

RESEARCH ARTICLE

Efficacy and Safety of Laser Surgery and Transurethral Resection of the Prostate for Treating Benign Prostate Hyperplasia: a Network Meta-analysis

Li Wang, Qiu-Yan Yu, Yan Liu, Zhen-Li Zhu, Yuan-Wei Huang, Ke Li*

Abstract

Background: Traditional meta-analyses or systematic reviews of randomized controlled trials (RCTs) have been used to compare laser surgeries and transurethral resection of the prostate (TURP) for benign prostate hyperplasia (BPH), but they cannot provide a hierarchy regarding efficacy and safety of treatment. **Objective:** We therefore performed a network meta-analysis (NMA) to compare and create hierarchies for efficacy and safety of TURP and laser surgeries for BPH. **Materials and Methods:** We searched for reports of RCTs published up to April 25, 2015. After methodological quality assessment and data extraction, we performed an NMA to compare TURP and laser surgeries for BPH. **Results:** We ranked the treatments of TURP and laser surgeries for BPH. For IPSS at 6 months, holmium laser resection of the prostate (HoLRP) ranked the first-best and at 12 months, holmium laser enucleation of the prostate (HoLEP). For Qmax at 6 and 12 months, HoLEP ranked the first-best; for operative time it was TURP; for catheter removal time, diode laser enucleation of the prostate (DiLEP) ranked the first-best. **Conclusions:** Although TURP is considered the gold standard for treating BPH, it is not better in terms of efficacy and safety compared with the laser surgery. Our NMA created hierarchies for the 9 types of surgery in terms of efficacy and safety, which should help clinicians choose the best approach for the individual patient.

Keywords: TURP - BPH - laser surgery - meta-analysis

Asian Pac J Cancer Prev, 17 (9), 4281-4288

Introduction

Benign prostatic hyperplasia (BPH), one of the most common and serious diseases affecting men, is considered the main reason for urinary tract symptoms. The disease affects about 50% men by the age of 60 years and 90% by the age of 85 (Roberts et al., 1998; Roehrborn et al., 2000). Various surgical treatments for treatment include transurethral resection of the prostate (TURP), open prostatectomy, holmium laser enucleation of the prostate (HoLEP), and photoselective vaporization of prostate (PVP). Although TURP is considered the gold standard treatment for BPH, the procedure has some limitations. Several studies (Oesterling, 1995; Shingleton et al., 1999; Lertakyamanee et al., 2002; Mebust et al., 2002; Committee, 2003; Rassweiler et al., 2006) reported complications following TURP, including transfusions, infections, urethral stricture, sexual dysfunction, urinary incontinence, urinary retention, clot retention and TUR syndrome.

Other treatments, such as laser prostatectomy, including photoselective vaporization of prostate (PVP); thulium laser enucleation of the prostate (ThuLEP) and

thulium laser resection of the prostate (TmLRP); HoLEP, holmium laser resection of the prostate (HoLRP) and holmium laser ablation of the prostate (HoLAP); and diode laser enucleation of the prostate (DiLEP) and diode laser vaporisation of the prostate (DiLVP), have emerged as treatment. As compared with TURP, HoLEP has less blood transfusion rate, shorter catheterization duration time and hospital stay (Li et al., 2014), and PVP is less likely to have postoperative complications of blood transfusion and clot retention (Thangasamy et al., 2012).

Traditional meta-analyses or systematic reviews based on randomized controlled trials (RCTs) of laser surgeries and TURP for BPH cannot provide a hierarchy of the efficacy and safety of treatment. We performed a network meta-analysis (NMA) to evaluate and create hierarchies for the efficacy and safety of laser surgery and TURP for BPH.

Materials and Methods

Studies were eligible for inclusion

We included reports of RCTs that involved TURP and PVP, HoLEP, ThuLEP, TmLRP, HoLRP, HoLAP,

DiLEP, or DiLVP as the intervention and control arms, respectively, and reported the efficacy, safety or perioperative outcomes international prostate symptom score (IPSS), maximum flow rate (Qmax) (ml/s), quality of life (QoL), postvoid residual volume (PVR) (ml), blood transfusion, urethral stricture, TUR syndrome, bladder neck contracture, reoperation, urinary tract infection (UTI), acute urinary retention (AUR), operating time (min), catheterization time (day), or hospital stay (day).

Search strategy

We searched MEDLINE via PubMed for reports of RCTs published in English up to April 15, 2015. The search algorithm was (“Prostatic Hyperplasia/surgery”[Mesh] AND (“lasers”[MeSH Terms] OR “lasers”[All Fields] OR “laser”[All Fields])) OR (“Prostatic Hyperplasia/surgery”[Mesh] AND “Transurethral Resection of Prostate”[Mesh]) AND Clinical Trial[ptyp]. We also searched ClinicalTrials.gov and reference lists of previous systematic reviews or meta-analyses (Ahyia et al., 2010; Mamoulakis et al., 2010; Thangasamy et al., 2012). We included published and unpublished reports of RCTs and excluded many from China to avoid systematic bias because many of these studies do not use an appropriate randomization procedure (13). Five reviewers (LW, QY, YL, ZZ and YH) independently assessed the titles and abstracts of the articles to determine inclusion.

Any discrepancies were resolved by consulting a sixth researcher (KL).

