

Platinum Priority – Review – Benign Prostatic Hyperplasia
Editorial by Steven A. Kaplan on pp. 714–715 of this issue

Prostatic Urethral Lift Improves Urinary Symptoms and Flow While Preserving Sexual Function for Men with Benign Prostatic Hyperplasia: A Systematic Review and Meta-analysis

Marlon Perera ^{a,b,†}, Matthew J. Roberts ^{a,b,c,d,†}, Suhail A.R. Doi ^{e,f}, Damien Bolton ^{g,h,*}

^a Mackay Base Hospital, Mackay, Queensland, Australia; ^b Urological Society of Australia and New Zealand, Edgecliff, New South Wales, Australia; ^c School of Medicine, The University of Queensland, Brisbane, Queensland, Australia; ^d Centre for Clinical Research, The University of Queensland, Brisbane, Queensland, Australia; ^e School of Population Health, The University of Queensland, Brisbane, Queensland, Australia; ^f Department of Endocrinology, Princess Alexandra Hospital, Brisbane, Queensland, Australia; ^g Department of Surgery, University of Melbourne, Melbourne, Victoria, Australia; ^h Ludwig Institute for Cancer Research, Austin Hospital, Studley Road, Heidelberg, Victoria, Australia

Article info

Article history:
Accepted October 21, 2014

Keywords:
Prostate
Prostatic urethral lift
Urolift
Benign prostatic hyperplasia
Urethra
Minimally invasive surgical therapy
Lower urinary tract symptoms

Abstract

Context: Treatment for lower urinary tract symptoms resulting from benign prostatic hyperplasia (BPH) is varied, and significant side effects, particularly concerning sexual function, affect uptake. The prostatic urethral lift (PUL) procedure is a recent addition to the armamentarium for BPH treatment, with independent reports suggesting improvement of symptoms, sexual function, and urinary flow.

Objective: We undertook a systematic review and meta-analysis of reported symptomatic, functional, and sexual outcomes following the PUL procedure.

Evidence acquisition: We performed a critical review of Medline, Embase, ScienceDirect, Cochrane Library, and Web of Science databases in May 2014 according to the Preferred Reporting Items for Systematic Review and Meta-Analysis statement. Quality assessment was performed using a modification of the Methodological Index for Non-Randomized Studies tool. All retrospective, prospective, and controlled trials were included for analysis. Symptom scores, sexual health scores, and functional outcomes were pooled and meta-analysed using quality and random-effects models.

Evidence synthesis: Ten articles comprising six independent patient cohorts were included for analysis. Pooled estimates from between 452 and 680 patients suggested overall improvement following PUL, including symptoms (large gain; standardised mean gain range of 1.3–1.6, International Prostate Symptom Score difference of –7.2 to –8.7 points), maximum flow rate (3.8–4.0 ml/s), and quality of life (2.2–2.4 points). Sexual function was preserved with a small improvement estimated at 12 mo (standardised mean gain range of 0.3–0.4). Pooled estimates were mostly heterogeneous across study groups.

Conclusions: PUL is a well-tolerated, minimally invasive therapy for BPH that provides favourable symptom, sexual health, and functional outcomes during follow-up to 12 mo. Longer follow-up and larger randomised studies are required to further confirm these preliminary results.

Patient summary: We reviewed the early results of an innovative procedure directed towards the management of prostate enlargement. The results revealed a well-tolerated procedure that produces improvement in urinary symptoms and function while preserving sexual function.

© 2014 European Association of Urology. Published by Elsevier B.V. All rights reserved.

[†] Contributed equally.

* Corresponding author. 5/210 Burgundy Street, Heidelberg, Victoria, 3084, Australia.
E-mail address: damiemb@unimelb.edu.au (D. Bolton).

1. Introduction

Lower urinary tract symptoms (LUTS) resulting from benign prostatic hyperplasia (BPH) are common, with moderate to severe LUTS estimated to affect up to 30% of men aged >50 yr [1,2]. Severe LUTS is associated with depression and reduced quality of life in otherwise healthy men [3], and an increasing population requiring treatment is expected, specifically 10.3 million men in the United States in 2020 [1,4]. Reduced healthcare-related quality of life causes significant economic burden [5]. Current methods of conservative treatment (α 1-blockers, 5 α -reductase inhibitors) total 11.6 million prescriptions per year across Europe [6] for modest improvements in the International Prostate Symptom Score (IPSS).

Up to 30% of patients require surgical intervention following failure of medical therapy, mostly due to dissatisfaction and side effect profile [1,7]. Transurethral resection of the prostate (TURP) produces a significant and reliable improvement in LUTS as a result of reducing bladder outlet obstruction [8] at the expense of morbidity, such as ejaculatory dysfunction (53–75%), erectile dysfunction (3.4–32%), urinary incontinence (2.2%), and urethral stricture (2–9%) [9]. Despite alternative therapeutic advances such as photoselective vaporisation of the prostate (PVP), the side effect profile remains prominent, with 8.8% suffering perioperative complications and 13.3% having long-term morbidity with this procedure [10,11]. Less invasive, or *minimally invasive*, surgical interventions such as transurethral microwave therapy (TUMT) and transurethral needle ablation (TUNA) spare a degree of the side effect profile at the expense of IPSS improvement [10].

Prostatic urethral lift (PUL) is a newly available minimally invasive procedure for LUTS secondary to BPH. Despite being categorised as minimally invasive, PUL is performed in the lithotomy position with the support of a local or general anaesthetic. Initially reported in 2005, the procedure results in anterolateral traction of the lateral lobes of the prostate towards the capsule, expanding the urethral lumen and relieving obstruction [12]. The procedure has been described in detail previously [13]. The lateral lobes are secured by small permanent suture-based implants administered by a preloaded custom implant-delivery device (UroLift System; NeoTract Inc., Pleasanton, CA, USA). Given this targeted mechanism on the lateral lobes, it has been postulated that PUL may have limited efficacy for patients with obstructing median lobes, which has been an important exclusion criterion for many previously published reports. This interventional technique is mechanical and avoids resection or ablation of prostatic tissue. Early results using PUL suggest a beneficial therapeutic effect while avoiding many of the morbidities and complications associated with more conventional surgery.

The aim of this study was to collate available data on PUL using a systematic search strategy and to quantify global treatment effects using meta-analysis. This article was produced without consultation or input from NeoTract Inc.

2. Evidence acquisition

A systematic review was performed in accordance with Cochrane Collaboration and Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines [14,15].

2.1. Search strategy

Scientific literature databases (Medline, Embase, ScienceDirect, Cochrane Library, and Web of Science) were systematically searched in May 2014 using several keywords including *prostate*, *benign prostate hyperplasia*, *lower urinary tract symptoms*, and *urethral lift* (Supplementary Table 1). Article selection was performed by two independent evaluators (M.P., M.J.R.), and any discrepancies were resolved.

