissue, which then ensures rapid vaporization, leaving a 0.2cm rim of residual coagulated tissue [13]. It may also be the case that the fluid medium used for PVP procedures is saline solution rather than glycine, therefore TUR syndrome does not occur in PVP. However, further research is necessary to understand this treatment related complication.

Additional postoperative complications such as acute urinary retention, UTIs, bladder neck contracture and urethral stricture were analyzed although no significant differences between TURP and PVP interventions were identified. However, PVP had two distinct disadvantages when compared with TURP. PVP appears to be associated

with a higher risk of developing dysuria and for re-intervention. Dysuria rates after PVP have been reported to be between 6% and 30% [33, 43]. There may be several reasons for this, although most likely postoperative dysuria is caused by thermal damage and edema in urethral tissue. Also, shorter catheterization times could be another cause of this irritable symptom. That said, research suggests this symptom is generally classified as mild to moderate across all patients, and therefore can be effectively managed, if not resolved altogether within two months of follow-up [27, 33]. As such, transient dysuria is not a serious PVP complication, the more serious complication is re-intervention.

There may be a number of reasons post-PVP patients are at a higher risk of re-intervention. There may be inadequate energy delivery, leading to incomplete tissue removal which might play an important role regarding the outcome of the procedure [38, 44]. According to our analysis, those who received an 80W PVP intervention were at significantly higher risk of re-intervention compared with TURP. However, researchers have found the differences between other higher power PVP laser groups (i.e., 120W, 160W and 180W) and TURP cohort are not statistically significant. Although, the GOLIATH study suggests that the 180W XPS laser system is superior to TURP when considering this particular parameter. Logically, this type of adverse event would markedly decrease with the advent of higher power laser systems.

As well as having a higher risk of dysuria and re-intervention, PVP is administered in the absence of histologic tissue examination, which might limit opportunities to incidentally identify prostate cancer. In order to address this, clinicians might want to consider when there is a rapidly increasing, or higher levels of prostate-specific antigen

(PSA), it might be more beneficial to use TURP rather than laser evaporation techniques. In addition, an extensive examination including PSA measures, digital rectal examinations and ultrasonography could be used to guide prostate biopsies administration, if cancer is suspected [12, 45]. Prostate cancer is often diagnosed in the late stages which is nearly always too late and therefore *opportunities* to diagnose this insidious disease must not be disregarded.

LUTS manifest secondarily through BPH and is a chronic health condition. The management of these symptoms create additional economic burden for patients and healthcare systems, generally [2, 46]. It is vital to evaluate the cost effectiveness of the two surgical therapies in clinical practice. Based upon a cost-effectiveness analysis, Armstrong et al suggest that the PVP procedure is unlikely to be cost effective because of the relatively expensive consumables [47]. However, Patel argues that there is an absence of high-quality and long-term data, in fact only two RCTs with short term follow-ups were available at the time [48]. This meta-analysis suggests that any initial investment in equipment and surgeon's training may be at least partially offset by shorter lengths of hospitalization and lower incidence of post-operative complications for PVP compared to TURP. Considering high number of cases each year, PVP may actually lower the demand for medical resources in this field although this also requires further research.

This meta-analysis was undertaken using all currently available comparative clinical studies, however; there are some limitations. First of all, despite designing a systematic search strategy, our inclusion criteria meant that non-English documents

were omitted, therefore there must be some language bias. Secondly, there are very few RCTs with long-term follow-up endpoints in this field of interest which must be addressed. To overcome this, we designed this study to incorporate five prospective cohort studies which added a layer of sophistication to this analysis.

None of the RCTs included described blinding methods which is considered a distinct quality deficit but this is to be expected given the nature of the interventions explored. Actually, this perhaps highlights the need to use the CONSORT quality appraisal method or the Delphi method in further studies. While studies have demonstrate high levels of agreement [49] between these quality assessment tools and the methods implemented in this meta-analysis, the CONSORT and Delphi methods contain an increased number of variables and are therefore more likely to differentiate. A more substantial concern however is that several studies did not report withdrawal or drop outs. This appears to have been is significant factor in our quality assessment and must be addressed in further research. Thirdly, there was consistently, substantial to extreme heterogeneity across this study sample. Sensitivity analysis only partially accounted for such high levels of heterogeneity. Increased sample sizes, or multi-centre trials involving larger numbers of participants as well as reporting age stratification may elaborate on our present understanding. Despite these limitations, this study provides the most up-to-date information concerning the comparison of PVP and TURP in surgical management of BPH.

CONCLUSION

These findings confirm previous studies which suggested that PVP is superior in

long-term efficacy to TURP. PVP appears to have only slightly increased IPSS, *Q*max, QoL, PVR and IIEF benefit, but is associated with fewer complications. As such, we recommend PVP is offered as the first-line treatment for LUTS secondary to BPH rather than the traditional TURP method. The only addendum is that PVP cannot acquire histological tissue examination which removes an opportunity to identify prostate cancer. Withdrawals and drop outs are not always reported in full and there is a need to use a more comprehensive quality assessment tool to appraise studies in this field. Further research is of course necessary, and should be conducted with larger samples, over longer periods.

AUTHOR CONTRIBUTIONS

SCL and PXP designed and conducted the systematic search to identify all relevant studies. SCL and PXP then assessed eligibility and the quality of each study, before extracting data and conducting statistical analysis. TXD and HMH coordinated the study and performed data acquisition. XW, WZ and YGZ participated in data interpretation and drafting this article. SS, ML and JYW reviewed and revised this report for critical content and scientific rigour. All authors read and approved the final manuscript

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Legend

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow chart

Figure 2. Forest plot of IPSS at 3 months (a1), 6 months (a2), 12 months (a3) and 24 months (a4); Forest plot of Qmax at 3 months (b1), 6 months (b2), 12 months (b3) and 24 months (b4); Forest plot of PVR at 3 months (c1), 6 months (c2), 12 months (c3) and 24 months (c4); Forest plot of Qol at 3 months (d1), 6 months (d2), 12 months (d3) and 24 months (d4); Forest plot of IIEF at 3 months (e1), 6 months (e2), 12 months (e3) and 24 months (e4). (IPSS = International Prostate Symptom Score; QoL = quality of life; Qmax = maximum flow rate; PVR = postvoid residual volume; IIEF=international index of erectile function)

Figure 3. Sensitivity analysis of the Qmax at 24-month follow-up (a); PVR at 3-month follow-up (b); operation times (c); and period of hospitalization (d). (Qmax = maximum flow rate; PVR = postvoid residual volume).

Table 1 Baseline characteristics of comparative studies.

Table 2 Meta-analytical outputs summarizing baseline parameters of PVP compared with TURP.

Table 3 Meta-analytical outputs for the safety of PVP compared with TURP.

Supplementary file

Supplement file 1 Electronic search strategy in PUBMED.

Table 1. Baseline characteristics of comparative studies

Authors and year	Design	Group	Laser power (W)	No. of patients	Age (years)	Prostate size (ml)	IPSS	*Q*max (mL/s)	PVR (mL)	QoL	IIEF	Follow-up, (months)	LE	Study quality
Kumar et al 2013	RCT	PVP	120	58	64.58±6.64	52.79±16.13	20.05±2.75	6.68±2.00	143.35±52.67	3.60±1.01	16.65±2.80	12	2a	3*
		TURP		60	63.68±6.57	52.20±15.93	20.71±2.68	7.00±1.97	139.25±54.28	3.73±0.97	16.95±2.86			
Lukacs et al 2012	RCT	PVP	120	68	66.9±7.8	50.54±16.53	22 (17–26)	7.79±2.75	89.5 (30-158)	70 (68–80)	N/A	12	2a	3*
		TURP		68	67.6±7.6	50.11±14.73	20 (15–23)	7.76±2.64	75 (28–126)	75 (65–85)	N/A			
Pereira-Correia et al 2012	RCT	PVP	120	10	66.4（52 – 76）	43.4(30– 58）	22 (9 – 33)	10（3 – 18）	150（25 – 250）		23（22 – 24）	24	2a	2*
		TURP		10	63.5（56 – 78）	47（30– 60）	25(15 – 31）	6.4（4 – 11）	177（50 – 300）		23（22 – 25）			
Capitan et al 2011	RCT	PVP	120	50	69.8±8.44	51.29±14.72	23.74±5.24	8.03±3.14		4.52±0.27		12	2a	3*
		TURP		50	67.7±6.7	53.10±13.75	23.52±4.38	3.88±2.71		4.14±1.06				
Al-Ansari et al 2010	RCT	PVP	120	60	66.3±9.4	61.8±22	27.2±2.3	6.9±2.2	53.2±25			36	2a	3*
		TURP		60	67.1±8	60.3±20	27.9±2.7	6.4±2	57±21					
Xue et al 2013	RCT	PVP	120	100	72.1±11.3	65.8 ± 23.6	23.0 ± 5.1	8.0 ± 3.6	148.3 ± 101.6	4.2 ± 0.9		36	2a	2*
		TURP		100	71.0±10.8	67.3 ± 24.7	23.2 ± 5.0	8.2 ± 3.8	151.1 ± 105.2	4.3 ± 0.8				
Horasanli et al 2008	RCT	PVP	80	39	69.2±7.1	86.1±8.8	18.9±5.1	8.6±5.2	183±50.1		19.9±5.1	6	2a	2*
		TURP		37	68.3±6.7	88±9.2	20.2±6.8	9.2±5.6	176.9±45.3		20.1±5.5			
Mohanty et al 2012	RCT	PVP	80	60	66.68±8.62	44.77±14.09	19.98±3.27	7.41±2.07	145.8±70.33	3.97±0.82	17.98±3.55	12	2a	3*
		TURP		57	65.74±9.09	49.02±15.93	20.88±3.87	6.75±1.63	143.23±65.96	3.91±0.78	17.40±4.76			
Bouchier-Hayes et al 2009	RCT	PVP	80	60	>50		25.28±5.93	8.81±2.55	129.2±155.7	4.74±1.23		12	2a	3*
		TURP		59			25.41±5.72	8.86±2.99	111.3±113.7	5.08±0.94				
Bachmann et al 2014	RCT	PVP	180	136	65.9±6.8	48.6±19.2	21.2±5.9	9.5±3.0	110.1±88.5	4.6±1.1	13.2±7.6	6	2a	3*
		TURP		133	65.4±6.6	46.2±19.1	21.7±6.4	9.9±3.5	109.8±103.9	4.5±1.4	13.7±7.5			
Bachmann et al	RCT	PVP	180	136	65.9±6.8	48.6±19.2	21.2±5.9	9.5±3.0	110.1±88.5	4.6±1.1	13.2±7.6	12	2a	2*