Data extraction and quality assessment

The data were extracted independently by the 5 reviewers; disagreements were resolved by discussion. We used the Cochrane Collaboration tool 17 to assess the quality of reports, including sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting of outcomes and other possible sources of bias. Two reviewers (LW, QY) independently performed the quality assessment. For every comparison of TURP and/or laser surgical treatments (PVP, HoLEP, ThuLEP, TmLRP, HoLRP, HoLAP, DiLEP, DiLVP), the standardized mean difference Hedges’s adjusted g (SMD) was calculated as the relative effect size for continuous outcomes and the odds ratio (OR) for binary outcomes.

Outcome measures

Primary outcomes were Qmax and IPSS at 6 and 12 months. Secondary outcomes were operative time, hospital time, catheter removal time and complications such as urethral stricture.

Statistical analysis

Bayesian-framework, network/multi-treatment meta-analysis integrates direct and indirect effects for all relative

Table 1. Baseline characteristics of the studies included

Study	Surgery types	No. of studies	Age(year)	IPSS		Qmax	Laser types
				T1/T2	T1/T2		
Ehab A.Elzayat et al.	HoLAP/PVP	57/52	72.7/71.6	20/18.4	6.7/6.4	6.7/6.4	Ho:YAG/Green Light
Ahmed M.Elshal et al.	HoLEP/PVP	50/53	71/74.1	22.4/23	7.5/8	7.5/8	Ho:YAG/Green Light
Hazem Elmansy et al.	HoLEP/PVP	43/37	71.5/73.2	22.4/21.8	8.1/8.9	8.1/8.9	Ho:YAG/Green Light
Fengbo Zhang et al.	ThuLEP/HoLEP	71/62	76.2/73.4	24.6/22.8	6.8/7.3	6.8/7.3	Tm:YAG/Ho:YAG
Po Hui Chiang et al.	PVP/DiLVP	84/55	69.1/72.7	21.6/20.1	4.3/5.5	4.3/5.5	Green Light/Diode Laser
Stephen S.Yang et al.	DiLEP/TURP	74/52	70.7/71	na	na/na	na/na	Diode Laser/-
Mohammad Reza Razzaghi et al.	DiLVP/TURP	50/52	68.5/68.2	23.6/24.6	6.8/6.3	6.8/6.3	Diode Laser/-
A.H.H.TAN et al.	TURP/HoLEP	30/31	70.3/71.7	23.7/26	8.3/8.4	8.3/8.4	-/Ho:YAG
FRANCESCO MONTORSI et al.	TURP/HoLEP	48/52	64.5/65.1	21.9/21.6	7.8/8.2	7.8/8.2	-/Ho:YAG
ANDRE WESTENBERG et al.	TURP/HoLEP	59/61	66.8/66.9	23/21.9	9.1/8.9	9.1/8.9	-/Ho:YAG
RAINER M.KUNTZ et al.	TURP/HoLEP	100/100	68.7/68	22.1/21.4	5.9/4.9	5.9/4.9	-/Ho:YAG
R.M.Mavuduru et al.	TURP/HoLEP	15/15	66.46/69.86	21.4/22.53	6.9/5.79	6.9/5.79	-/Ho:YAG
Nao Sun et al.	TURP/HoLEP	82/82	71.91/72.16	24.55/24.4	5.69/5.28	5.69/5.28	-/Ho:YAG
PETER J.GILLING et al.	TURP/HoLRP	59/61	66.8/66.9	23/21.9	9.1/8.9	9.1/8.9	-/Ho:YAG
Alexander Bachmann et al.	TURP/PVP	142/139	65.4/65.9	21.7/21.2	9.9/9.5	9.9/9.5	-/Green Light
Boxin Xue et al.	TURP/PVP	100/100	71/72.1	23.2/23	8.2/8	8.2/8	-/Green Light
Carlos Capitan et al.	TURP/PVP	50/50	67.7/69.8	23.52/23.75	8.68/8.03	8.68/8.03	-/Green Light
Bogdan Geavlete et al.	TURP/PVP	80/75	na/na	24.4/24.2	6.3/6.2	6.3/6.2	-/Green Light
Abdulla Al et al.	TURP/PVP	60/60	67.1/66.3	27.9/27.2	6.4/6.9	6.4/6.9	-/Green Light
David M.Bouchier et al.	TURP/PVP	59/60	66.36/65.06	25.41/25.28	5.08/4.74	5.08/4.74	-/Green Light
Kaya Horasanll et al.	TURP/PVP	37/39	68.3/69.2	20.2/18.9	9.2/8.6	9.2/8.6	-/Green Light
Volkan Tugcu et al.	TURP/PVP	98/112	66.3/67.5	17.7/17.7	7.2/6.9	7.2/6.9	-/Green Light
DAVID M. BOUCHIER et al.	TURP/PVP	38/38	66.23/65.23	na/na	na/na	na/na	-/Green Light
W. BRUCE SHINGLETON et al.	TURP/PVP	50/50	67.4/68.2	21/22	6.9/8	6.9/8	-/Green Light
Shu-Jie Xia et al.	TURP/TmLRP	48/52	69.3/68.9	20.8/21.9	8.3/8	8.3/8	-/Tm:YAG
Di Cui et al.	TURP/TmLRP	49/47	70.4/67.8	20.2/21.1	8.4/8.62	8.4/8.62	-/Tm:YAG
Hao Yan et al.	TURP/TmLRP	40/40	74.5/72.5	22.6/21.7	7.8/7.5	7.8/7.5	-/Tm:YAG