2.2. Inclusion and exclusion criteria

Retrospective and prospective studies evaluating functional and sexual outcomes following the PUL procedure for LUTS resulting from BPH were included in the analysis. No language or sample-size restrictions were used. Conference proceedings were unable to be robustly assessed for study quality and thus were excluded. If duplicate study populations or analyses of repeated data were identified, the publication reporting a larger sample size was preferentially assessed.

2.3. Quality assessment

Initially, studies were quality assessed based on the Cochrane Handbook for Systematic Reviews of Interventions 5.02 [15,16]. A quality-appraisal tool was adapted for the current research question from the recommendations by Ramsey et al [17]. Each paper was scored independently by two evaluators (M.J.R., M.P.), and these scores were used to appropriately weight each study when performing *quality effects* meta-analysis [18] (Supplementary Table 2).

2.4. Data extraction and analysis

Data extracted from the eligible studies included demographic information (eg, patient age, prostate volume), operative details (eg, number of implants, operative time, perioperative complications), and postoperative outcomes. Primary outcome measures that were assessed included prostate symptoms (IPSS, American Urological Association Symptom Index, BPH Impact Index [BPHII]), sexual health (International Index of Erectile Dysfunction [IIEF], Sexual Health Inventory for Men, Male Sexual Health Questionnaire [MSHQ] for ejaculatory function [MSHQ-EjD] and bother [MSHQ-Bother]), and functional parameters including maximum urine flow rate (Q_{max}) and postvoid residual volume (PVR).

Extracted data were collated in Excel (Microsoft Corporation, Redmond, WA, USA). Quality and random-effects

meta-analysis was performed using MetaXL 2.0 [18–20] (<http://www.epigear.com>). If results from one scoring system (eg, quality of life score, Q_{\max} , PVR) were pooled, the effect size extracted was the gain in mean score or mean gain (MG) plus or minus standard error (SE) from before (time point 1 [T1]) to after (time point 2 [T2]) the intervention. The following calculations were used:

$$MG \pm SE = \bar{X}_{T2} - \bar{X}_{T1} \pm \sqrt{\frac{2s_p^2(1-r)}{n}}$$

in which $s_p^2 = (s_{T1}^2 + s_{T2}^2)/2$

If multiple scales were used to measure the same outcome, a standardised MG (SMG) was calculated by considering the MG in the context of the pooled standard deviation (s_p) [21]. The following calculations were used:

$$SMG \pm SE = \frac{\bar{X}_{T2} - \bar{X}_{T1}}{s_p} \pm \sqrt{\frac{2(1-r)}{n} + \frac{SMG^2}{2n}}$$

in which $s_p = \sqrt{(s_{T1}^2 + s_{T2}^2)/2}$

The interpretation of SMG is similar to Cohen's d [22], for which small, medium, large, and very large effect-size thresholds are defined as 0.2, 0.5, 0.8, and 1.3, respectively.

To aid in clinical understanding, interpretation of the SMG as a difference in IPSS (the IPSS is a 35-point scale with 7 points being a large difference) was undertaken by multiplying the SMG and its 95% confidence interval (CI) by 5.5, which represents a typical standard deviation for the IPSS scores. This interpretation should be considered indicative only.

Random-effects model results were reported only in Supplementary Table 3 for comparison purposes because the results of this model are known to underestimate the statistical error and defaults to the arithmetic mean when heterogeneity is large. It also ignores the risk of bias from individual studies; as such, results that differ from the quality effects model results may not be meaningful. Heterogeneity in effect sizes was defined as τ^2 greater than zero or Q -statistic >50 [23].

3. Evidence synthesis

Using the systematic search strategy outlined in Supplementary Table 1, 581 articles were identified, of which 58 were duplicate records that were excluded (Fig. 1). Of the remaining 523 records, 462 were not relevant to the research question and 23 were conference abstracts that could not be quality assessed and thus were excluded. From

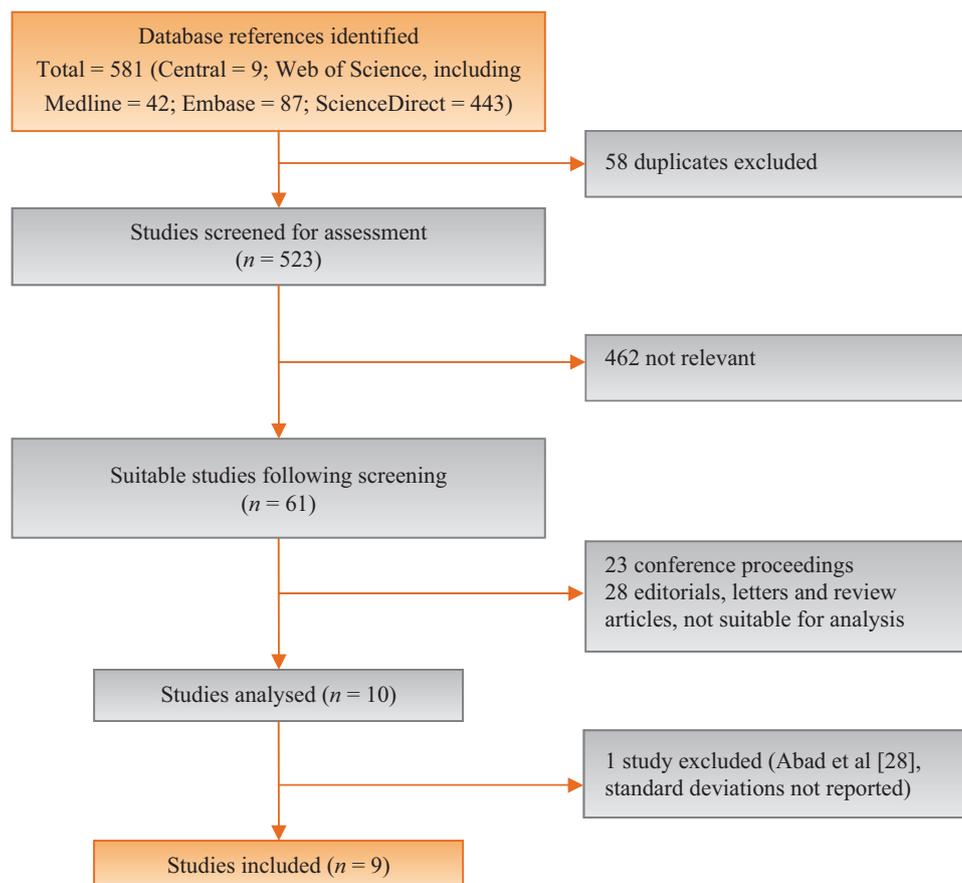


Fig. 1 – Study selection.