2015		TURP		133	65.4±6.6	46.2±19.1	21.7±6.4	9.9±3.5	109.8±103.9	4.5±1.4	13.7±7.5			
Thomas et al 2016	RCT	PVP	180	136	65.9±6.8	48.6±19.2	21.2±5.9	9.5±3.0	110.1±88.5	4.6±1.1	13.2±7.6	24	2a	3*
		TURP		133	65.4±6.6	46.2±19.1	21.7±6.4	9.9±3.5	109.8±103.9	4.5±1.4	13.7±7.5			
Telli et al 2015	RCT	PVP	120	39	67 (51–87)	60 (41–75)	20 (12–30)	10.6 (5–17)	60 (20–220)			24	2a	2*
		TURP		62	69 (56–87)	55 (40–72)	19 (10–31)	12.5 (3–21)	65 (10–220)					
Kumar et al 2016	RCT	PVP	120	58	64.58±6.64	52.79±16.13	20.05±2.75	6.68±2.00	143.35±52.67	3.60±1.01	16.65±2.80	36	2a	2*
		TURP		60	63.68±6.57	52.20±15.93	20.71±2.68	7.00±1.97	139.25±54.28	3.73±0.97	16.95±2.86			
Mordasini et al 2018	RCT	PVP	80	112	68.4±8.7	36.1±11.5	20.3±7.0	8.9±4.1	91.1±88.3	4.2±1.1		60	2a	2*
		TURP		126	67.6±8.4	37.9±14.3	20.4±7.5	8.5±4.6	114.5±136.4	4.3±14				
Chen et al 2011	PCS	PVP	160	57	69.5±7.4	60.2±27.8	19.7±6.0	6.9±4.0	93.7±79.7			6	2b	9#
		TURP		51	67.1±6.9	58.3±26.2	21.8±7.3	6.8±2.3	102.2±70.1					
Bachmann et al 2005	PCS	PVP		37	71.0±9.3	65.1±36.9	18.1±5.9	6.9±2.2	146.1±106.9	3.3±1.7		6	2b	9#
		TURP		64	68.7±7.9	48.9±21.2	17.3±6.3	6.9±2.2	120.7±49.0	3.4±1.6				
Ruszat et al 2008	PCS	PVP	80	113	62.3±5.0	56.3±27.4	20±6.4	8.5±4.1	203±226			24	2b	9#
		TURP		75	61.7±5.5	45.3±21.0	19±6.9	9.8±5.0	104±108					
		PVP		91	75.0±2.8	64.8±26.8	18.6±5.8	7.3±2.7	215±247					
		TURP		40	74.0±2.6	54.2±21.2	16.0±7.1	9.2±5.4	124±141					
		PVP		65	84.3±3.1	69.3±32.7	14.1±7.4	7.1±4.2	200±219					
		TURP		12	82.4±2.8	44.9±22.1	15.5±6.7	7.6±3.9	231±350					
Tasci et al 2008	PCS	PVP		40	71.8±5.9	108.4±15.8	22.3±5.6	6.2±2.2	116.5±60.5	3.6±0.7		24	2b	9#
		TURP		41	70.1±5.4	104.2±12.5	22.6±3.9	6.5±1.8	110.7±59.8	3.5±0.6				
Tugcu et al 2008	PCS	PVP		112	67.5±7.4	49.1±11.9	17.9±4.9	6.9±1.9	107.9±63.0	3.4±0.6		24	2b	9#
		TURP		98	66.3±7.9	47.7±8.4	17.7±3.5	7.2±1.7	100.3±57.1	3.4±0.5				
Nomura et al 2009	PCS	PVP	80	78	72.0(67.0,78.0)	50.5(38.6,70.3)	23 (17, 27)	6.8 (5.2, 9.5)	69 (31, 139)	5 (5, 6)		12	2b	9#
		TURP		51	70.5 (66.5, 76.0)	42.8 (34.6, 54.0)	22 (16, 27)	7.3 (5.3, 10.2)	60 (31, 140)	5 (4, 5)				
Guo et al 2015	PCS	PVP	80	257	69.7±8.9	52.3±19.3	19.4±6.3	8.3±6.0	119.5±83.8	3.7±1.7		60	2b	9#

		TURP		104	66.4±8.4	44.2±19.1	18.4±6.3	10.0±5.2	95.6±98.4	3.7±1.3		

LE = level of evidence;# Using Newcastle-Ottawa Scale (score from 0 to 9)； * Using Jadad scale (score from 0 to 5); RCT= randomized controlled trial; IPSS = International Prostate Symptom Score; QoL = quality of life; Qmax = maximum flow rate; PVR = postvoid residual volume; TURP = transurethral resection of the prostate; PVP=Photoselective vaporization of the prostate; IIEF=international index of erectile function; PCS=prospective cohort study.

Bachmann et al 2014， Bachmann et al 2015 and Thomas et al 2016 are from the same trials in different period; Kumar et al 2013 and Kumar et al 2016 are from the same trials in different period.

Table 2. Meta-analytical outputs summarizing baseline parameters of PVP compared with TURP

Parameter	No.of studies	Sample size		Heterogeneity(Total)				MD (95%CI)	Test for overall effect	
		PVP	TURP	chi^2	df	I^2(%)	P value			
IPSS										
Baseline	14	1179	989	11.32	13	0	0.58	-0.29 [-0.68, 0.10]	Z=1.47	p=0.14
Qmax										
Baseline	14	1179	989	70.23	13	81	<0.01	0.05[-0.51, 0.61]	Z=0.17	p=0.87
PVR										
Baseline	12	1016	864	9.24	11	0	0.6	2.19[-3.22,7.61]	Z=0.79	p=0.43
Qol										
Baseline	10	910	766	11.15	9	19	0.27	0.01 [-0.07,0.10]	Z=0.33	P=0.74
IIEF										
Baseline	5	351	297	1.58	4	0	0.81	-0.13 [-0.86,0.60]	Z=0.34	P=0.73

CI=confidence interval, MD=mean difference, RR=risk ratio; IPSS = International Prostate Symptom Score; PVP=Photoselective vaporization of the prostate; QoL = quality of life; PVR = postvoid residual volume; Qmax = maximum flow rate; IIEF=International Index of Erectile Function; TURP = transurethral resection of the prostate

Table 3. Meta-analytical outputs for the safety of PVP compared with TURP

Outcomes	No.of studies	Sample size		Heterogeneity(Total)				MD or RR(95%CI)	Test for overall effect	
		PVP	TURP	chi^2	df	I^2(%)	*P*		Z	*P*
Operation time	14	979	870	216.27	13	94	<0.01	15.24 [8.91,21.54]	4.72	<0.01
	6*	429*	428*	6.01*	5*	17*	0.31*	10.60 [8.39, 12.81]*	9.40*	<0.01*
Hospitalization time	11	819	723	600.62	10	98	<0.01	-1.98 [-2.56, -1.39]	6.59	<0.01
	3*	240*	229*	6.29*	2*	68*	<0.01*	-1.83 [-2.25, -1.40]*	8.42*	<0.01*
Catheterization time	14	861	794	964.75	13	99	<0.01	-1.25 [-1.58, -0.92]	7.48	<0.01
Blood loss	6	389	335	46.05	5	89	<0.01	-1.33 [-2.05, -0.61]	3.62	<0.01
Transfusion	14	1110	946	10.87	13	0	0.62	0.14 [0.08, 0.26]	6.10	<0.01
TUR syndrome	7	590	435	0.73	6	0	0.99	0.19 [0.06, 0.61]	2.82	<0.01
Capsular perforation	7	641	451	1.84	6	0	0.93	0.09 [0.03, 0.26]	4.51	<0.01
Clot retention	8	699	504	1.72	7	0	0.97	0.14 [0.07, 0.29]	5.32	<0.01
Urinary tract infection	13	1049	860	8.79	12	0	0.72	1.15 [0.85, 1.55]	0.89	0.38
Acute urinary retention	10	694	653	5.55	9	0	0.78	1.19[0.80, 1.75]	0.86	0.39
Urinary incontinence	4	296	263	4.28	3	30	0.23	1.45[0.74, 2.86]	1.08	0.28
Bladder neck contracture	8	523	520	4.32	7	0	0.74	1.05 [0.57, 1.94]	0.16	0.87
Urethral stricture	15	1172	980	9.37	14	0	0.81	0.81 [0.57, 1.16]	1.14	0.25
Retrograde ejaculation	4	320	314	15.06	3	80	<0.01	0.72 [0.49, 1.07]	1.62	0.11
Dysuria	12	1079	854	24.80	11	58	0.01	1.76 [1.17, 2.65]	2.71	<0.01

Re-intervention	12	980	809	14.58	11	25	0.20	1.81 [1.28, 2.56]	3.35	<0.01

* Using sensitivity analysis; CI=confidence interval; MD=mean difference; PVP=Photoselective vaporization of the prostate; RR=risk ratio; TURP = transurethral resection of the prostate; TUR syndrome= transurethral resection syndrome