Abbreviations: IPSS, international prostate symptom score; Qmax, maximum urinary flow rate; TURP, transurethral resection of the prostate; PVP, photoselective vaporisation of the prostate; HoLEP, holmium laser enucleation of the prostate; HoLAP, holmium laser ablation of the prostate; HoLRP, holmium laser resection of the prostate; TmLRP, thulium laser resection of the prostate; ThuLEP, thulium laser enucleation of the prostate; DiLEP, diode laser enucleation of the prostate; DiLVP, diode laser vaporisation of the prostate; na, not available; -, no parameter; T1, the first group; T2, the second group

treatments and provides estimates with maximum power (HIGGINS and Whitehead, 1996; Lu and Ades, 2004; Jansen et al., 2008; Salanti et al., 2008). Our NMA with

a Bayesian-framework to compare TURP with other laser treatments for BPH allowed for the integration of direct and indirect comparisons. We used forest plots to investigate statistical heterogeneity by the I² statistic (Higgins and JPT, 2008) with I² <25% considered low heterogeneity and >50% high heterogeneity (Schmid et al., 2013). We calculated probability of events with ORs and 95% confidence intervals (95% CIs) for binary outcomes and SMD and 95% CIs for continuous outcomes. Inconsistency was defined as the difference between direct and indirect evidence with 95% CI excluding 0; we checked for inconsistency with a triangular loop graph (Higgins et al., 2012). We calculated the probability of each surgical procedure being the best treatment and ranked treatments (Lu and Ades, 2004; Ades et al., 2006). Analyses involved use of Review Manager 5.3 (quality assessment of RCTs), STATA 12.0 (pairwise meta-analysis and I² calculations), R 3.0.3 (estimation of inconsistency between direct and indirect evidence, ranking treatments), and WinBUGS 1.4.3 (NMA models) (Salanti et al., 2011).

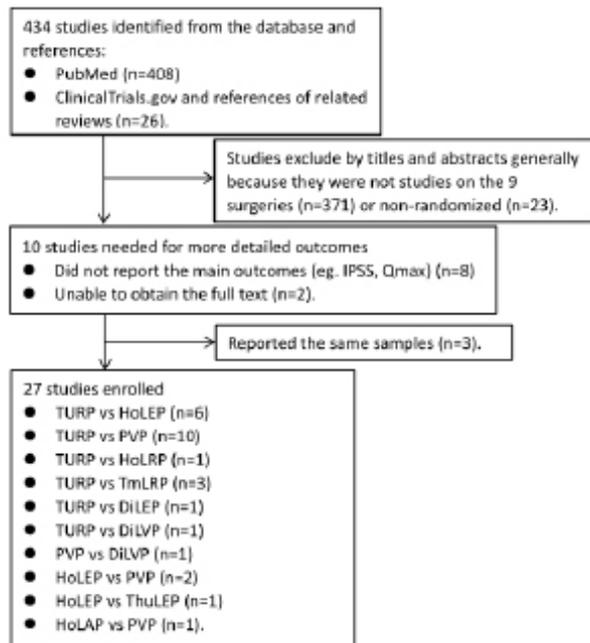


Figure 1. Flow Diagram of Screening Randomized Controlled Trials

Results

After screening, 27 reports of RCTs (Gilling et al., 1999; Shingleton et al., 1999; Tan et al., 2003; Kuntz et al., 2004; Montorsi et al., 2004; Westenberg et al., 2004; Bouchier-Hayes et al., 2006; Horasanli et al.,

Table 2. Heterogeneity between Studies

Variables	Comparisons	No. of studies	Heterogeneity
OT	TURP VS. PVP	5	$\chi^2=0.15, P=0.004, I^2=74.3\%$
	TURP VS. HoLEP	4	$\chi^2=9.60, P=0.022, I^2=68.7\%$
	PVP VS. HoLEP	2	$\chi^2=1.72, P=0.190, I^2=41.9\%$
	TURP VS. TmLRP	2	$\chi^2=3.53, P=0.060, I^2=71.6\%$
CT	TURP VS. PVP	7	$\chi^2=9.34, P=0.155, I^2=35.8\%$
	TURP VS. HoLEP	5	$\chi^2=17.85, P=0.001, I^2=77.6\%$
	TURP VS. HoLRP	2	$\chi^2=0.00, P=0.975, I^2=0.0\%$
	PVP VS. HoLEP	2	$\chi^2=0.42, P=0.516, I^2=0.0\%$
HT	TURP VS. PVP	7	$\chi^2=29.72, P=0.000, I^2=79.8\%$
	TURP VS. HoLEP	4	$\chi^2=10.77, P=0.013, I^2=72.1\%$
US	TURP VS. PVP	7	$\chi^2=6.06, P=0.416, I^2=1.0\%$
	TURP VS. HoLEP	5	$\chi^2=2.91, P=0.573, I^2=0.0\%$
	TURP VS. TmLRP	3	$\chi^2=0.51, P=0.776, I^2=0.0\%$
Qmax at 6 months	TURP VS. PVP	5	$\chi^2=14.70, P=0.005, I^2=72.8\%$
	TURP VS. HoLEP	4	$\chi^2=14.00, P=0.003, I^2=78.6\%$
Qmax at 12 months	TURP VS. PVP	3	$\chi^2=1.03, P=0.599, I^2=0.0\%$
	TURP VS. HoLEP	5	$\chi^2=17.62, P=0.001, I^2=77.3\%$
	TURP VS. TmLRP	2	$\chi^2=0.00, P=0.994, I^2=0.0\%$
IPSS at 6 months	TURP VS. PVP	4	$\chi^2=10.35, P=0.016, I^2=71.0\%$
	TURP VS. HoLEP	4	$\chi^2=13.74, P=0.003, I^2=78.2\%$
IPSS at 12 months	TURP VS. PVP	2	$\chi^2=0.37, P=0.541, I^2=0.0\%$
	TURP VS. HoLEP	5	$\chi^2=14.68, P=0.005, I^2=72.8\%$
	TURP VS. TmLRP	2	$\chi^2=0.00, P=0.944, I^2=0.0\%$