Table 1 – Characteristics of included studies

Series	Study type	Country	n	Inclusion criteria	Exclusion criteria	Follow-up (mo)	Outcome measures
Abad et al, 2013 [28]	Prospective cohort	Spain	20	Aged >50 yr, IPSS >20, Q _{max} <15 ml/s, no prior BPH treatment	PSA >10, obstructive median lobe, infection, previous prostate surgery	12	IPSS, BPHII, Q _{max}
Cantwell et al, 2014 [26]	Crossover trial	USA	53	Aged >50 yr, no prior BPH treatment, washed out or naive to medical therapy, IPSS >12, Q _{max} <12 ml/s, PV 30–80 ml	Obstructive median lobe, PVR >250 ml, infection, PSA >10 (unless negative biopsy), cystolithiasis, bacterial prostatitis	12	IPSS, QOL, BPHII, SHIM, MSHQ-EjD, MSHQ-Bother
Delongchamps, cited in Hoffman et al, 2012 [49]	Prospective cohort	France	4	NR	NR	1	IPSS, SHIM, MSHQ-EjD
LIFT study, Roehrborn et al, 2013 [24]	Blinded RCT	USA	140	Aged >50 yr, no prior BPH treatment, washed out or naive to medical therapy, IPSS >12, Q _{max} <12 ml/s, PV 30–80 ml	Obstructive median lobe, retention, PVR >250 ml, infection, PSA >10 (unless negative biopsy), cystolithiasis, bacterial prostatitis	12	AUASI, QOL, BPHII, Q _{max} , PVR
LIFT study, McVary et al, 2014 [25]	Blinded RCT	USA	137	As above	As above	12	IPSS, SHIM, MSHQ-EjD, Q _{max}
Shore et al, 2014 [27]	Prospective cohort	USA	51	Aged >50 yr, no prior BPH treatment, washed out or naive to medical therapy, IPSS >12, Q _{max} <12 ml/s, PV 30–80 ml	Obstructive median lobe, PVR >250 ml, infection, cystolithiasis, bacterial prostatitis	1	IPSS, QOL, BPHII, SHIM, MSHQ-EjD, MSHQ-Bother, Q _{max}
McNicholas et al, 2013 [13]	Prospective cohort	UK	102	PV <60 ml, IPSS >12, Q _{max} <15 ml/s, PVR <250 ml	NR	12	IPSS, QOL, BPHII, Q _{max} , PVR
Chin et al, 2012 [30]	Prospective cohort	Australia	64	IPSS >12, Q _{max} 5–12 ml/s, PVR <250 ml	PSA >10, retention, infection, previous prostate surgery, large median lobes, compromised renal function	24	IPSS, QOL, BPHII, SHIM, MSHQ-EjD, Q _{max} , PVR
Woo et al, 2012 [29]	Prospective cohort	Australia	64	IPSS >12, Q _{max} 5–12 ml/s, PVR <250 ml, washed out to medical therapy	Obstructive median lobe, retention, infection	12	IPSS, SHIM, MSHQ-EjD, MSHQ-Bother
Woo et al, 2011 [4]	Prospective cohort	Australia	15	PV 20–100 ml, IPSS >12, Q _{max} 5–12 ml/s, PVR <250 ml, washed out to medical therapy	Obstructive median lobe, infection, retention, PSA >10, significant medical comorbidities, previous surgery	12	IPSS, QOL, Q _{max} , PVR

AUASI = American Urological Association Symptom Index; BPH = benign prostatic hyperplasia; BPHII = Benign Prostatic Hyperplasia Impact Index; EjD = ejaculatory dysfunction; IPSS = International Prostate Symptom Score; MSHQ = Male Sexual Health Questionnaire; NR = not reported; QOL = quality of life; PSA = prostate-specific antigen; PV = prostate volume; PVR = postvoid residual; Q_{max} = maximum flow rate; RCT = randomised controlled trial; SHIM = Sexual Health Inventory for Men.

Table 2 – Baseline functional scores prior to prostatic urethral lift intervention

Series	n	Age	PV, ml, mean (SD)	IPSS, mean (SD)	BPHII, mean (SD)	HRQOL, mean (SD)	IIEF-5 or SHIM, mean (SD)	MSHQ- EjD, mean (SD)	MSHQ- Bother, mean (SD)	Q _{max} , ml/s, mean (SD)	PVR, ml, mean (SD)
Abad et al, 2013 [28]	20	74.3 ± NR	42.6 (NR)	26.7 (6.0)	8.4 (2.3)	NR	NR	NR	NR	8.6 (2.9)	NR
Cantwell et al, 2014 [26]	53	64 ± 8.0	40.3 (9.9)	23.3 (5.5)	6.3 (3.0)	4.5 (1.2)	12.8 (8.3)	9.5 (10.0)	NR	8.8 (4.2)	67.8 (66.4)
Delongchamps, cited in Hoffman et al, 2012 [49]	4	63.5 ± 11.1	55 (19)	20.8 (3.1)	NR	NR	NR	5.5 (6.1)	NR	6 (2.3)	115 (72)
LIFT study, Roehrborn et al, 2013 [24]	140	67 ± 8.6	44.5 (12.4)	22.2 (5.4)	NR	4.6 (1.1)	13.0 (8.4)	8.7 (3.2)	NR	8.9 (2.2)	85.5 (69.2)
LIFT study, McVary et al, 2014 [25]	137	67 ± NR	NR	22.2 (5.4)	NR	4.6 (1.1)	18.0 (5.6)	9.1 (3.1)	2.0 (1.6)	8.0 (2.4)	NR
Shore et al, 2014 [27]	51	66 ± 7.6	41.3 (11.6)	21.5 (5.4)	6.7 (3.1)	4.6 (1.0)	16.5 (7.3)	9.95 (2.6)	NR	8.2 (2.2)	77.1 (74.9)
McNicholas et al, 2013 [13]	102	68 ± 10.0	48 (10.5)	23.2 (6.1)	NR	4.7 (1.0)	NR	NR	NR	8.7 (4.0)	NR
Chin et al, 2012 [30]	64	67 ± 7.3	51 (11.5)	22.6 (5.4)	NR	NR	NR	NR	NR	8.3 (2.2)	NR
Woo et al, 2012 [29]	64	67 ± 7.3	51 (11.5)	22.9 (5.4)	NR	NR	11.7 (8.6)	9.0 (3.7)	1.7 (1.5)	NR	NR
Woo et al, 2011 [4]	15	66 ± 6	NR	NR	NR	NR	NR	NR	NR	NR	NR

BPHII = Benign Prostatic Hyperplasia Impact Index; EjD = ejaculatory dysfunction; HRQOL = health-related quality of life; IIEF-5 = International Index of Erectile Function; IPSS = International Prostate Symptom Score; MSHQ = Male Sexual Health Questionnaire; NR = not reported; PV = prostate volume; PVR = postvoid residual; Q_{max} = maximum flow rate; RCT = randomised controlled trial; SD = standard deviation; SHIM = Sexual Health Inventory for Men.

the remaining 10 articles, 6 independent patient series were identified for analysis. Of these six, one represented a randomised controlled trial [24,25], one was an observational crossover cohort from the placebo group in the randomised controlled trial [26], two were prospective trials [27], and two were retrospective cohorts [4,13,28–30] (Table 1). Patient demographics and baseline symptom, functional, and sexual measures are outlined in Table 2. Five studies were included in the meta-analysis because one study did not report standard deviations and was excluded [28].