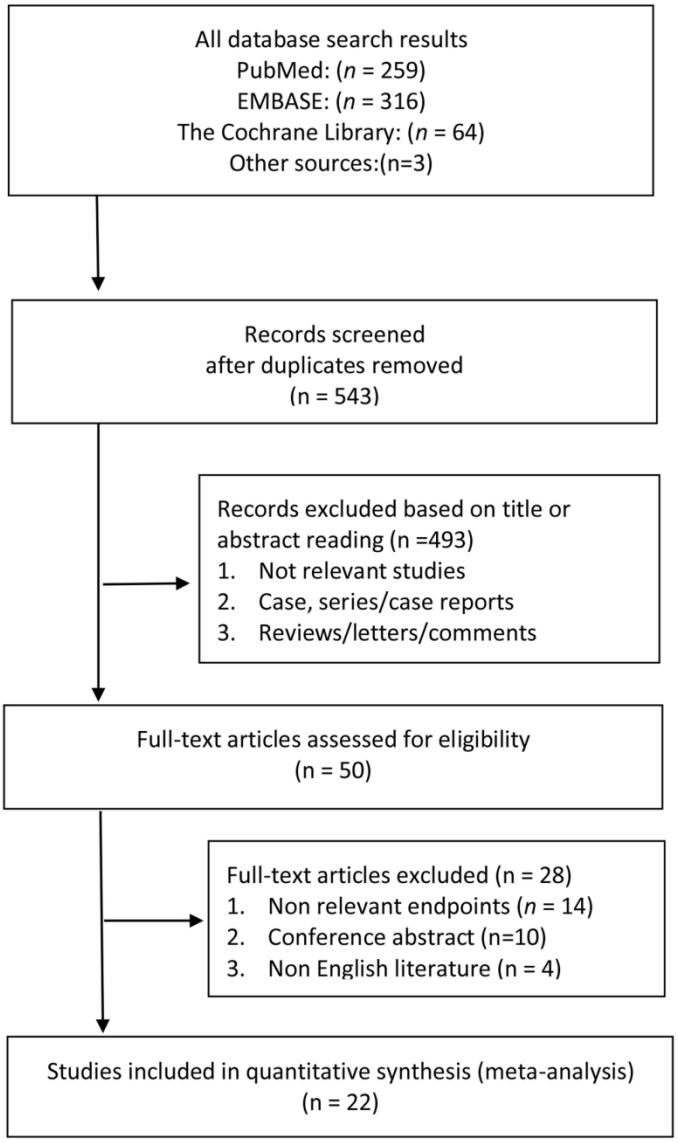

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow chart

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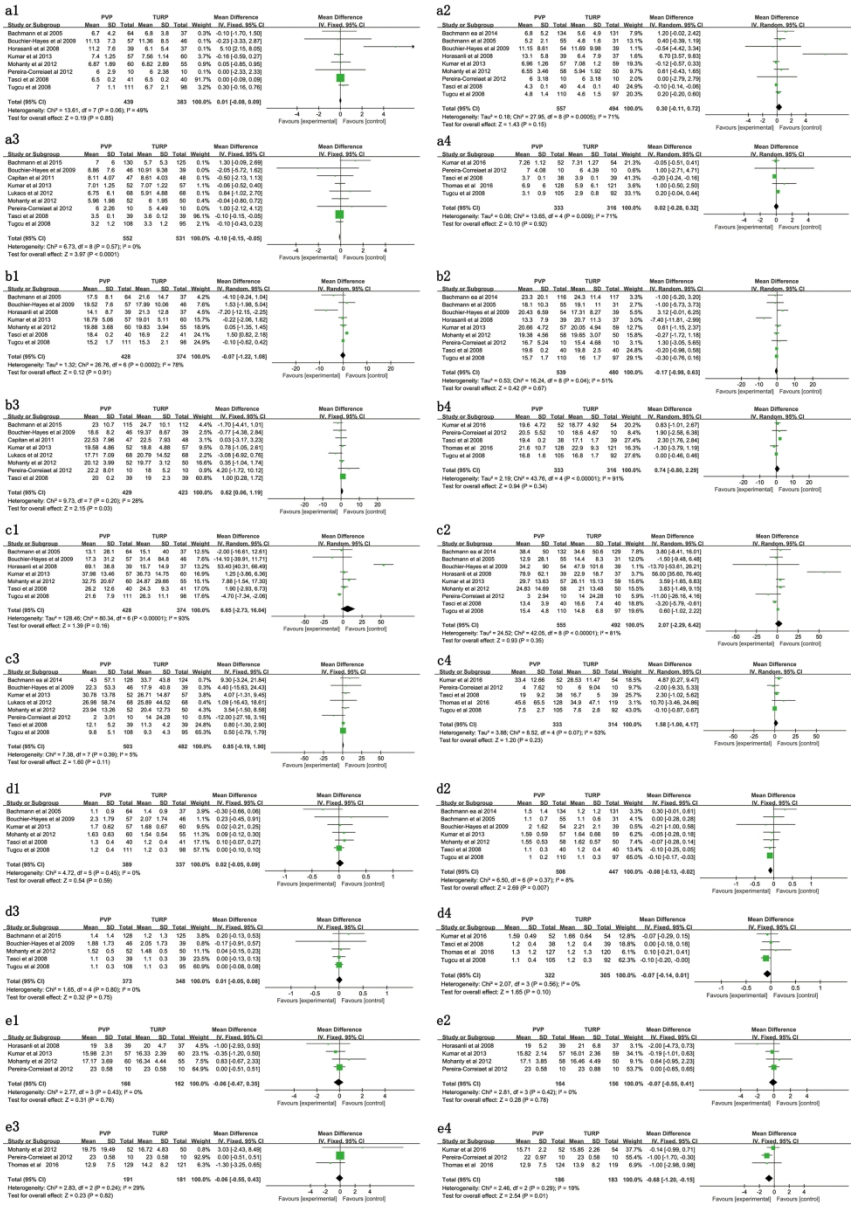

Figure 2. Forest plot of IPSS at 3 months (a1), 6 months (a2), 12 months (a3) and 24 months (a4); Forest plot of Qmax at 3 months (b1), 6 months (b2), 12 months (b3) and 24 months (b4); Forest plot of PVR at 3 months (c1), 6 months (c2), 12 months (c3) and 24 months (c4); Forest plot of QoI at 3 months (d1), 6 months (d2), 12 months (d3) and 24 months (d4); Forest plot of IIEF at 3 months (e1), 6 months (e2), 12 months (e3) and 24 months (e4). (IPSS = International Prostate Symptom Score; QoL = quality of life; Qmax = maximum flow rate; PVR = postvoid residual volume; IIEF=international index of erectile function)

209x296mm (300 x 300 DPI)

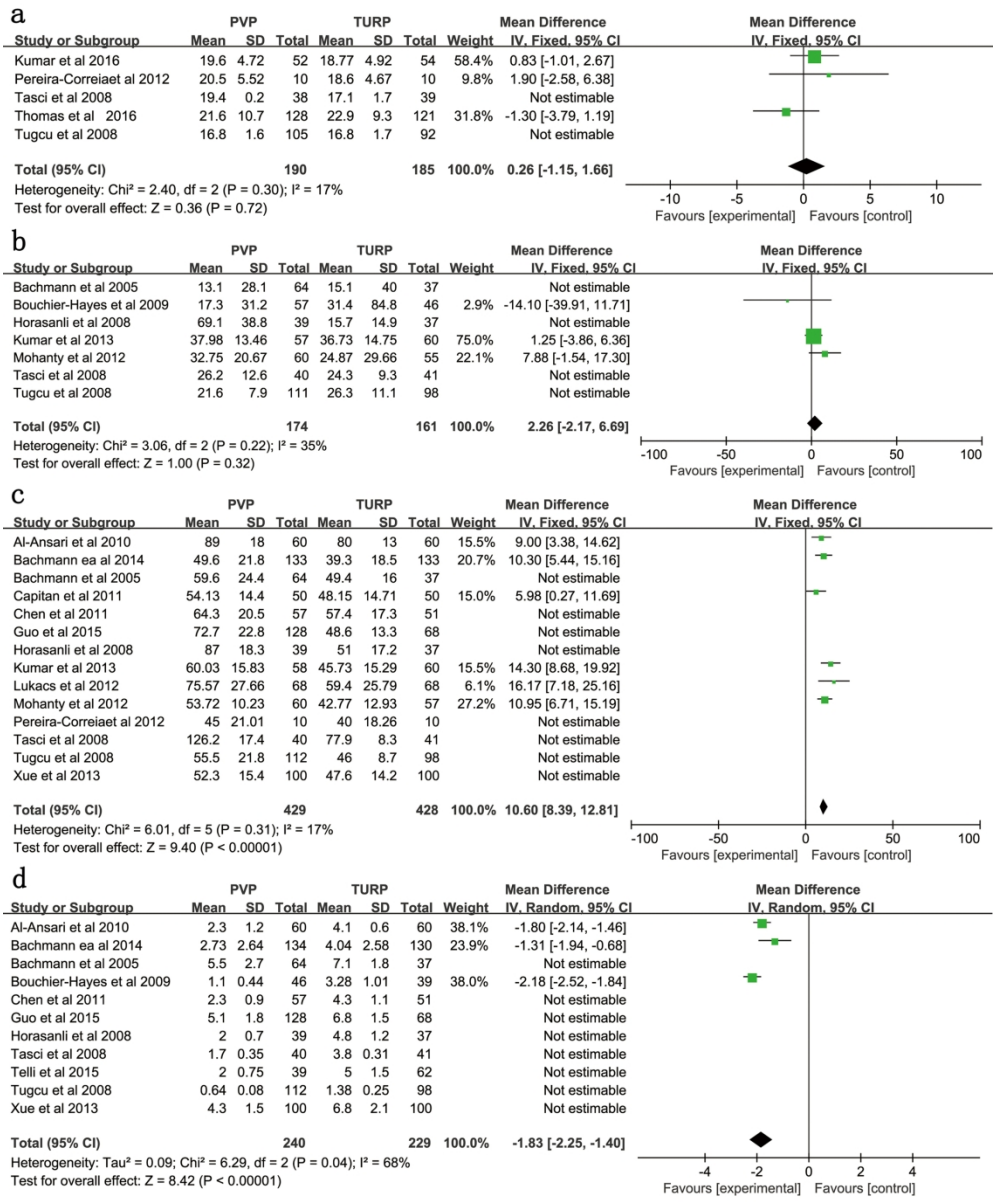

Figure 3. Sensitivity analysis of the Qmax at 24-month follow-up (a); PVR at 3-month follow-up (b); operation times (c); and period of hospitalization (d). (Qmax = maximum flow rate; PVR = postvoid residual volume).

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Comparison of photoselective green light laser vaporization versus traditional transurethral resection for benign prostate hyperplasia: an up-to-date systematic review and meta-analysis of randomized control trials and prospective studies

Search strategy in PUBMED

((((((((((((Hyperplasia, Prostatic) OR Prostatic Hypertrophy) OR Adenoma, Prostatic) OR Adenomas, Prostatic) OR Prostatic Adenomas) OR Prostatic Adenoma) OR Benign Prostatic Hyperplasia) OR Prostatic Hyperplasia, Benign) OR Prostatic Hypertrophy, Benign) OR Benign Prostatic Hypertrophy) OR Hypertrophy, Benign Prostatic)) AND ((((((((((((Prostate Transurethral Resection) OR Prostate Transurethral Resections) OR Transurethral Prostate Resection) OR Prostate Resection, Transurethral) OR Prostate Resections, Transurethral) OR Resection, Transurethral Prostate) OR Resections, Transurethral Prostate) OR Transurethral Prostate Resections) OR TURP) OR TURPs) OR Prostatectomy, Transurethral) OR Prostatectomies, Transurethral) OR Transurethral Prostatectomies) OR Transurethral Prostatectomy)) AND (((PVP) OR photoselective vaporisation) OR green-light laser)

The last quest was updated on December 20, 2018

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	6-7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	None
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7-8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7-8
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8-9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9-10
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-14
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-14
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10-14
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11-13
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	14-19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	19-20
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	20-21
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	21

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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BMJ Open

Comparison of photoselective green light laser vaporization versus traditional transurethral resection for benign prostate hyperplasia: an updated systematic review and meta-analysis of randomized controlled trials and prospective studies