Abbreviations: CT, catheter removal time; HT, hospital time; IPSS, international prostate symptom score; OT, operative time; Qmax, maximum urinary flow rate; TURP, transurethral resection of the prostate; PVP, photoselective vaporisation of the prostate; HoLEP, holmium laser enucleation of the prostate; TmLRP, thulium laser resection of the prostate; US, urethral stricture

Table 3. Efficacy (IPSS and Qmax at 6 months) of All the Surgeries (SMD with 95% CI)

TURP	-1.27 (-3.52,0.78)	-0.33 (-2.48,1.77)	-0.17 (-4.94,4.36)	1.29 (-3.41,6.53)	-3.19 (-8.49,2.43)	0.01 (-3.35,3.61)
1.22 (-1.24,4.13)	PVP	0.94 (-1.90,3.42)	1.1 (-3.46,6.40)	2.56 (-2.62,7.77)	-1.93 (-7.22,3.74)	1.28 (-2.19,5.18)
-2.4 (-5.01,0.58)	-3.61 (-7.06,-0.12)	HoLEP	0.16 (-4.69,4.80)	1.62 (-3.50,7.24)	-2.87 (-8.73,2.53)	0.34 (-3.63,4.29)
-1.22 (-7.82,5.57)	-2.43 (-9.61,4.78)	1.18 (3.65,8.34)	HoLRP	1.46 (-5.06,8.21)	-3.03 (-10.06,4.20)	0.18 (-5.44,5.69)
-1.65 (-8.06,4.52)	-2.86 (-9.76,3.64)	0.75 (-5.99,7.47)	-0.43 (-9.55,8.34)	TmLRP	-4.49 (-11.87,2.47)	-1.28 (-7.22,4.64)
3.34 (-3.03,10.47)	2.13 (-4.08,8.66)	5.74 (-1.72,12.99)	4.56 (-4.45,14.80)	4.99 (-4.27,14.45)	HoLAP	3.21 (-2.96,9.47)
2.23 (-2.19,6.72)	1.02 (-3.53,5.30)	4.63 (-0.48,9.79)	3.45 (-4.55,11.14)	3.88 (-3.81,11.90)	-1.11 (-9.06,6.68)	DiLVP

Table 4. Efficacy (IPSS and Qmax at 12 months) of All the Surgeries (SMD with 95% CI)

TURP	0.2436 (-1.21,1.91)	1.09 (-0.07,2.23)	0.44 (-1.81,2.59)	0.07 (-2.99,3.28)	2.23 (-1.71,5.78)	-0.54 (-2.76,1.75)
0.62 (-0.81,2.67)	PVP	0.85 (-0.99,2.45)	0.20 (-2.58,2.75)	-0.18 (-3.84,3.27)	1.99 (-1.58,5.06)	-0.79 (-2.86,1.09)
-2.4721 (-3.84,-1.05)	-3.09 (-5.46,-1.23)	HoLEP	-0.65 (-3.31,1.69)	-1.02 (-4.41,2.41)	1.14 (-2.74,4.86)	-1.63 (-4.02,0.79)
0.09 (-2.27,2.30)	-0.54 (-3.60,2.16)	2.56 (-0.18,5.17)	HoLRP	-0.38 (-4.27,3.49)	1.79 (-2.70,5.85)	-0.99 (-3.81,2.02)
-4.88 (-9.16,-0.33)	-5.5 (-10.47,-0.80)	-2.4 (-6.85,2.30)	-4.96 (-10.14,0.48)	TmLRP	2.16 (-2.97,6.91)	-0.61 (-4.35,3.19)
1.8 (-2.67,6.44)	1.18 (-3.06,5.37)	4.27 (-0.30,9.14)	1.72 (-3.37,7.14)	6.68 (0.85,13.12)	HoLAP	-2.77 (-14.97,44.97)
2.73 (0.49,4.98)	2.11 (-0.83,4.38)	5.2 (2.44,7.64)	2.64 (-0.52,5.92)	7.6 (2.42,12.70)	0.93 (-3.94,5.71)	DiLVP

Table 5. Safety (Urethral stricture(RR with 95% CI)) and Efficacy (Length of hospital stay (SMD with 95% CI) of All the Surgeries