Patient inclusion and exclusion criteria remained relatively constant across study groups, with patients aged >50 yr with IPSS >12 and Q_{max} <12–15 ml/s. Accepted prostate volumes varied between studies but generally included patients with volumes 20–100 ml, with a cut-off of ≤80 ml applied in the randomised controlled trial. The most consistently reported exclusion criteria were obstructive median lobes, active urinary infection, acute urinary retention (or PVR >250 ml), and prostate-specific antigen (PSA) >10 ng/ml (unless normal biopsy). Patient demographics across the six series were comparable, with a median age range of 64–74.3 yr and mean operative time range of 19.1–66 min. Anaesthesia methods varied, with most US-based series completed under local anaesthetic, with or without penile block (95–99%). The procedure was well tolerated across all series, with a serious complication rate (defined as a Clavien-Dindo [31] score of ≥2) of 2.5–18%. As shown in Table 3, the most frequent complications reported within 3 mo postoperatively included dysuria (25–53%), haematuria (16–75%), pelvic pain (3.7–19.3%), urgency (7.8–10%), transient incontinence (1.9–16%), and urinary tract infection (3.2–10%). Varied definitions and terminology limited statistical comparison.

The pooled SMG estimates for prostate symptom scores (IPSS and BPHII) and sexual health scores (IIEF, MSHQ-EjD, MSHQ-Bother) incorporated between 888 and 1298 responses from 452 to 680 patients. The SMG for prostatic symptom scores ranged between –1.3 (95% CI, –1.4 to –1.2) and –1.6 (95% CI, –1.7 to –1.3), suggesting a large decrease in symptoms across the 12-mo follow-up period (Table 3; Fig. 2A). Interpretation of the SMG in terms of difference in IPSS score suggests that the change in score was –7.2 points (95% CI, –7.9 to –6.5) at 1 mo, –8.3 points (95% CI, –9.1 to –7.5) at 3 mo, –8.7 points (95% CI, –9.4 to –7.9) points at 6 mo, and –8.0 points (95% CI, –8.8 to –7.2) at 12-mo follow-up. Prostate weight, number of implants, urethral length, degree of median lobe obstruction, and other prognostic factors identifying patients likely to have a greater therapeutic effect have not been reported and thus were not available for analysis.

The SMG in sexual health scores ranged between 0.3 (95% CI, 0.2–0.4) and 0.4 (95% CI, 0.3–0.5), suggesting a small improvement [22]. Pooled estimates were mostly heterogeneous, with some homogeneity observed (prostate symptom score at 6 mo, sexual health score at 12 mo).

Mean improvement in quality-of-life scores were estimated to be between 2.2 points (95% CI, –2.5 to –2.0) and 2.4 points (95% CI, –2.6 to –2.2) (MG) using responses from between 452 and 628 patients (Table 3; Fig. 2B). A homogeneous pooled estimate from three studies was observed for data at 12 mo, with the remainder being heterogeneous.

Assessment of functional outcomes (Q_{max}, PVR) was limited due to inconsistent reporting, specifically at selected intervals in selected studies. Nevertheless, favourable pooled estimates were observed for Q_{max}, with an improvement of between 3.8 ml/s (95% CI, 3.0–4.6) and

Table 3 – Operative details and complications

Series	Local anaesthetic	Operative time, min, mean (SD)	Implants, mean (range)	Postoperative catheter	Early postoperative complications					Progression to TURP at 12 mo
					Dysuria	Haematuria	Pelvic pain	UTI	Incontinence	
Abad et al, 2013 [28]	0/20 (0)	19.1 (NR)	3.8 (2–6)	NR	14/20 (70)	6/20 (30)	NR	NR	0/20	1/20 (5)
Cantwell et al, 2014 [26]	46/53 (88)	53 (15)	4.4 (2–8)	26/53 (49)	19/53 (36)	14/53 (26)	11/53 (21)	1/53 (2)	2/53 (3.8)	1/53 (2)
Delongchamps, cited in Hoffman et al, 2012 [49]	NR	11 (4.7)	5.5 (3–9)	4/4 (100)	0/4 (0)	1/4 (25)	0/4 (0)	0/4 (0)	0/4 (0)	NA
LIFT study, Roehrborn et al, 2013 [24]	NR	66 (24)	4.9 (2–11)	72/140 (51)	48/140 (34)	36/140 (26)	25/140 (18)	4/140 (2.9)	5/140 (3.6)	2/140 (1.4)
LIFT study, McVary et al, 2014 [25]	NR	NR	4.9 (NR)	72/137 (53)	NR	NR	NR	NR	NR	2/137 (1.5)
Shore et al, 2014 [27]	51/51 (100)	52 (22)	3.7 (2–6)	10/51 (20)	27/51 (53)	38/51 (75)	8/51 (16)	NR	2/51 (4)	NA
McNicholas et al, 2013 [13]	17/102 (17)	58 (16)	4.5 (2–9)	43/102 (42)	25/102 (25)	16/102 (16)	NR	3/102 (3)	NR	4/102 (3.9)
Chin et al, 2012 [30]	26/64 (41)	NR	NR	34/64 (53)	NR	NR	NR	7/64 (11)*	5/64 (8)	12/64 (19)*
Woo et al, 2012 [29]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Woo et al, 2011 [4]	0/15 (0)	NR	3.5 (2–5)	11/19 (58)	11/19 (58)	12/19 (63)	1/19 (5)	3/19 (10)†	3/19 (16)	3/19 (16)

NA = not available; NR = not reported; SD = standard deviation; TURP = transurethral resection of the prostate; UTI = urinary tract infection.

Data are shown as frequency (%) unless indicated otherwise.

* Over 24-mo follow-up period.

† Over 12-mo follow-up period.