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Complete List of Authors:	Lai, Shicong; Department of Urology, Beijing Hospital of the Ministry of Health, Beijing 100730, China, ; Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China Peng, Panxin; Peking University China-Japan Friendship School of Clinical Medicine, Beijing 100029, China; China-Japan Friendship Hospital, Department of Urology Diao, Tongxiang; Beijing Hospital, National Center of Gerontology, China; Peking university fifth school of clinical medicine Hou, Huimin; Beijing Hospital, National Center of Gerontology, China; Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China Wang, Xuan; Beijing Hospital, National Center of Gerontology, China Zhang, Wei; Beijing Hospital, National Center of Gerontology, China; Peking university fifth school of clinical medicine Liu, Ming; Beijing Hospital, National Center of Gerontology, China Zhang, Yaoguang; Beijing Hospital, National Center of Gerontology, China Seery, Samuel; Chinese Academy of Medical Sciences and Peking Union Medical College, School of Humanities and Social Sciences Wang, Jianye; Beijing Hospital, National Center of Gerontology, China
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Secondary Subject Heading:	Urology, Surgery
Keywords:	Prostate disease < UROLOGY, UROLOGY, Adult urology < UROLOGY

Comparison of photoselective green light laser vaporization versus traditional transurethral resection for benign prostate hyperplasia: an updated systematic review and meta-analysis of randomized controlled trials and prospective studies

Shi-Cong Lai[1,2#], Pan-Xin Peng[3,4#], Tong-Xiang Diao[1,5], Hui-Min Hou[1,2], Xuan Wang[1], Wei Zhang[1,5], Ming Liu[1], Yao-Guang Zhang[1], Samuel Seery[6]， Jian-Ye Wang[1]*

[1] Department of Urology, Beijing Hospital, National Center of Gerontology, Beijing 100730, China

[2] Graduate School of Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China

[3] Peking University China-Japan Friendship School of Clinical Medicine, Beijing 100029, China

[4] Department of Urology, China-Japan Friendship Hospital, Beijing 100029, China

[5] Peking university fifth school of clinical medicine

[6] School of Humanities and Social Sciences, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100730, China

 # Shi-Cong Lai and Pan-xin Peng contributed as the co-first author

*** Correspondence author: Jian-Ye Wang**

5. Address for correspondence:

Jian-Ye Wang, No.1 Da Hua Road, Dong Dan, Beijing 100730, P.R. China

Email: **wangjy@bjhmoh.cn**

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Abstract

Objective: To assess the efficacy and safety of green-light laser photoselective vaporisation of the prostate (PVP) compared with transurethral resection of the prostate (TURP) for lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH).

Design: Systematic review and meta-analysis, conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement.

Data sources: PubMed, EMBASE, The Cochrane Library until October 2018

Eligibility criteria: Randomized controlled trials and prospective studies comparing the safety and efficacy of PVP versus TURP for LUTS manifesting through BPH.

Data extraction and synthesis: Perioperative parameters, complications rates and functional outcomes including treatment-related adverse events such as International Prostate Symptom Score (IPSS), maximum flow rate (Qmax), postvoid residual (PVR), Quality of Life (Qol) and International Index of Erectile Function (IIEF).

Results: 22 publications consisting of 2665 patients were analyzed. Pooled analysis revealed PVP is associated with reduced blood loss, transfusion, clot retention, TUR syndrome, capsular perforation, catheterization time and hospitalization, but also with a higher re-intervention rate and longer intervention duration (all $p < 0.05$). No significant difference in IPSS, *Q*max, QoL, PVR or IIEF at 3, 24, 36 or 60 months was identified. There was a significant difference in Qol at 6 months (MD = -0.08; 95%CI

-0.13 to -0.02; p = 0.007), and IPSS (MD = −0.10; 95%CI −0.15 to −0.05; p<0.0001) and Qmax (MD = 0.62; 95% CI 0.06 to 1.19; p=0.03) at 12 months although these differences were not clinically relevant.

Conclusion: PVP is an effective alternative, holding additional safety benefits. PVP has equivalent long-term IPSS, Qmax, QoL, PVR, IIEF efficacy, and fewer complications. The main drawbacks are dysuria and re-intervention although both can be managed with non-invasive techniques. The additional shortcoming is that PVP does not acquire histological tissue examination which removes an opportunity to identify prostate cancer.

Keywords: Benign prostatic hyperplasia (BPH), Lower urinary tract symptoms (LUTS), Meta-analysis, Photoselective vaporisation of the prostate (PVP), Transurethral resection of the prostate (TURP)

Strengths and limitations of this study

- This updated meta-analysis included a larger number of studies involving more participants which adds precision to previous findings
- This study analyzed both safety and efficacy, focusing on sexual functioning and quality of life measures because LUTS treatment related adverse events have a hugely detrimental impact on ones' psychological well-being
- Quality assessment methods used did not highlight substantial differences between studies because blinding is not possible given the characteristics of the two interventions under investigation
- Due to the limited number of studies in this field, we were unable to conduct subgroup analysis around laser power (i.e., 80W, 120W, 180W etc.) which is necessary to identify the most effective/efficient standard
- Surgical experience with laser technology, drop outs and withdrawals as well as other important factors were seldom reported in any detail which inhibits further analysis

INTRODUCTION

Lower urinary tract symptoms (LUTS) commonly occur in the aging male population, affecting more than 1 in 4 of those above 50 years of age. LUTS manifest through benign prostatic hyperplasia (BPH) and often have a hugely negative impact on quality of life (Qol) [1]. Treatments for BPH range from medicinal interventions to surgery, where transurethral resection of the prostate (TURP) remains the surgical gold standard. Surgical therapy is recommended for patients whom have not benefitted from medical interventions such as, 5-alpha-reductase inhibitors and alpha-blockers [1, 2]. TURP has been found to have a high success rate and low re-intervention rate at long-term follow-up [3], however; increasingly evidence indicates this invasive procedure is also associated with serious complications such as bleeding, urethral strictures, urinary incontinence and transurethral resection (TUR) syndrome [4-6]. Consequently, there is an urgent need to develop minimally-invasive therapies which do not have such a negative impact on patients' lives.

Laser therapies offer a new direction in BPH therapies and photoselective vaporization of the prostate (PVP) is increasingly being studied as a potential new first line treatment [7-11]. This technique is generally performed with a 532-nm green laser generated using potassium-titanyl-phosphate (KTP) or lithium triborate crystals [12]. Unlike other types of laser, the green laser is easily absorbed by soft tissue haemoglobin, while hardly at all by other fluid mediums, which leads to improved coagulation and lowers the risk of deeper tissue injuries during vaporization [13, 14]. Numerous studies

provide supporting evidence of increased benefit, demonstrating that PVP has superior mid-term clinical efficacy compared with TURP across functional outcomes including International Prostate Symptom Score (IPSS), maximum flow rate (Qmax), postvoid residual volume (PVR), International Index of Erectile Function (IIEF) and QoL [15, 16].

In a previous meta-analysis published in 2013, Teng et al [17] found that PVP and TURP have similar treatment efficacies although due to the minimally invasive nature, PVP offers several potential benefits. While this early research provided some optimism, studies have yet to compare sexual function outcomes or efficacy results at 24 months, and across all available RCTs and prospective studies. Consequently, we sought to conduct an updated systematic review and meta-analysis of high quality studies to support clinical decision-makers treating BPH.

MATERIALS AND METHODS

Patient and Public Involvement

Neither patients nor the public were involved in the design and planning of the study.

Literature Search and Article Selection

A comprehensive literature search was performed using biomedical databases including PubMed, EMBASE, and the Cochrane Library up until October 2018. The following MeSH terms and free text words were used: benign prostatic hyperplasia,

BPH, transurethral resection of the prostate, TURP, green-light laser, vaporization, photoselective vaporization of the prostate and PVP. These terms were used singly and in combination (for further details please see supplement file 1). Additionally, manual searches were commenced for references and citations included within pertinent reviews. Language was restricted to English and the search and selection strategy was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement [18]. Randomized controlled trials and prospective studies meeting the following criteria were included: (1) studies comparing the safety and efficacy of PVP versus TURP for surgical treatment of LUTS secondary to manifesting BPH, (2) endpoints such as treatment-related adverse events and functional outcomes such as IPSS, Qmax, PVR, Qol and IIEF when available, and (3) providing the full text of the study could be accessed.

Literature searching, selection, and data extraction was undertaken independently by two reviewers (SL and PP) which was then cross-checked. Any discrepancies were resolved through discussion. A flowchart representing the search and selection process is presented in **Fig. 1**.

Assessment of Study Quality

Study quality was assessed in accordance with criteria recommended by the Oxford Centre for Evidence Based Medicine [19] Methodological reporting quality of RCTs was assessed using Jadad [20] and the Newcastle–Ottawa scale [21] was used to evaluate the quality of the prospective cohort studies included.

Data Extraction and Statistical Analysis

Preoperative parameters were extracted together with intraoperative data including operation times, changes in hemoglobin and transfusion rates. Postoperative data including length of hospitalization, duration of catheterization and treatment-related complications were also analyzed. Functional results including IPSS, Qmax, PVR, Qol and IIEF were assessed at 3, 6, 12, 24, 36 and 60 months after surgery.

Mean difference (MD) was used to assess continuous parameters. Authors were contacted when data were expressed as medians with corresponding range values. Otherwise, the statistical formula elaborated by Hozo et al [22] was implemented to back-calculate means and standard deviation in accordance with the recommended methods described in the Cochrane Handbook for Systematic Reviews [23].

Results were expressed as risk ratios (RR) with corresponding 95% confidence interval (CI) for dichotomous variables. I^2 was utilized to assess heterogeneity across studies. An I^2 <50% is generally considered an acceptable level of heterogeneity therefore a fixed effect model was applied. In instances where the I^2 >50% a random effects model was applied as is the standard procedure for higher levels of heterogeneity. Pooled effects were synthesized using Z test and a p value <0.05 was set at the threshold for statistical significance.

Sensitivity analysis

Sensitivity analysis was conducted to assess the reliability of the findings of this study. As such, Qmax at 24 months, PVR at 3-months, operation times, and period of

hospitalization were further analysed by removing non-RCTs. All data analyses were conducted with Review Manager 5.3 software.

RESULTS

The predetermined search and selection criteria yielded 22 publications [2, 7-11, 24-39], reporting 19 separate clinical studies. Three studies (i.e., Bachman et al., 2014 [10], 2015 [29] and Thomas et al. 2016 [30]) refer to an identical study, and two studies (Kumar et al. 2013 [24] and 2016 [31]) were from the same trials over different periods of time. In total, there were 2,665 patients involved, 1,455 of whom had been treated with PVP and 1,210 with TURP. Patient characteristics and study characteristics are summarized in **Table 1**. Overall, RCTs included in this meta-analysis can be considered of reasonably high quality with 8 studies achieving a score of 3, while 7 slightly lower quality achieved Jadad scores of 2. All prospective studies included can be considered high quality having been awarded 9 using the Newcastle-Ottowa Scale.