TURP	0.48 (0.12,1.13)	0.93 (0.21,2.61)	0.51 (0.02,2.12)	3.77 (0.07,10.09)	0.39 (0.00,2.43)	0.87 (0.02,4.56)
1.77 (1.13,2.41)	PVP	2.82 (0.36,11.34)	1.52 (0.04,8.55)	21.84 (0.19,36.59)	0.95 (0.01,4.89)	2.02 (0.07,10.14)
1.26 (0.49,1.97)	-0.51 (-1.42,0.38)	HoLEP	0.81 (0.02,3.93)	63.68 (0.08,20.77)	0.87 (0.00,3.92)	1.48 (0.02,7.32)
1.91 (0.28,3.45)	0.14 (-1.69,1.87)	0.65 (0.10,2.41)	TmLRP	40.07 (0.13,99.52)	3.74 (0.00,19.71)	11.99 (0.03,40.31)
0.87 (-0.63,2.44)	-0.9 (-2.60,0.82)	-0.39 (-2.06,1.40)	-1.04 (-3.17,1.07)	HoLRP	0.85 (0.00,4.00)	2.06 (0.01,11.78)
1.84 (0.19,3.43)	0.07 (-1.38,1.66)	0.58 (-1.13,2.39)	-0.07 (-2.45,2.25)	0.97 (-1.27,3.30)	HoLAP	18.31 (0.07,32.10)
0.68 (-0.89,2.28)	-1.09 (-2.81,0.66)	-0.58 (-2.38,1.31)	-1.23 (-3.51,1.16)	-0.19 (-2.55,2.01)	-1.16 (-3.53,1.34)	DiLEP
1.45 (-0.19,2.92)	-0.33 (-2.07,1.31)	0.18 (-1.54,1.80)	-0.47 (-2.56,1.80)	0.57 (-1.65,2.74)	-0.39 (-2.45,1.80)	0.76 (-1.42,2.97)
						DiLVP

2008; Tugcu et al., 2008; Xia et al., 2008; Elzayat and Al, 2009; Mavuduru et al., 2009; Al-Ansari et al., 2010; Bouchier-Hayes et al., 2010; Geavlete et al., 2010; PhD et al., 2010; Capitán et al., 2011; Elmansy et al., 2012; Yang et al., 2012; Zhang et al., 2012; Cui et al., 2013; Xue et al., 2013; Yan et al., 2013; Bachmann et al., 2014; Elshal et al., 2014; Razzaghi et al., 2014; Sun et al., 2014) were

included (Figure 1) in our multiple-treatments NMA of the 9 surgical treatments (Figure 2). Quality assessment is in Figure 3. Most RCTs were not blinded, and some reports did not include details about concealment. All trials were two-arm studies.

A total of 14 articles of RCTs (1,664 patients) reported the IPSS at 6 months and 14 (1,524 patients) at 12 months

Table 6. Efficacy (operative time and catheter remove time) of All the Surgeries (SUMC with 95% CI)

TURP	-11.49 (-15.77 to -7.24)	-14.34 (-19.84 to -8.55)	-25.07 (-37.51 to -13.10)	-0.99 (-9.53 to 7.24)	-25.73 (-40.03 to -11.65)	-4.91 (-20.55 to 10.16)	-5.84 (-17.15 to 7.03)
1.30 (0.91 to 1.67)	PVP	-2.85 (-9.71 to 3.85)	-13.57 (-26.23 to -0.66)	10.51 (0.46 to 20.15)	-14.24 (-27.68 to -0.67)	6.58 (-9.12 to 23.14)	5.65 (-6.53 to 19.33)
1.18 (0.75 to 1.63)	-0.12 (-0.62 to 0.44)	HoLEP	-10.72 (-22.77 to 0.42)	13.36 (2.78 to 23.22)	-11.39 (-26.09 to 3.22)	9.43 (-7.46 to 25.19)	8.50 (-4.63 to 22.17)
1.26 (0.14 to 2.36)	-0.04 (-1.25 to 1.10)	0.07 (-0.97 to 1.07)	ThuLEP	24.08 (8.82 to 39.63)	-0.66 (-19.61 to 17.04)	20.16 (0.20 to 39.98)	19.23 (1.61 to 36.80)
1.43 (0.55 to 2.23)	0.13 (-0.83 to 1.05)	0.25 (-0.73 to 1.13)	0.17 (-1.32 to 1.57)	TmLRP	-24.74 (-40.89 to -7.34)	-3.92 (-21.29 to 14.28)	-4.85 (-19.24 to 10.05)
-0.36 (-3.58 to 2.71)	-1.66 (-5.01 to 1.41)	-1.54 (-4.93 to 1.53)	-1.61 (-5.01 to 1.51)	-1.79 (-4.92 to 1.34)	HoLRP		
0.86 (-0.53 to 2.28)	-0.44 (-1.74 to 0.89)	-0.32 (-1.74 to 1.12)	-0.39 (-2.01 to 1.41)	-0.57 (-2.11 to 1.14)	1.22 (-2.04 to 4.77)	HoLAP	20.82 (-0.35 to 42.92)
1.12 (-0.13 to 2.50)	-0.18 (-1.59 to 1.16)	-0.06 (-1.42 to 1.41)	-0.14 (-1.88 to 1.63)	-0.31 (-1.86 to 1.42)	1.48 (-1.82 to 5.10)	0.26 (-1.65 to 2.16)	19.89 (1.75 to 39.63)
2.87 (1.82 to 3.97)	1.57 (0.43 to 2.73)	1.69 (0.55 to 2.85)	1.62 (0.03 to 3.19)	1.44 (0.20 to 2.87)	3.23 (-0.06 to 6.61)	2.01 (0.16 to 3.68)	1.75 (0.08 to 3.43)
							DiLVP (-21.02 to 17.99)