4.0 ml/s (95% CI, 3.4–4.6) observed in meta-analysed studies (1, 3, and 12 mo), which were homogeneous (Table 4; Fig. 2C). Pooled PVR estimates were significantly variable, owing to inconsistent reporting, and demonstrated very high heterogeneity estimates (Table 4). Figure 2 also indicates that effects due to the intervention were seen early and were sustained over 12 mo.

At 12-mo follow-up, 1.5–16% of patients experienced insufficient IPSS or Q_{max} improvements and progressed to TURP. Several studies reported results of routine follow-up cystoscopic evaluation of the PUL implants. At 6 mo postoperatively, no study reported implant encrustation or removal of troublesome implant. At 12-mo follow-up, no appropriately placed implants developed encrustation; however, 14 of 27 implants exposed to the bladder experienced encrustation, and 2 of 14 were symptomatic and were removed with endoscopic forceps [24,25]. Implant failure or infection requiring removal was not reported.

3.1. Discussion

PUL is a well-described, minimally invasive addition to the armamentarium for BPH treatment. The results of the current systematic review and meta-analysis suggest that PUL produces improved prostatic symptoms and urinary function with relative preservation of sexual function.

A large [22] improvement of LUTS symptoms was observed in the pooled analysis of symptom scores (IPSS and BPHII). When estimated on the IPSS scale, an improvement of –8.0 points (95% CI, –8.8 to –7.2) was estimated at 12-mo follow-up. The mechanical improvement resulting from superolateral traction of the lateral prostatic lobes provided by the PUL procedure is estimated to be more effective than medical therapies and placebo, which both improve IPSS at 12 mo by 3.5–7.5 points [1]. Alternative minimally invasive therapies, including TUNA and TUMT, produce similar improvements in IPSS of 9.3–12.4 points at 12-mo follow-up when compared with the PUL procedure [10,32]. Both TURP and PVP have been shown to produce excellent improvements in IPSS at 12 mo of up to 14.9 points [10,33,34] but have operation-associated morbidity and inpatient hospital costs. Compared with TURP and PVP, PUL is minimally invasive without a requirement of general anaesthesia and with potentially shorter operative time, which may provide cost benefits, although these have not been assessed to date. Furthermore, the long-term durability of PUL in improving IPSS is uncertain in the published literature, with maintained outcomes reported at 24-mo follow-up in a single study [30].

Functional benefits of PUL were also observed in the pooled estimates, specifically, improvements of up to 3.80 ml/s in Q_{max} during 1 mo and 12 mo in three studies; however, this analysis of the early outcomes of the PUL procedure demonstrated heterogeneity for Q_{max} outcomes. Consequently, the values obtained are not suitable for direct comparison with alternative therapies, and the resulting improvements in Q_{max} should be considered with caution. The functional improvements observed in the current meta-analysis appear noninferior when compared with current

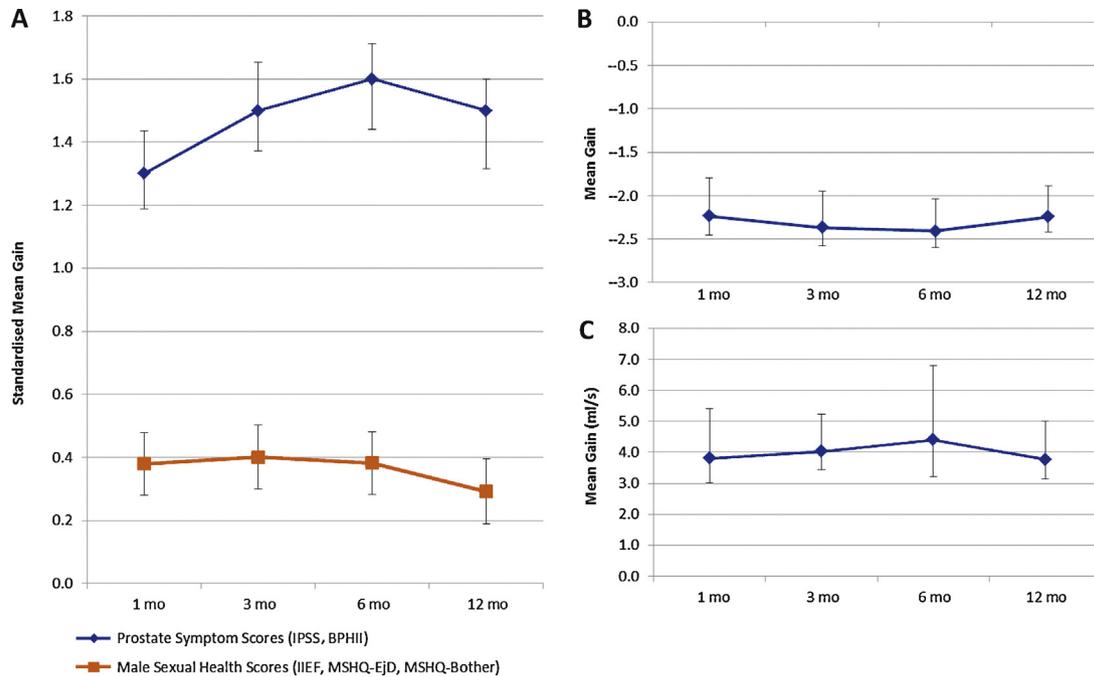


Fig. 2 – Pooled estimates (with 95% confidence intervals) following quality-effects meta-analysis at follow-up periods (1, 3, 6, and 12 mo): (A) symptom and sexual health outcomes (pooled benefit estimates as standardised mean gain); (B) quality of life scales (pooled estimate as mean gain); (C) maximum flow rate (pooled estimate as mean gain in millilitres per second). BPHII = Benign Prostatic Hyperplasia Impact Index; EjD = ejaculatory dysfunction; IIEF = International Index of Erectile Function; IPSS = International Prostate Symptom Score; MSHQ = Male Sexual Health Questionnaire.

medical [1,35] and minimally invasive [36–38] therapies. Functional improvements following PUL are fewer than those following surgical interventions including TURP and PVP, which are associated with an improved Q_{max} of between 10 and 13 ml/s [33,34,39,40] at 12-mo follow-up. Significant heterogeneity retards the comparison of PVR estimates, for which benefits were also observed following sham procedures (with associated cystoscopy), presumably as result of urethral dilation resulting from both approaches. Current evidence suggests that the currently described PUL procedure requires alteration to improve functional performance for equivalence with surgical interventions.