1. Meta-analysis of functional outcomes

Baseline data including IPSS, *Q*max, PVR, QoL and IIEF for all participants in both the PVP and TURP groups were similar (**Table 2**).

1.1. IPSS at 3, 6, 12, and 24 month follow-up

Pooled analysis suggests there is no significant difference in IPSS at the 3, 6, or 24 month follow-up points. At 3 months the MD = 0.01 (p = 0.85) please see **Fig. 2 a1.**

At 6 months the MD = 0.30 (p = 0.15), see **Fig. 2 a2. A**t the 12 month follow-up stage there was a statistically significant difference with a MD = -0.10 ($p < 0.01$), see **Fig. 2 a3**, however; at 24 months there was no significant difference (MD = 0.02, p = 0.92), see **Fig. 2 a4**.

1.2. Qmax at 3, 6, 12, and 24 month follow-up

Pooled analysis suggests there is no significant difference between PVP and TURP regarding Qmax at the 3 month follow-up stage with an MD = -0.07 (p = 0.91), see **Fig. 2 b1.** At the 6 months follow up the MD = -0.17 (p = 0.67), see **Fig. 2 b2**. At 12 months Qmax measures were slightly higher in the PVP group (MD = 0.62), which may be considered a statistically significant difference (p = 0.03), although only *borderline* when considering confidence intervals (95%CI= 0.06 to 1.19), see **Fig. 2 b3** for details. At 24 months the MD = 0.74 although was again non significant (p = 0.34), see **Fig. 2 b4** for details. However, an extreme level of heterogeneity were observed (I^2 = 91%) hence sensitivity analysis was conducted at the 24-month follow-up point which yielded an MD = 0.26, although this was not a significant finding (p = 0.72), see **Fig. 3a**.

1.3. PVR at 3, 6, 12, and 24 month follow-up

PVR between the two groups, yielded no significant difference at 3 months (MD =6.65, p = 0.16), see **Fig. 2 c1**, at 6 months (MD = 2.07, p = 0.35), see **Fig. 2 c2**, at 12 months (MD = 0.85, p = 0.11), see **Fig. 2 c3,** or at the 24 month follow-up point (MD = 1.58, p = 0.23), see **Fig. 2 c4**. Again, a high level of heterogeneity (I^2 = 93%) was

observed and so sensitivity analysis was conducted at the 3 month follow-up juncture. This did not highlight a significant difference between groups (p = 0.38), see **Fig. 3b** for details.

1.4. Qol at 3, 6, 12, and 24-month follow-up

There was no clinically relevant difference in QoL across the time points analysed. At the 3-month point there was an MD = 0.02, (p = 0.59) see **Fig. 2 d1**. However; there was one statistically significant difference at six months (MD = -0.08), although this is not clinically relevant and can only be considered of borderline significance (95%CI = -0.13 to -0.02), despite the low p value (p = 0.007), see **Fig. 2 d2**. At 12 months (MD = 0.01, p = 0.75), see **Fig. 2 d3** and at 24 months (MD = -0.07, p = 0.10), see **Fig. 2 d4**, there was no significant difference.

1.5. IIEF at 6, 12, and 24 month follow-up

An analysis of sexual functioning was performed using IIEF. There was no significant difference between the two groups in terms of the IIEF at the 3 month point (MD = -0.06, p = 0.76) see **Fig. 2 e1**, at the 6-month (MD = -0.07, p = 0.78) see **Fig. 2 e2** or at the 12 month point (MD = -0.06, p = 0.82) see **Fig. 2 e3**. Pooled analysis does highlight a lower IIEF at the 24 month follow-up in the PVP group compared to the TURP group with a MD = -0.68, which is statistically significant but again must be interpreted with caution because to the upper confidence interval is so close to zero (95%CI= -1.20 to -0.15, p = 0.01), see **Fig. 2 e4.**

2. Meta-analysis of perioperative parameters

2.1. Operation time

Fourteen studies comparing PVP against TURP reported operation times. Overall, TURP takes less time than PVP with a MD=15.24 minutes, and this was a significant finding (p <0.01) see **Table 3**. However, there was extreme heterogeneity across this sample (I^2 = 94%). As such, sensitivity analysis was conducted by removing low-quality trials (**Fig. 3c**) which lowered the level of heterogeneity (I^2 = 17%) and lowered the mean difference to 10.60 minutes (95%CI 8.39 to 12.81, p <0.01), see **Table 3**.

2.2. Operative blood loss

Six studies involving 724 participants (PVP n = 389, TURP n = 335) provided blood loss estimates during operations. The pooled statistic suggested that the drop in hemoglobin levels in the PVP group was significantly lower than in the TURP group with a MD of –1.33g/dl (p <0.01*),* see **Table 3** for details.

2.3. Periods of hospitalization

Eleven studies involving 1,542 participants met our inclusion criteria for the analysis of periods of hospitalization. Pooled statistics highlighted a significant reduction in hospitalization times with a MD = -1.98 days (p <0.01) for PVP compared with TURP. However, again the level of heterogeneity across this sample was extreme (I^2 = 98%) therefore sensitivity analysis (**Fig.3d**) was again performed although this had a negligible impact on the results (MD = -1.83 days, 95% CI -2.25 to -1.40, p <0.01). See **Table 3** for further details.

2.3. Catheterization time

Fourteen available studies including 1,655 participants (861 in the PVP group and 794 in the TURP group) were involved in this meta-analysis. Pooled data revealed that the PVP group had a significantly shorter catheterization time with an MD = -1.25 days, (p <0.01) see **Table 3**.

3. Meta-analysis of Complications

3.1. Perioperative complications

The overall effect of perioperative complications including bleeding-related transfusion, TUR syndrome, capsular perforation, clot retention, urinary tract infection and acute urinary retention are summarized in **Table 3**. According to this meta-analysis, PVP was found to have significantly lower incidence of transfusion with an RR=0.14 (p <0.01), and clot retention (RR=0.14, p <0.01). There was also a substantial and significant difference in the occurrence of TUR syndrome (RR=0.19, p <0.01) and capsular perforations (RR=0.09, p <0.01). Furthermore, PVP appears to have a higher risk of mild to moderate dysuria (RR=1.76, 95%CI 1.17 to 2.65, p <0.01), although there was no substantial or significant difference regarding urinary tract infection (RR=1.15, 95% CI 0.85 to 1.55, p = 0.38) or acute urinary retention rate (RR=1.19, 95%CI 0.80 to 1.75, p = 0.39).

3.2. Long-term complications

Analysis of long-term complications such as bladder neck contracture, retrograde

ejaculation and urethral stricture, suggests there is no significant difference between PVP and TURP. Bladder neck contracture (RR=1.05, $p = 0.87$), retrograde ejaculation (RR = 0.72, $p = 0.11$) and urethral stricture (RR=0.81, $p = 0.25$), see **Table 3** for further details. However, PVP was found to have a significantly higher risk of re-intervention (RR=1.81, $p < 0.01$) see **Table 3** for details.

DISCUSSION

Over the past two decades TURP has remained the gold standard surgical intervention for symptomatic BPH despite having high rates of treatment-related morbidities and complications which have a hugely negative impact on approximately 20% of those receiving this intervention [3, 6, 11]. Urologists continue to search for safer techniques without diminishing clinical efficacy compared to TURP.

Endoscopic technologies are being developed, and PVP emerged as a promising intervention which attracted our attention because this is a minimally-invasive surgical procedure. The first generation PVP laser system utilized high-powered KTP lasers (60W) at 532 nm and was initially introduced in 1998 [40]. More advanced generations including the KTP laser (80W)，the Green-light high-performance system (HPS) laser (120W) , the Green-light lithium triboride (LBO) laser (160W) and the Green-light X-ray photoelectron spectroscopy (XPS) laser (180W) systems were then sequentially introduced up until 2018, raising hopes of treating symptomatic BPH, effectively and safely.

Previous research comparing PVP and TURP has demonstrated that there is no

significant difference in medium term efficacy or safety when treating BPH, however; the long-term efficacy between these two techniques remains controversial. In this updated systematic review and meta-analysis, we reviewed all available RCTs and prospective studies (n = 22) up until October 2018 which involved a total of 2,665 participants. Pooled analyses and sensitivity analysis suggests both PVP and TURP have similar long-term function outcomes, which were analyzed using both subjective (IPSS, QoL) and objective (*Q*max, PVR) measures. IPSS at 12 month follow-up，*Q*max at 6 months and QoL at 12 months highlighted a statistically significant difference, although the differences were only small.

This study adds to the current evidence base in terms of understanding sexual functioning post-intervention. Previous clinical studies have evaluated retrograde ejaculation rates although conclusions could not be provided with any authority because findings were generally inconsistent and gathered over relatively short periods of time [7, 10, 25, 27, 38]. The longest running RCT which compared PVP with TURP had a 60 month follow-up, and suggested there is similar improvement in IPSS, Qmax, PVR, Qol and IIEF [36, 39].

Previously conducted meta-analyses have not had the opportunity to evaluate IIEF due to the relatively small number of studies collecting and reporting this particular outcome. Fortunately, IIEF is increasingly being used to analyze sexual functioning which enabled us to design and perform this meta-analysis given the increased availability of evidence in this area. Pooled analysis however suggests there is no

significant difference in the retrograde ejaculation rate nor is there a significant difference in IIEF outcomes between PVP and TURP.

This meta-analysis did highlight substantial differences in perioperative factors analyzed across this sample of studies. Pooled analyses and sensitivity analyses show that operation times are significantly longer for PVP, whereas the duration of hospitalization and catheterization are significantly shorter. Prolonged operative duration involved in PVP interventions appears to be associated with laser power and individual surgeon's experience and related skills. Laser power is determined for each individual device, and evidence from previous studies suggest that overall operation times are prolonged by approximately 23 minutes for PVP with an 80W laser, approximately 9 minutes with 120W and 7 minutes with 120W and 160W lasers. Furthermore, literature shows a surgeon's overall technical skills and confidence place him/her at a point on a learning curve for new technologies which is likely to be an important factor in the length of operations.

Safety is another key issue because the most serious TURP complications, such as bleeding and TUR syndrome are known to correlate with prostate size and longer operative times [6, 41]. This analysis highlighted additional benefits, in that the incidence of perioperative complications including bleeding, blood transfusion, clot retention, capsule perforation and TUR syndrome are significantly lower for those receiving the PVP intervention. Although, this can be explained by the characteristics of the green light laser, where the 532-nm wavelength is easily absorbed by hemoglobin

in prostatic tissues but not by water [13]. Likewise in vaporization, high-power laser energy is instantly absorbed by the blood, ensuring quicker vaporization into the tissue which creates a prostate cavity with minimal blood loss [42].