Table 7. The rank of all treatments (efficacy and safety). Abbreviations: CT, catheter removal time; HT, hospital time; US, urethral stricture; OT, operative time

	IPSS 6months mean(95%CI)	Qmax 6 months mean(95%CI)	IPSS 12 months mean(95%CI)	Qmax 12 months mean(95%CI)	US mean(95%CI)	OT mean(95%CI)	CT mean(95%CI)	HS mean(95%CI)
Rank								
TURP	3.27(1.00,6.00)	3.72(2.00,6.00)	4.94(3.00,7.00)	3.88(3.00,6.00)	5.75(4.00,7.00)	1.87(1.00,3.00)	8.27(7.00,9.00)	7.61(6.00,8.00)
PVP	5.18(2.00,7.00)	4.95(3.00,7.00)	4.33(2.00,7.00)	4.76(3.00,6.00)	3.34(2.00,6.00)	4.78(3.00,6.00)	4.21(2.00,7.00)	2.79(1.00,5.00)
HoLEP	3.89(1.00,7.00)	1.95(1.00,4.00)	1.94(1.00,5.00)	1.24(1.00,3.00)	4.85(2.00,7.00)	5.67(4.00,7.00)	4.90(2.00,7.00)	4.58(2.00,7.00)
ThuLEP						7.38(66.00,8.00)	4.49(2.00,8.00)	
TmLRP	3.68(1.00,7.00)	3.11(1.00,7.00)	3.92(1.00,7.00)	4.11(2.00,6.02)	3.15(1.00,7.00)	2.21(1.00,4.00)	3.73(2.00,7.00)	2.73(1.00,7.00)
HoLRP	2.37(1.00,7.00)	2.85(1.00,7.00)	4.53(1.00,7.00)	1.91(1.00,3.00)	5.26(1.00,7.00)		7.53(2.00,9.00)	4.45(1.00,8.00)
HoLAP	6.20(1.00,7.00)	5.83(1.00,7.00)	2.52(1.00,7.00)	5.55(2.00,7.00)	1.85(1.00,7.00)	7.39(5.00,8.00)	5.81(2.00,9.00)	2.95(1.00,7.00)
DiLEP						3.26(1.00,7.00)	4.96(2.00,8.00)	5.95(1.00,8.00)
DiLVP	3.41(1.00,7.00)	5.58(2.00,7.00)	5.81(2.00,7.00)	6.55(5.00,7.00)	3.80(1.00,7.00)	3.44(1.00,6.00)	1.11(1.00,2.00)	3.95(1.00,7.00)
Best								
TURP	0.05(0.00,1.00)	0.00(0.00,0.00)	0.00(0.00,0.00)	0.00(0.00,0.00)	0.00(0.00,0.00)	0.36(0.00, 1.00)	0.00(0.00,0.00)	0.00(0.00,0.00)
PVP	0.01(0.00,0.00)	0.00(0.00,0.00)	0.01(0.00,0.00)	0.00(0.00,0.00)	0.02(0.00,0.00)	0.00(0.00, 0.00)	0.00(0.00,0.00)	0.11(0.00,1.00)
HoLEP	0.05(0.00,1.00)	0.36(0.00,1.00)	0.68(0.00,1.00)	0.83(0.00,1.00)	0.02(0.00,0.00)	0.00(0.00, 0.00)	0.00(0.00,0.00)	0.01(0.00,0.00)
ThuLEP						0.00(0.00, 0.00)	0.01(0.00,0.00)	
TmLRP	0.19(0.00,1.00)	0.28(0.00,1.00)	0.08(0.00,1.00)	0.01(0.00,0.00)	0.18(0.00,1.00)	0.30(0.00,1.00)	0.01(0.00,0.00)	0.37(0.00,1.00)
HoLRP	0.51(0.00,1.00)	0.32(0.00,1.00)	0.09(0.00,1.00)	0.15(0.00,1.00)	0.03(0.00,1.00)		0.02(0.00,0.00)	0.04(0.00,1.00)
HoLAP	0.03(0.00,1.00)	0.03(0.00,1.00)	0.13(0.00,1.00)	0.01(0.00,0.00)	0.64(0.00,1.00)	0.00(0.00,0.00)	0.01(0.00,0.00)	0.31(0.00,1.00)
DiLEP						0.22(0.00,1.00)	0.02(0.00,0.00)	0.03(0.00,1.00)
DiLVP	0.16(0.00,1.00)	0.01(0.00,0.00)	0.01(0.00,0.00)	0.00(0.00,0.00)	0.11(0.00,1.00)	0.12(0.00,1.00)	0.92(0.00,1.00)	0.14(0.00,1.00)