Sexual health outcomes in the current meta-analysis included five cohorts reporting IIEF, MSHQ-EjD, and MSHQ-Bother in patients undergoing PUL. Pooled estimates of overall sexual function scores suggested a consistently small improvement [41] throughout follow-up (Table 3) that is favourable compared with medical and surgical alternatives. Because LUTS is well established as an independent risk factor for sexual dysfunction [42–44], precipitation or exacerbation of sexual dysfunction commonly complicates medical and surgical treatment. Impact on sexual function following medical therapies (α 1-blockers, 5 α -reductase inhibitors) has been reported inconsistently but generally is considered to be due to loss of libido with erectile and ejaculatory dysfunction [25,35,45–48]. Minimally invasive therapies, including TUMT and TUNA, are characterised by increased risk of erectile dysfunction (0–18.2%) and retrograde ejaculation (9.2–22.2%) [49,50]. More invasive options,

including TURP or PVP, are associated with high rates of erectile dysfunction (14–26%) and ejaculatory dysfunction (15–63%) [10,50,51]. The causative mechanism for these side effects is unclear, with hypotheses including diathermy-induced autonomic nerve injury and injury to the bladder neck or musculus ejaculatorius [10,11,52,53]. Regardless of the hypothesis, these vital structures are prone to functional compromise following treatment with ablative modalities. Improved sexual function following the preservation of native prostatic tissue achieved with the PUL technique is a key benefit of this minimally invasive treatment alternative for LUTS secondary to BPH.

PUL is a novel, minimally invasive treatment modality for LUTS secondary to BPH. The targeted mechanism on the lateral lobes leaves the median lobe relatively unchanged following the implantation of this device. Intuitively, patients with obstructing median lobes may receive limited therapeutic benefit. To date, all prospective trials are characterised by the exclusion of patients with obstructing median lobes. As such, the effect in such patients has not been studied and is largely unknown. Similarly, other variables including high prostate volumes and long prostatic urethral length may limit the benefit obtained. Such variables have not been assessed in the current literature and represent the scope for further research. The use of PUL in patients with elevated PSA has been addressed, with many studies outlining a preoperative PSA >10 ng/ml as a relative exclusion criteria for the PUL procedure [13,24,25,30]; however, several studies subsequently include these patients following normal prostatic biopsy and report relative safety.

Table 4 – Pooled estimates of outcome measures following the prostatic urethral lift procedure

	1 mo	3 mo	6 mo	12 mo
Prostate symptom scores (IPSS, BPHII)				
No. of data sources, response sample size (<i>n</i>)	9 (1298)	6 (1050)	6 (1022)	6 (888)
Effect size (95% CI)	−1.30 (−1.4 to −1.2)	−1.50 (−1.7 to −1.4)	−1.6 (−1.7 to −1.3)	−1.5 (−1.6 to −1.3)
Heterogeneity (τ^2)	0.1	0.1	0.00	0.00
Male sexual health scores (IIEF, MSHQ-EjD, MSHQ-Bother)				
No. of data sources, response sample size (<i>n</i>)	13 (1042)	9 (889)	9 (908)	9 (786)
Effect size (95% CI)	0.4 (0.3–0.5)	0.4 (0.3–0.5)	0.4 (0.3–0.5)	0.3 (0.2–0.4)
Heterogeneity (τ^2)	0.00	0.00	0.00	0.00
Health-related quality of life				
No. of data sources, response sample size (<i>n</i>)	4 (628)	3 (508)	3 (496)	3 (452)
Effect size (95% CI)	−2.2 (−2.5 to −2.0)	−2.4 (−2.6 to −2.2)	−2.4 (−2.6 to −2.2)	−2.2 (−2.4 to −2.1)
Heterogeneity (τ^2)	0.2	0.1	0.1	0.00
Maximum flow rate				
No. of data sources, response sample size (<i>n</i>)	3 (242)	3 (488)	1* (106)	3 (362)
Effect size (95% CI)	3.8 (3.0–4.6)	4.0 (3.4–4.6)	4.4 (3.2–5.6)	3.8 (3.1–4.4)
Heterogeneity (τ^2)	0.4	0.03	NA	0.2
Postvoid residual				
No. of data sources, response sample size (<i>n</i>)	2 (128)	2 (396)	1* (122)	2 (350)
Effect size (95% CI)	15.5 (12.6–18.6)	−6.2 (−10.1 to −2.8)	−11 (−13 to −9)	−4.0 (−10.5 to 2.6)
Heterogeneity (τ^2)	1732	24	NA	219

BPHII = Benign Prostatic Hyperplasia Impact Index; CI = confidence interval; EjD = ejaculatory dysfunction; IIEF = International Index of Erectile Function; IPSS = International Prostate Symptom Score; MSHQ = Male Sexual Health Questionnaire.
* Individual study data reported, no meta-analysis performed.

Further prostatic intervention following implementation of the PUL implants has been considered to the extent possible in the available literature. Published series' report extrusion into the bladder lumen and subsequent encrustation of bladder neck implants, a vast majority of which were asymptomatic and managed conservatively. At 24-mo follow-up, only one series documented the removal of implants in the context of significant encrustation. Progression to TURP or PVP following the PUL procedure was reported, outlining the ability of the resectoscope to instantaneously melt the monofilament implants without problems [4,30]. The presence of implants was reported to have no influence on surgical routine during TURP or PVP. No publication to date has reported outcomes following investigation or management of a subsequent diagnosis of prostate cancer, including prostatic biopsy, brachytherapy, or prostatectomy after the PUL procedure.

As with any therapeutic intervention, benefits secondary to placebo may confound results. To date, a sole multicentre randomised controlled trial for the PUL procedure has been published [24,25]. The aforementioned study performed a sham procedure during cystoscopy, which allowed the postoperative physiologic changes associated with cystoscopic dilation of the urinary tract to be differentiated from the PUL. The resulting symptom scores and functional measures following PUL were superior within 3 mo postoperatively [24]. Sexual function and satisfaction scores improved following PUL but did not differ significantly within 3 mo from the placebo-control cohort [25]. An inability to maintain long-term benefits may be due to cystoscopic dilation as well as to the placebo effect. Study participants were blinded until 3 mo postoperatively and then subsequently offered PUL, with these results reported as a crossover-type analysis [26]. It is clear that further

research is required with prolonged follow-up of placebo-control and study participants over the prior 6 mo and with more participants.

The ultimate place of PUL in the management of BPH has yet to be determined. The ability of this technique to provide symptom benefits following a single short procedure, without the risk of retrograde ejaculation, positions it as a potential alternative to both medical and more invasive surgical procedures for which this side effect is more prominent. Currently it would seem to have a justifiable role in the management of men with moderate BPH (prostate volume <80 g) for whom the potential for this side effect as a consequence of treatment would either reduce their quality of life or lead them to defer intervention even at the risk of more significant complications. Longer term evaluation (>3 yr of data) of durability and symptomatic improvement produced by PUL will play a key role in determining its ultimate place in the management of BPH.