Other bleeding-related complications occur less frequently for those receiving PVP. However, another possible explanation could be that KTP laser energy penetrates only 1 to 2 mm of tissue. Therefore, high-power laser energy might be concentrated into the surface coat of prostatic tissue, which then ensures rapid vaporization, leaving a 0.2cm rim of residual coagulated tissue [13]. It may also be the case that the fluid medium used for PVP procedures is saline solution rather than glycine, therefore TUR syndrome does not occur in PVP. However, further research is necessary to understand this treatment related complication.

Additional postoperative complications such as acute urinary retention, UTIs, bladder neck contracture and urethral stricture were analyzed although no significant differences between TURP and PVP interventions were identified. However, PVP had two distinct disadvantages when compared with TURP. PVP appears to be associated with a higher risk of developing dysuria and for re-intervention. Dysuria rates after PVP have been reported to be between 6% and 30% [33, 43]. There may be several reasons for this, although most likely postoperative dysuria is caused by thermal damage and edema in urethral tissue. Also, shorter catheterization times could be another cause of this irritable symptom. That said, research suggests this symptom is generally classified as mild to moderate across all patients, and therefore can be effectively managed, if not

resolved altogether within two months of follow-up [27, 33]. As such, transient dysuria is not a serious PVP complication, the more serious complication is re-intervention.

There may be a number of reasons post-PVP patients are at a higher risk of re-intervention. There may be inadequate energy delivery, leading to incomplete tissue removal which might play an important role regarding the outcome of the procedure [38, 44]. According to our analysis, those who received an 80W PVP intervention were at significantly higher risk of re-intervention compared with TURP. However, researchers have found the differences between other higher power PVP laser groups (i.e., 120W, 160W and 180W) and TURP cohort are not statistically significant. Although, the GOLIATH study suggests that the 180W XPS laser system is superior to TURP when considering this particular parameter. Logically, this type of adverse event would markedly decrease with the advent of higher power laser systems.

As well as having a higher risk of dysuria and re-intervention, PVP is administered in the absence of histologic tissue examination, which might limit opportunities to incidentally identify prostate cancer. In order to address this, clinicians might want to consider when there is a rapidly increasing, or higher levels of prostate-specific antigen (PSA), it might be more beneficial to use TURP rather than laser evaporation techniques. In addition, an extensive examination including PSA measures, digital rectal examinations and ultrasonography could be used to guide prostate biopsies administration, if cancer is suspected [12, 45]. Prostate cancer is often diagnosed in the late stages which is nearly always too late and therefore *opportunities* to diagnose this

insidious disease must not be disregarded.

LUTS manifest secondarily through BPH and is a chronic health condition. The management of these symptoms create additional economic burden for patients and healthcare systems, generally [2, 46]. It is vital to evaluate the cost effectiveness of the two surgical therapies in clinical practice. Based upon a cost-effectiveness analysis, Armstrong et al suggest that the PVP procedure is unlikely to be cost effective because of the relatively expensive consumables [47]. However, Patel argues that there is an absence of high-quality and long-term data, in fact only two RCTs with short term follow-ups were available at the time [48]. This meta-analysis suggests that any initial investment in equipment and surgeon's training may be at least partially offset by shorter lengths of hospitalization and lower incidence of post-operative complications for PVP compared to TURP. Considering high number of cases each year, PVP may actually lower the demand for medical resources in this field although this also requires further research.

This meta-analysis was undertaken using all currently available comparative clinical studies, however; there are some limitations. First of all, despite designing a systematic search strategy, our inclusion criteria meant that non-English documents were omitted, therefore there must be some language bias. Secondly, there are very few RCTs with long-term follow-up endpoints in this field of interest which must be addressed. To overcome this, we designed this study to incorporate five prospective cohort studies which added a layer of sophistication to this analysis.

None of the RCTs included described blinding methods which is considered a distinct quality deficit but this is to be expected given the nature of the interventions explored. Actually, this perhaps highlights the need to use the CONSORT quality appraisal method or the Delphi method in further studies. While studies have demonstrate high levels of agreement [49] between these quality assessment tools and the methods implemented in this meta-analysis, the CONSORT and Delphi methods contain an increased number of variables and are therefore more likely to differentiate. A more substantial concern however is that several studies did not report withdrawal or drop outs. This appears to have been is significant factor in our quality assessment and must be addressed in further research. Thirdly, there was consistently, substantial to extreme heterogeneity across this study sample. Sensitivity analysis only partially accounted for such high levels of heterogeneity. Increased sample sizes, or multi-centre trials involving larger numbers of participants as well as reporting age stratification may elaborate on our present understanding. Despite these limitations, this study provides the most up-to-date information concerning the comparison of PVP and TURP in surgical management of BPH.

CONCLUSION

These findings confirm previous studies which suggested that PVP is superior in long-term efficacy to TURP. PVP appears to have only slightly increased IPSS, *Q*max, QoL, PVR and IIEF benefit, but is associated with fewer complications. As such, we recommend PVP is offered as the first-line treatment for LUTS secondary to BPH rather

than the traditional TURP method. The only addendum is that PVP cannot acquire histological tissue examination which removes an opportunity to identify prostate cancer. Withdrawals and drop outs are not always reported in full and there is a need to use a more comprehensive quality assessment tool to appraise studies in this field. Further research is of course necessary, and should be conducted with larger samples, over longer periods.

AUTHOR CONTRIBUTIONS

SCL and PXP designed and conducted the systematic search to identify all relevant studies. SCL and PXP then assessed eligibility and the quality of each study, before extracting data and conducting statistical analysis. TXD and HMH coordinated the study and performed data acquisition. XW, WZ and YGZ participated in data interpretation and drafting this article. SS, ML and JYW reviewed and revised this report for critical content and scientific rigour. All authors read and approved the final manuscript

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DATA AVAILABLITY STATEMENT

No additional unpublished data were available.

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Legend

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow chart

Figure 2. Forest plot of IPSS at 3 months (a1), 6 months (a2), 12 months (a3) and 24 months (a4); Forest plot of Qmax at 3 months (b1), 6 months (b2), 12 months (b3) and 24 months (b4); Forest plot of PVR at 3 months (c1), 6 months (c2), 12 months (c3) and 24 months (c4); Forest plot of Qol at 3 months (d1), 6 months (d2), 12 months (d3) and 24 months (d4); Forest plot of IIEF at 3 months (e1), 6 months (e2), 12 months (e3) and 24 months (e4). (IPSS = International Prostate Symptom Score; QoL = quality of life; Qmax = maximum flow rate; PVR = postvoid residual volume; IIEF=international index of erectile function)

Figure 3. Sensitivity analysis of the Qmax at 24-month follow-up (a); PVR at 3-month follow-up (b); operation times (c); and period of hospitalization (d). (Qmax = maximum flow rate; PVR = postvoid residual volume).

Table 1 Baseline characteristics of comparative studies.

Table 2 Meta-analytical outputs summarizing baseline parameters of PVP compared with TURP.

Table 3 Meta-analytical outputs for the safety of PVP compared with TURP.

Supplementary file

Supplement file 1 Electronic search strategy in PUBMED.

Table 1. Baseline characteristics of comparative studies

Authors and year	Design	Group	Laser power (W)	No. of patients	Age (years)	Prostate size (ml)	IPSS	*Q*max (mL/s)	PVR (mL)	QoL	IIEF	Follow-up, (months)	LE	Study quality
Kumar et al 2013	RCT	PVP	120	58	64.58±6.64	52.79±16.13	20.05±2.75	6.68±2.00	143.35±52.67	3.60±1.01	16.65±2.80	12	2a	3*
		TURP		60	63.68±6.57	52.20±15.93	20.71±2.68	7.00±1.97	139.25±54.28	3.73±0.97	16.95±2.86			
Lukacs et al 2012	RCT	PVP	120	68	66.9±7.8	50.54±16.53	22 (17–26)[%]	7.79±2.75	89.5 (30,158)[%]	70 (68,80)[%]		12	2a	3*
		TURP		68	67.6±7.6	50.11±14.73	20 (15–23)[%]	7.76±2.64	75 (28,126)[%]	75 (65,85)[%]				
Pereira-Correia	RCT	PVP	120	10	66.4(52 ,76)[$]	43.4(30, 58)[$]	22 (9, 33)[$]	10(3, 18)[$]	150(25,250)[$]		23(22,24)[$]	24	2a	2*
et al 2012		TURP		10	63.5(56, 78)[$]	47(30,60)[$]	25(15, 31)[$]	6.4(4,11)[$]	177(50, 300)[$]		23(22, 25)[$]			
Capitan et al 2011	RCT	PVP	120	50	69.8±8.44	51.29±14.72	23.74±5.24	8.03±3.14		4.52±0.27		12	2a	3*
		TURP		50	67.7±6.7	53.10±13.75	23.52±4.38	3.88±2.71		4.14±1.06				
Al-Ansari et al 2010	RCT	PVP	120	60	66.3±9.4	61.8±22	27.2±2.3	6.9±2.2	53.2±25			36	2a	3*
		TURP		60	67.1±8	60.3±20	27.9±2.7	6.4±2	57±21					
Xue et al 2013	RCT	PVP	120	100	72.1±11.3	65.8 ± 23.6	23.0 ± 5.1	8.0 ± 3.6	148.3 ± 101.6	4.2 ± 0.9		36	2a	2*

		TURP		100	71.0±10.8	67.3 ± 24.7	23.2 ± 5.0	8.2 ± 3.8	151.1 ± 105.2	4.3 ± 0.8				
Horasanli et al 2008	RCT	PVP	80	39	69.2±7.1	86.1±8.8	18.9±5.1	8.6±5.2	183±50.1		19.9±5.1	6	2a	2*
		TURP		37	68.3±6.7	88±9.2	20.2±6.8	9.2±5.6	176.9±45.3		20.1±5.5			
Mohanty et al 2012	RCT	PVP	80	60	66.68±8.62	44.77±14.09	19.98±3.27	7.41±2.07	145.8±70.33	3.97±0.82	17.98±3.55	12	2a	3*
		TURP		57	65.74±9.09	49.02±15.93	20.88±3.87	6.75±1.63	143.23±65.96	3.91±0.78	17.40±4.76			
Bouchier-Hayes et al 2009	RCT	PVP	80	60	>50		25.28±5.93	8.81±2.55	129.2±155.7	4.74±1.23		12	2a	3*
		TURP		59			25.41±5.72	8.86±2.99	111.3±113.7	5.08±0.94				
Bachmann et al 2014	RCT	PVP	180	136	65.9±6.8	48.6±19.2	21.2±5.9	9.5±3.0	110.1±88.5	4.6±1.1	13.2±7.6	6	2a	3*
		TURP		133	65.4±6.6	46.2±19.1	21.7±6.4	9.9±3.5	109.8±103.9	4.5±1.4	13.7±7.5			
Bachmann et al 2015	RCT	PVP	180	136	65.9±6.8	48.6±19.2	21.2±5.9	9.5±3.0	110.1±88.5	4.6±1.1	13.2±7.6	12	2a	2*
		TURP		133	65.4±6.6	46.2±19.1	21.7±6.4	9.9±3.5	109.8±103.9	4.5±1.4	13.7±7.5			
Thomas et al 2016	RCT	PVP	180	136	65.9±6.8	48.6±19.2	21.2±5.9	9.5±3.0	110.1±88.5	4.6±1.1	13.2±7.6	24	2a	3*
		TURP		133	65.4±6.6	46.2±19.1	21.7±6.4	9.9±3.5	109.8±103.9	4.5±1.4	13.7±7.5			
Telli et al 2015	RCT	PVP	120	39	67 (51,87)$	60 (41,75)$	20 (12,30)$	10.6 (5,17)$	60 (20,220)$			24	2a	2*