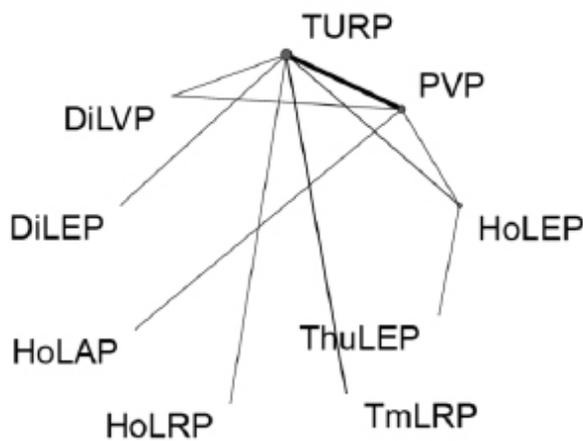


Figure 2. Network of Treatment Comparisons (Thickness of connecting lines indicates the number of available comparisons. The size of the nodes indicates the number of trials that study the treatments)

(Table 1); 15 (1,754 patients) reported the Qmax at 6 months and 15 (1,586 patients) at 12 months. Overall, 17 reports (2,033 patients) described operative time, 21 (2559 patients) catheter removal time, 17 (2,236 patients) hospital stay time and 19 (2,420 patients) urethral

stricture. Statistical heterogeneity was moderate (Table 2), although for some comparisons, I² was > 50%, for high heterogeneity, so we chose a Bayesian framework for the random-effects NMA (Borenstein et al., 2010). We found no inconsistency between direct and indirect comparisons.

Surgeries for BHP ranked by outcome

At 6 months, Qmax was lower for PVP than HoLEP (95% CI -7.06 to -0.12) and was higher for HoLEP than HoLRP (95% CI 3.65 to 8.34) (Table 3). For IPSS at 12 months, surgeries did not significantly differ (Table 4). At 12 months, Qmax was lower for TURP than HoLEP (95% CI -3.84 to -1.04) and TmLRP (95% CI -9.16 to -0.33) but higher than DiLVP (0.49 to 4.98). Qmax was lower for PVP than HoLEP (95% CI -5.46 to -1.23) and TmLRP (-10.47 to -0.80) and higher for HoLEP than DiLEP (95% CI 2.44 to 7.64) and TmLRP than HoLAP (95% CI 0.85 to 13.12) and DiLEP (95% CI 2.42 to 12.70).

Urethral stricture did not differ among treatments (Table 5). Hospital stay was longer with TURP than PVP (95% CI 1.13 to 2.41), HoLEP (95% CI 0.49 to 1.97), TmLRP (95% CI 0.28 to 3.45) and HoLAP (95% CI 0.19 to 3.43) and for HoLEP than TmLRP (95% CI 0.10 to 2.41).

Operative time was shorter with TURP than PVP

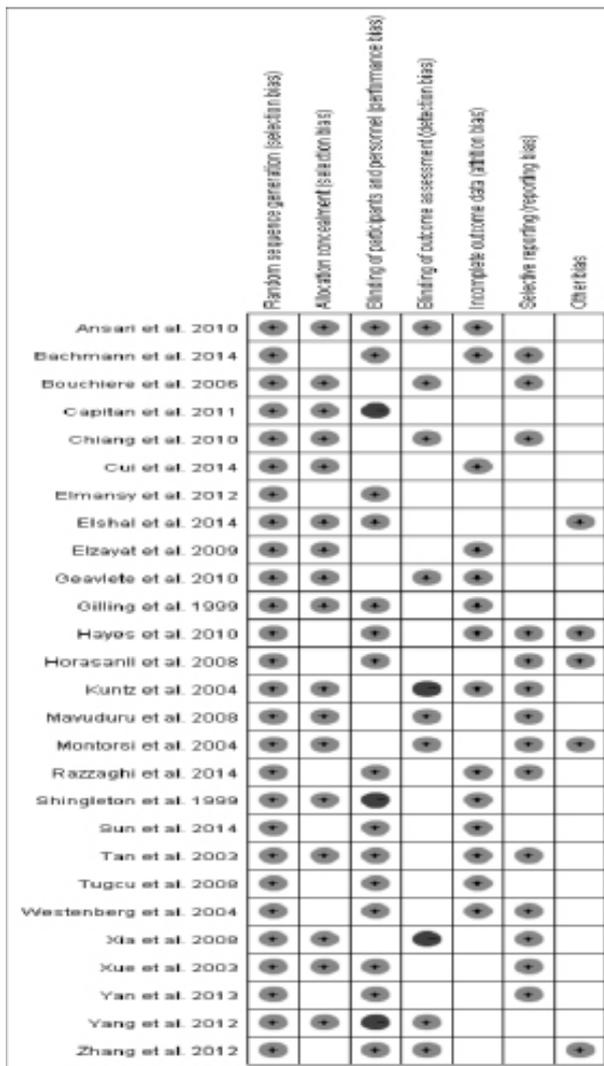


Figure 3. Quality Evaluation of Randomized Controlled Trials

(95% CI -15.77 to -7.24), HoLEP (95% CI -19.84 to -8.55), ThuLEP (95% CI -37.51 to -13.10) and HoLAP (95% CI -40.03 to -11.65) (Table 6). It was shorter with PVP than ThuLEP (95% CI -26.23 to -0.66) and HoLAP (95% CI -27.68 to -0.67); and TmLRP than HoLAP (95% CI -40.89 to -7.34). Operative time was longer with PVP than TmLRP (95% CI 0.46 to 20.15); HoLEP than TmLRP (95% CI 2.78 to 23.22); ThuLEP than TmLRP (95% CI 8.82 to 39.63), DiLEP (95% CI 0.20 to 39.98) and DiLVP (95% CI 1.61 to 36.80); and HoLAP than DiLVP (95% CI 1.75 to 39.63).