The present meta-analysis has several limitations. Limited published reports examining this procedure required that all studies, of varying quality, be included in the meta-analysis. As such, the inherent high risk of bias was adjusted for use of quality scoring of individual studies, which was statistically incorporated into the quality effects pooled estimates. Further limitations owe to the naïve standing of the PUL procedure for treatment of LUTS secondary to BPH because this allowed meta-analysis of effect sizes only at 12-mo follow-up. Thus, the long-term durability of this device cannot be commented on appropriately. In light of these limitations of the studies and the respective results assessed with appropriate adjustment, a high degree of heterogeneity was obtained. This was particularly evident in pooled analysis of overall symptoms and sexual function. Furthermore, publication bias and favourable reporting owing to

commercial interests with the current method of PUL cannot be discounted.

4. Conclusion

We identified five independent series evaluating the symptomatic, sexual, and functional outcomes following PUL. Our results suggest that this procedure is associated with minimal perioperative morbidity, whereas meta-analysis estimates suggest improvements in symptomatic and functional outcomes that are durable through 12-month follow-up. Preservation of the bladder neck and subsequent control of sexual function following PUL provide stark contrast to the medical and surgical alternatives for treatment of BPH. Further comparative trials with longer follow-up periods and cost–benefit analyses are required to guide clinicians as to the suitability of PUL in routine clinical practice.

Author contributions: Damien Bolton had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Perera, Roberts, Doi.

Acquisition of data: Perera, Roberts.

Analysis and interpretation of data: Roberts, Doi.

Drafting of the manuscript: Perera, Roberts, Bolton.

Critical revision of the manuscript for important intellectual content: Doi, Bolton.

Statistical analysis: Roberts, Doi.

Obtaining funding: None.

Administrative, technical, or material support: None.

Supervision: Bolton.

Other (specify): None.

Financial disclosures: Damien Bolton certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: M.J.R. is supported by a Doctor in Training Research Scholarship from Avant Mutual Group Ltd., Cancer Council Queensland PhD Scholarship and Professor William Burnett Research Fellowship from the Discipline of Surgery, School of Medicine, The University of Queensland.

Funding/Support and role of the sponsor: None.

Acknowledgment statement: The authors are grateful to Professor RA “Frank” Gardiner (University of Queensland; Royal Brisbane and Women’s Hospital, Australia) for critical revisions of the manuscript.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.eururo.2014.10.031>.

References

- [1] Roehrborn CG. Current medical therapies for men with lower urinary tract symptoms and benign prostatic hyperplasia: achievements and limitations. *Rev Urol* 2008;10:14–25.
- [2] Nordling J. Efficacy and safety of two doses (10 and 15 mg) of alfuzosin or tamsulosin (0.4 mg) once daily for treating symptomatic benign prostatic hyperplasia. *BJU Int* 2005;95:1006–12.
- [3] Rom M, Schatzl G, Swietek N, Rucklinger E, Kratzik C. Lower urinary tract symptoms and depression. *BJU Int* 2012;110:E918–21.
- [4] Woo HH, Chin PT, McNicholas TA, et al. Safety and feasibility of the prostatic urethral lift: a novel, minimally invasive treatment for lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH). *BJU Int* 2011;108:82–8.
- [5] Speakman M, Kirby R, Doyle S, Ioannou C. Burden of male lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) - focus on the UK. *BJU Int*. In press. <http://dx.doi.org/10.1111/bju.12745>
- [6] Cornu J-N, Cussenot O, Haab F, Lukacs B. A widespread population study of actual medical management of lower urinary tract symptoms related to benign prostatic hyperplasia across Europe and beyond official clinical guidelines. *Eur Urol* 2010;58:450–6.
- [7] Verhamme KM, Dieleman JP, Bleumink GS, Bosch JL, Stricker BH, Sturkenboom MC. Treatment strategies, patterns of drug use and treatment discontinuation in men with LUTS suggestive of benign prostatic hyperplasia: the Triumph project. *Eur Urol* 2003;44:539–45.
- [8] Oelke M, Bachmann A, Descazeaud A, et al. EAU guidelines on the treatment and follow-up of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. *Eur Urol* 2013;64:118–40.
- [9] Rassweiler J, Teber D, Kuntz R, Hofmann R. Complications of transurethral resection of the prostate (TURP)—incidence, management, and prevention. *Eur Urol* 2006;50:969–80, discussion 980.
- [10] McVary KT, Roehrborn CG, Avins AL, et al. Update on AUA guideline on the management of benign prostatic hyperplasia. *J Urol* 2011;185:1793–803.
- [11] Ahyai SA, Gilling P, Kaplan SA, et al. Meta-analysis of functional outcomes and complications following transurethral procedures for lower urinary tract symptoms resulting from benign prostatic enlargement. *Eur Urol* 2010;58:384–97.
- [12] Barkin J, Giddens J, Incze P, Casey R, Richardson S, Gange S. UroLift system for relief of prostate obstruction under local anesthesia. *Can J Urol* 2012;19:6217–22.
- [13] McNicholas TA, Woo HH, Chin PT, et al. Minimally invasive prostatic urethral lift: surgical technique and multinational experience. *Eur Urol* 2013;64:292–9.
- [14] Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;339:b2700.
- [15] Higgins JP, Green S, editors. *Cochrane handbook for systematic reviews of interventions*. Hoboken, NJ: Wiley-Blackwell; 2008.
- [16] Higgins JP, Altman DG, Sterne JA. Assessing risk of bias in included studies. In: Higgins JP, Green S, eds. *Cochrane handbook for systematic reviews of interventions*, ed 5.1.0. Cochrane Collaboration Web site. <http://handbook.cochrane.org/>.
- [17] Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE. Interrupted time series designs in health technology assessment: lessons from two systematic reviews of behavior change strategies. *Int J Technol Assess Health Care* 2003;19:613–23.
- [18] Doi SA, Thalib L. A quality-effects model for meta-analysis. *Epidemiology* 2008;19:94–100.
- [19] Roberts MJ, Williamson DA, Hadway P, Doi SA, Gardiner RA, Paterson DL. Baseline prevalence of antimicrobial resistance and subsequent infection following prostate biopsy using empirical or altered prophylaxis: a bias-adjusted meta-analysis. *Int J Antimicrob Agents* 2014;43:301–9.