		TURP		62	69 (56,87)$	55 (40,72)$	19 (10,31)$	12.5 (3,21)$	65 (10,220)$					
Kumar et al 2016	RCT	PVP	120	58	64.58±6.64	52.79±16.13	20.05±2.75	6.68±2.00	143.35±52.67	3.60±1.01	16.65±2.80	36	2a	2*
		TURP		60	63.68±6.57	52.20±15.93	20.71±2.68	7.00±1.97	139.25±54.28	3.73±0.97	16.95±2.86			
Mordasini et al 2018	RCT	PVP	80	112	68.4±8.7	36.1±11.5	20.3±7.0	8.9±4.1	91.1±88.3	4.2±1.1		60	2a	2*
		TURP		126	67.6±8.4	37.9±14.3	20.4±7.5	8.5±4.6	114.5±136.4	4.3±14				
Chen et al 2011	PCS	PVP	160	57	69.5±7.4	60.2±27.8	19.7±6.0	6.9±4.0	93.7±79.7			6	2b	9#
		TURP		51	67.1±6.9	58.3±26.2	21.8±7.3	6.8±2.3	102.2±70.1					
Bachmann et al 2005	PCS	PVP		37	71.0±9.3	65.1±36.9	18.1±5.9	6.9±2.2	146.1±106.9	3.3±1.7		6	2b	9#
		TURP		64	68.7±7.9	48.9±21.2	17.3±6.3	6.9±2.2	120.7±49.0	3.4±1.6				
Ruszat et al 2008	PCS	PVP	80	113	62.3±5.0	56.3±27.4	20±6.4	8.5±4.1	203±226			24	2b	9#
		TURP		75	61.7±5.5	45.3±21.0	19±6.9	9.8±5.0	104±108					
		PVP		91	75.0±2.8	64.8±26.8	18.6±5.8	7.3±2.7	215±247					
		TURP		40	74.0±2.6	54.2±21.2	16.0±7.1	9.2±5.4	124±141					
		PVP		65	84.3±3.1	69.3±32.7	14.1±7.4	7.1±4.2	200±219					

		TURP		12	82.4±2.8	44.9±22.1	15.5±6.7	7.6±3.9	231±350				
Tasci et al 2008	PCS	PVP		40	71.8±5.9	108.4±15.8	22.3±5.6	6.2±2.2	116.5±60.5	3.6±0.7	24	2b	9#
		TURP		41	70.1±5.4	104.2±12.5	22.6±3.9	6.5±1.8	110.7±59.8	3.5±0.6			
Tugcu et al 2008	PCS	PVP		112	67.5±7.4	49.1±11.9	17.9±4.9	6.9±1.9	107.9±63.0	3.4±0.6	24	2b	9#
		TURP		98	66.3±7.9	47.7±8.4	17.7±3.5	7.2±1.7	100.3±57.1	3.4±0.5			
Nomura et al 2009	PCS	PVP	80	78	72.0(67.0,78.0)$	50.5(38.6,70.3)$	23 (17, 27)$	6.8 (5.2, 9.5)$	69 (31, 139)$	5 (5, 6)$	12	2b	9#
		TURP		51	70.5 (66.5, 76.0)$	42.8 (34.6, 54.0)$	22 (16, 27)$	7.3 (5.3, 10.2)$	60 (31, 140)$	5 (4, 5)$			
Guo et al 2015	PCS	PVP	80	257	69.7±8.9	52.3±19.3	19.4±6.3	8.3±6.0	119.5±83.8	3.7±1.7	60	2b	9#
		TURP		104	66.4±8.4	44.2±19.1	18.4±6.3	10.0±5.2	95.6±98.4	3.7±1.3			

LE = level of evidence;# Using Newcastle-Ottawa Scale (score from 0 to 9)； * Using Jadad scale (score from 0 to 5); RCT= randomized controlled trial; IPSS = International Prostate Symptom Score; QoL = quality of life; Qmax = maximum flow rate; PVR = postvoid residual volume; TURP = transurethral resection of the prostate; PVP=Photoselective vaporization of the prostate; IIEF=international index of erectile function; PCS=prospective cohort study.

Continuous variables were expressed as (mean±standard deviation) ,mean (range)$ or median (interquartile range)%.

Bachmann et al 2014， Bachmann et al 2015 and Thomas et al 2016 are from the same trials in different period; Kumar et al 2013 and Kumar et al 2016 are from the same trials in different period.

Table 2. Meta-analytical outputs summarizing baseline parameters of PVP compared with TURP

Parameter	No.of studies	Sample size		Heterogeneity(Total)				Mean Difference (95%CI)	Test for overall effect	
		PVP	TURP	chi^2	df	I^2(%)	P value			
IPSS										
Baseline	14	1179	989	11.32	13	0	0.58	-0.29 [-0.68, 0.10]	Z=1.47	p=0.14
Qmax										
Baseline	14	1179	989	70.23	13	81	<0.01	0.05[-0.51, 0.61]	Z=0.17	p=0.87
PVR										
Baseline	12	1016	864	9.24	11	0	0.6	2.19[-3.22,7.61]	Z=0.79	p=0.43
Qol										
Baseline	10	910	766	11.15	9	19	0.27	0.01 [-0.07,0.10]	Z=0.33	P=0.74
IIEF										
Baseline	5	351	297	1.58	4	0	0.81	-0.13 [-0.86,0.60]	Z=0.34	P=0.73

CI=confidence interval, RR=risk ratio; IPSS = International Prostate Symptom Score; PVP=Photoselective vaporization of the prostate; QoL = quality of life; PVR = postvoid residual volume; Qmax = maximum flow rate; IIEF=International Index of Erectile Function; TURP = transurethral resection of the prostate

Table 3. Meta-analytical outputs for the safety of PVP compared with TURP

Outcomes	No.of studies	Sample size		Heterogeneity(Total)				MD or RR(95%CI)	Test for overall effect	
		PVP	TURP	chi^2	df	I^2(%)	*P*		Z	*P*
Operation time	14	979	870	216.27	13	94	<0.01	15.24 [8.91,21.54]	4.72	<0.01
	6*	429*	428*	6.01*	5*	17*	0.31*	10.60 [8.39, 12.81]*	9.40*	<0.01*
Hospitalization time	11	819	723	600.62	10	98	<0.01	-1.98 [-2.56, -1.39]	6.59	<0.01
	3*	240*	229*	6.29*	2*	68*	<0.01*	-1.83 [-2.25, -1.40]*	8.42*	<0.01*
Catheterization time	14	861	794	964.75	13	99	<0.01	-1.25 [-1.58, -0.92]	7.48	<0.01
Blood loss	6	389	335	46.05	5	89	<0.01	-1.33 [-2.05, -0.61]	3.62	<0.01
Transfusion	14	1110	946	10.87	13	0	0.62	0.14 [0.08, 0.26]	6.10	<0.01

TUR syndrome	7	590	435	0.73	6	0	0.99	0.19 [0.06, 0.61]	2.82	<0.01
Capsular perforation	7	641	451	1.84	6	0	0.93	0.09 [0.03, 0.26]	4.51	<0.01
Clot retention	8	699	504	1.72	7	0	0.97	0.14 [0.07, 0.29]	5.32	<0.01
Urinary tract infection	13	1049	860	8.79	12	0	0.72	1.15 [0.85, 1.55]	0.89	0.38
Acute urinary retention	10	694	653	5.55	9	0	0.78	1.19[0.80, 1.75]	0.86	0.39
Urinary incontinence	4	296	263	4.28	3	30	0.23	1.45[0.74, 2.86]	1.08	0.28
Bladder neck contracture	8	523	520	4.32	7	0	0.74	1.05 [0.57, 1.94]	0.16	0.87
Urethral stricture	15	1172	980	9.37	14	0	0.81	0.81 [0.57, 1.16]	1.14	0.25
Retrograde ejaculation	4	320	314	15.06	3	80	<0.01	0.72 [0.49, 1.07]	1.62	0.11
Dysuria	12	1079	854	24.80	11	58	0.01	1.76 [1.17, 2.65]	2.71	<0.01
Re-intervention	12	980	809	14.58	11	25	0.20	1.81 [1.28, 2.56]	3.35	<0.01

* Using sensitivity analysis; CI=confidence interval; MD=mean difference; PVP=Photoselective vaporization of the prostate; RR=risk ratio; TURP = transurethral resection of the prostate; TUR syndrome= transurethral resection syndrome

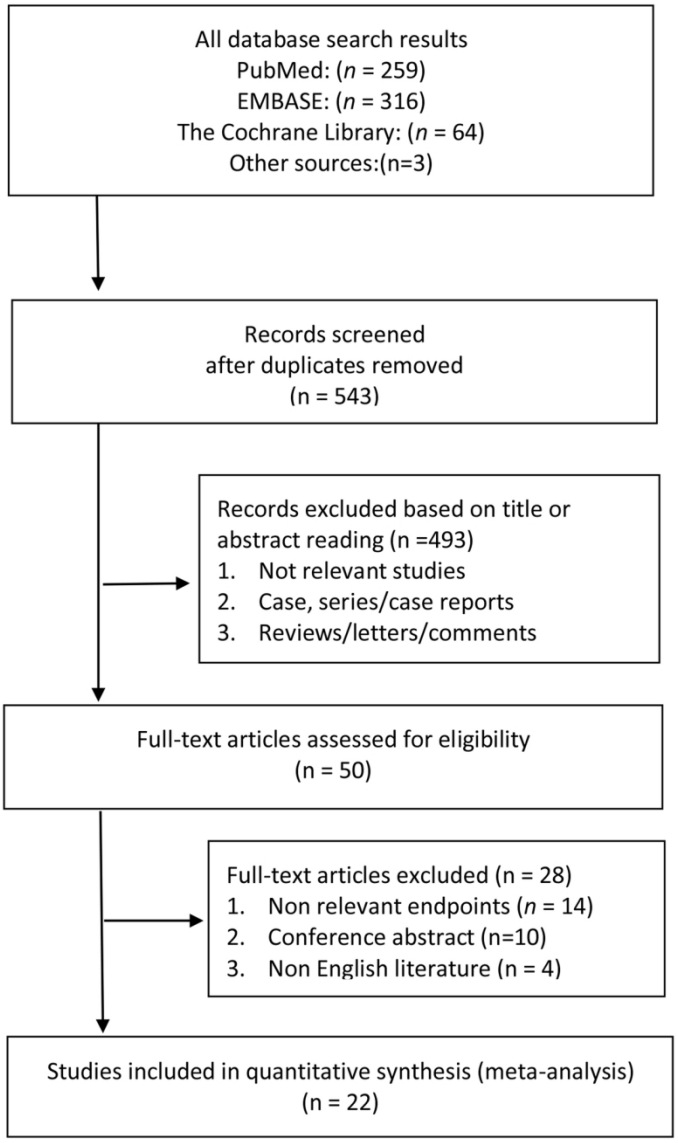

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow chart

119x184mm (300 x 300 DPI)