- [20] Doi SA, Barendregt JJ, Mozkewich EL. Meta-analysis of heterogeneous clinical trials: an empirical example. *Contemp Clin Trials* 2011;32:288–98.
- [21] Lipsey M, Wilson D. *Practical meta-analysis*. Thousand Oaks, CA: Sage; 2000.
- [22] Cohen J. *Statistical power analysis for the behavioral sciences*. ed 2. London, UK: Lawrence Erlbaum Associates; 1988.
- [23] Takkouche B, Cadarso-Suarez C, Spiegelman D. Evaluation of old and new tests of heterogeneity in epidemiologic meta-analysis. *Am J Epidemiol* 1999;150:206–15.
- [24] Roehrborn CG, Gange SN, Shore ND, et al. The prostatic urethral lift for the treatment of lower urinary tract symptoms associated with prostate enlargement due to benign prostatic hyperplasia: the LIFT study. *J Urol* 2013;190:2161–7.
- [25] McVary KT, Gange SN, Shore ND, et al. Treatment of LUTS secondary to BPH while preserving sexual function: randomized controlled study of prostatic urethral lift. *J Sex Med* 2014;11:279–87.
- [26] Cantwell AL, Bogache WK, Richardson SF, et al. Multicentre prospective crossover study of the 'prostatic urethral lift' for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. *BJU Int* 2014;113:615–22.
- [27] Shore N, Freedman S, Gange S, et al. Prospective multi-center study elucidating patient experience after prostatic urethral lift. *Can J Urol* 2014;21:7094–101.
- [28] Abad PG, del Peso AC, Ojas BS, Arjona MF. Urolift®, a new minimally invasive treatment for patients with low urinary tract symptoms secondary to BPH. Preliminary results [in Spanish]. *Arch Esp Urol* 2013;66:584–91.
- [29] Woo HH, Bolton DM, Laborde E, et al. Preservation of sexual function with the prostatic urethral lift: a novel treatment for lower urinary tract symptoms secondary to benign prostatic hyperplasia. *J Sex Med* 2012;9:568–75.
- [30] Chin PT, Bolton DM, Jack G, et al. Prostatic urethral lift: two-year results after treatment for lower urinary tract symptoms secondary to benign prostatic hyperplasia. *Urology* 2012;79:5–11.
- [31] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205–13.
- [32] Lourenco T, Armstrong N, N'Dow J, et al. Systematic review and economic modelling of effectiveness and cost utility of surgical treatments for men with benign prostatic enlargement. *Health Technol Assess* 2008;12:iii, ix–x, 1–146, 169–515.
- [33] Thangasamy IA, Chalasani V, Bachmann A, Woo HH. Photoselective vaporisation of the prostate using 80-W and 120-W laser versus transurethral resection of the prostate for benign prostatic hyperplasia: a systematic review with meta-analysis from 2002 to 2012. *Eur Urol* 2012;62:315–23.
- [34] Teng J, Zhang D, Li Y, et al. Photoselective vaporization with the green light laser vs transurethral resection of the prostate for treating benign prostate hyperplasia: a systematic review and meta-analysis. *BJU Int* 2013;111:312–23.
- [35] McConnell JD, Roehrborn CG, Bautista OM, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med* 2003;349:2387–98.
- [36] Namiki K, Shiozawa H, Tsuzuki M, Mamiya Y, Matsumoto T, Miki M. Efficacy of transurethral needle ablation of the prostate for the treatment of benign prostatic hyperplasia. *Int J Urol* 1999;6:341–5.
- [37] Ohigashi T, Nakamura K, Nakashima J, Baba S, Murai M. Long-term results of three different minimally invasive therapies for lower urinary tract symptoms due to benign prostatic hyperplasia: comparison at a single institute. *Int J Urol* 2007;14:326–30.
- [38] Lim YW, Tay KJ, Ho HSS. The minimally invasive treatments for benign prostatic hyperplasia. *Proc Singapore Healthcare* 2014;23:65–73.
- [39] Bouchier-Hayes DM, Van Appledorn S, Bugeja P, Crowe H, Challacombe B, Costello AJ. A randomized trial of photoselective vaporization of the prostate using the 80-W potassium-titanyl-phosphate laser vs transurethral prostatectomy, with a 1-year follow-up. *BJU Int* 2010;105:964–9.
- [40] Lukacs B, Loeffler J, Bruyère F, et al. Photoselective vaporization of the prostate with GreenLight 120-W laser compared with monopolar transurethral resection of the prostate: a multicenter randomized controlled trial. *Eur Urol* 2012;61:1165–73.
- [41] Takeshima N, Sozu T, Tajika A, Ogawa Y, Hayasaka Y, Furukawa TA. Which is more generalizable, powerful and interpretable in meta-analyses, mean difference or standardized mean difference? *BMC Med Res Methodol* 2014;14:30.
- [42] McVary K. Lower urinary tract symptoms and sexual dysfunction: epidemiology and pathophysiology. *BJU Int* 2006;97(Suppl 2):23–8, discussion 44–5.
- [43] Laumann EO, Paik A, Glasser DB, et al. A cross-national study of subjective sexual well-being among older women and men: findings from the Global Study of Sexual Attitudes and Behaviors. *Arch Sex Behav* 2006;35:145–61.
- [44] Rosen R, Altwein J, Boyle P, et al. Lower urinary tract symptoms and male sexual dysfunction: the Multinational Survey of the Aging Male (MSAM-7). *Eur Urol* 2003;44:637–49.
- [45] Wilt TJ, Mac Donald R, Rutks I. Tamsulosin for benign prostatic hyperplasia. *Cochrane Database Syst Rev* 2003;CD002081.
- [46] Rosen RC, Fitzpatrick JM. Ejaculatory dysfunction in men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia. *BJU Int* 2009;104:974–83.
- [47] van Dijk MM, de la Rosette JJ, Michel MC. Effects of alpha(1)-adrenoceptor antagonists on male sexual function. *Drugs* 2006;66:287–301.
- [48] Shelbaia A, Elsaied WM, Elghamrawy H, Abdullah A, Salaheldin M. Effect of selective alpha-blocker tamsulosin on erectile function in patients with lower urinary tract symptoms due to benign prostatic hyperplasia. *Urology* 2013;82:130–5.
- [49] Hoffman RM, Monga M, Elliott SP, et al. Microwave thermotherapy for benign prostatic hyperplasia. *Cochrane Database Syst Rev* 2012;CD004135.
- [50] Friebe RW, Lin HC, Hinh PP, Berardinelli F, Canfield SE, Wang R. The impact of minimally invasive surgeries for the treatment of symptomatic benign prostatic hyperplasia on male sexual function: a systematic review. *Asian J Androl* 2010;12:500–8.
- [51] Hoffman RM, MacDonald R, Wilt TJ. Laser prostatectomy for benign prostatic obstruction. *Cochrane Database Syst Rev* 2004;CD001987.
- [52] Martin DJ, Mulhall JP. Enlarging the scope of managing benign prostatic hyperplasia: addressing sexual function and quality of life. *Int J Clin Pract* 2005;59:579–90.
- [53] Alloussi SH, Lang C, Eichel R, Alloussi S. Ejaculation-preserving transurethral resection of prostate and bladder neck: short- and long-term results of a new innovative resection technique. *J Endourol* 2014;28:84–9.