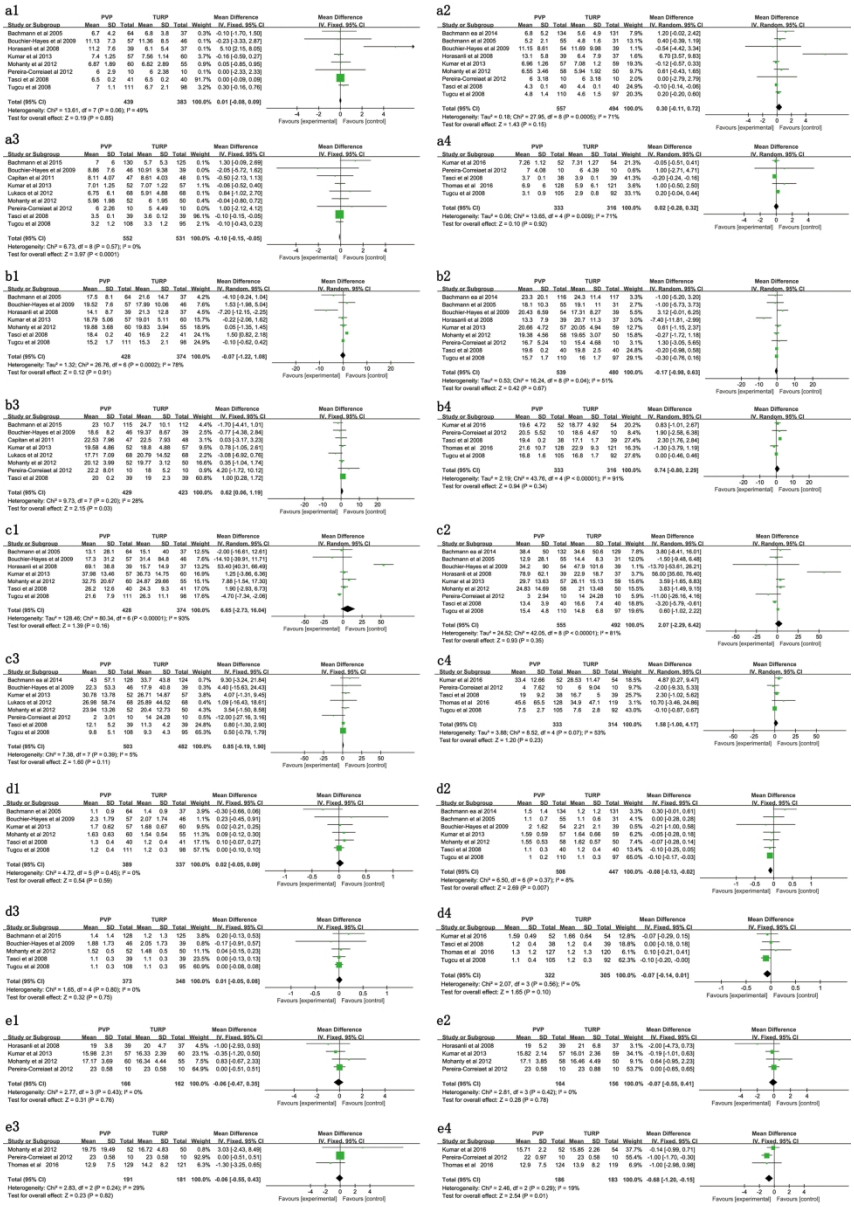

Figure 2. Forest plot of IPSS at 3 months (a1), 6 months (a2), 12 months (a3) and 24 months (a4); Forest plot of Qmax at 3 months (b1), 6 months (b2), 12 months (b3) and 24 months (b4); Forest plot of PVR at 3 months (c1), 6 months (c2), 12 months (c3) and 24 months (c4); Forest plot of QoI at 3 months (d1), 6 months (d2), 12 months (d3) and 24 months (d4); Forest plot of IIEF at 3 months (e1), 6 months (e2), 12 months (e3) and 24 months (e4). (IPSS = International Prostate Symptom Score; QoL = quality of life; Qmax = maximum flow rate; PVR = postvoid residual volume; IIEF=international index of erectile function)

209x296mm (300 x 300 DPI)

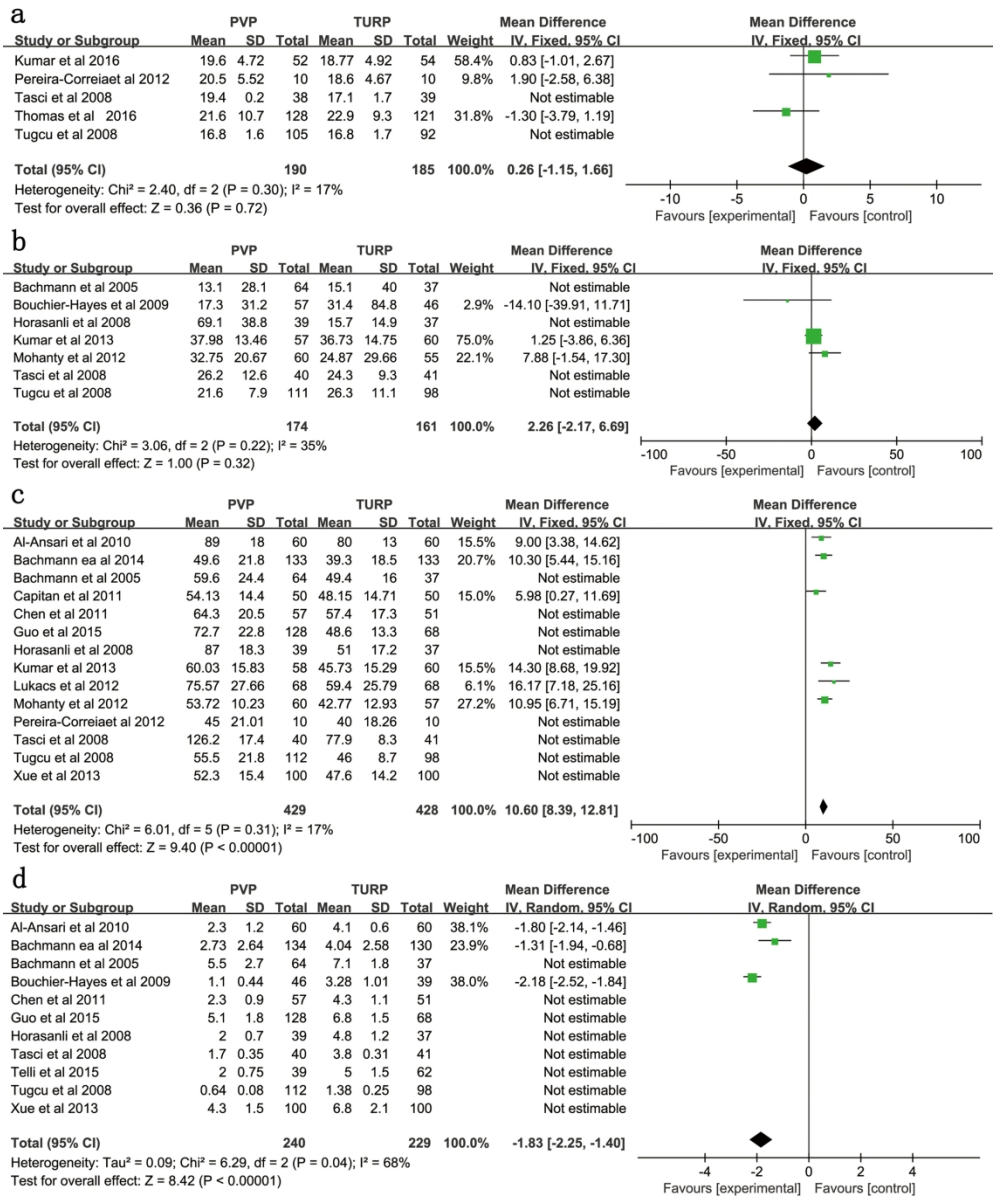

Figure 3. Sensitivity analysis of the Qmax at 24-month follow-up (a); PVR at 3-month follow-up (b); operation times (c); and period of hospitalization (d). (Qmax = maximum flow rate; PVR = postvoid residual volume).

209x254mm (300 x 300 DPI)

Comparison of photoselective green light laser vaporization versus traditional transurethral resection for benign prostate hyperplasia: an up-to-date systematic review and meta-analysis of randomized control trials and prospective studies

Search strategy in PUBMED

((((((((((((Hyperplasia, Prostatic) OR Prostatic Hypertrophy) OR Adenoma, Prostatic) OR Adenomas, Prostatic) OR Prostatic Adenomas) OR Prostatic Adenoma) OR Benign Prostatic Hyperplasia) OR Prostatic Hyperplasia, Benign) OR Prostatic Hypertrophy, Benign) OR Benign Prostatic Hypertrophy) OR Hypertrophy, Benign Prostatic)) AND ((((((((((((Prostate Transurethral Resection) OR Prostate Transurethral Resections) OR Transurethral Prostate Resection) OR Prostate Resection, Transurethral) OR Prostate Resections, Transurethral) OR Resection, Transurethral Prostate) OR Resections, Transurethral Prostate) OR Transurethral Prostate Resections) OR TURP) OR TURPs) OR Prostatectomy, Transurethral) OR Prostatectomies, Transurethral) OR Transurethral Prostatectomies) OR Transurethral Prostatectomy)) AND (((PVP) OR photoselective vaporisation) OR green-light laser)

The last quest was updated on December 20, 2018

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	6-7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	None
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7-8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7-8
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8-9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9-10
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-14
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-14
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10-14
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11-13
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	14-19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	19-20
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	20-21
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	21

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