Catheter removal time was longer with TURP than PVP (94% CI 0.91 to 1.67), HoLEP (95% CI 0.75 to 1.63), ThuLEP (95% CI 0.14 to 2.36), TmLRP (95% CI 0.55 to 2.23) and DiLVP (95% CI 1.82 to 3.97) and PVP than DiLVP (95% CI 0.43 to 2.73); HoLEP than DiLVP (95% CI 0.55 to 2.85); ThuLEP than DiLVP (95% CI 0.03 to 3.19); TmLRP than DiLVP (95% CI 0.20 to 2.87); HoLAP than DiLVP (95% CI 0.16 to 3.68); and DiLEP than DiLVP (95% CI 0.08 to 3.43).

We used WinBUGS 1.4.3 to rank treatments (Schmid et al., 2013) (Table 7). For IPSS at 6 months, the order was HoLRP > TURP > DiLEP and at 12 months, HoLEP

> HoLRP > TURP. For Qmax at 6 months, the order was HoLEP > HoLRP > TmLRP and at 12 months, HoLEP > HoLRP > PVP. The order for operative time was TURP > TmLRP > DiLEP; for catheter removal time, DiLEP > TmLRP > PVP; for length of hospital stay, TmLRP > PVP > HoLAP; and for urethral stricture, HoLAP > TmLRP > PVP.

Discussion

Our NMA provided evidence-based hierarchies for the efficacy and safety of 8 laser surgeries and TURP for BHP. We integrated direct and indirect evidence from RCTs to compare the efficacy and safety of the 9 surgeries.

Our shortcoming was that we did not reported the powers of the surgeries in that we considered the surgeries with different powers as the same surgeries (e.g., we considered PVP-80w and PVP-120w as the same surgery) and some comparisons had few RCTs (e.g., DiLVP and ThuLEP), which may indicate bias when comparing the efficacy and safety of the surgeries.

Although TURP is considered the gold standard surgery for BPH, its efficacy and safety was not the best among the 9 surgeries. Catheter removal and hospital stay times were shorter for PVP than TURP. A conventional meta-analysis reported that blood transfusion were significantly less likely with PVP than TURP (Thangasamy et al., 2012). At 12 months, Qmax was higher and catheter removal time shorter for TmLRP than TURP; catheter removal time was shorter for DiLVP than TURP. We found no difference between DiLEP and TURP in operative time, catheter removal time or length of hospital stay. As well, at 12 months, Qmax was lower for TURP than HoLEP and TmLRP. Hospital stay was longer with TURP than PVP, TmLRP and HoLAP and catheter removal time was longer with TURP than PVP, HoLEP, ThuLEP, TmLRP and DiLVP.

Some studies (Elzayat et al., 2005; Rij and Gilling, 2012) reported that HoLEP may the new gold standard for BPH. A conventional meta-analysis (Tan et al., 2007) reported that at 12 months, Qmax and IPSS was better with HoLEP than TURP ($p < 0.0001$ and $p = 0.01$). HoLEP was associated with less blood loss ($p = 0.001$) and required shorter catheterization time ($p < 0.0001$) and hospital stay ($p = 0.001$) and lower blood transfusion rate ($p = 0.04$). We found HoLEP best in terms of Qmax at 6 and 12 months and IPSS at 12 months. Operative time was longer with HoLEP than TURP, some conventional meta-analyses also found the same results (Tan et al., 2007; Zhao et al., 2011). HoLEP may remove more tissue than TURP (Tan et al., 2003; Montorsi et al., 2004), and HoLEP requires extra time for fragmentation of prostatic lobes into pieces small enough to be evacuated through the resectoscope sheath (Montorsi et al., 2004).

In brief, although TURP is considered the gold standard surgery for BPH, our NMA comparing 8 other BHP laser treatments and TURP showed that it may not be the best in terms of efficacy and safety, HoLEP is more competitive, IPSS at 12 months and Qmax at 6 months and 12 months especially.

References

- Ades AE, Sculpher M, Sutton A, et al (2006). Bayesian methods for evidence synthesis in cost-effectiveness analysis. *Pharmacoeconomics*, **24**, 1-19.
- Ahyaia SA, Kaplan SA, Kuntz RM, et al (2010). Meta-analysis of functional outcomes and complications following transurethral procedures for lower urinary tract symptoms resulting from benign prostatic enlargement. *European Urol*, **58**, 384-97.
- Al-Ansari A, Younes N, Sampige VP, et al (2010). GreenLight HPS 120-W Laser Vaporization Versus Transurethral Resection of the Prostate for Treatment of Benign Prostatic Hyperplasia: A Randomized Clinical Trial with Midterm Follow-up. *Eur Urol*, **58**, 349-55.
- Bachmann A, Tubaro A, Barber N, et al (2014). 180-W XPS GreenLight Laser Vaporisation Versus Transurethral Resection of the Prostate for the Treatment of Benign Prostatic Obstruction: 6-Month Safety and Efficacy Results of a European Multicentre Randomised Trial-The GOLIATH Study. *Eur Urol*, **65**, 931-42.
- Borenstein M, Hedges LV, Higgins JPT, et al (2010). A basic introduction to fixed-effect and random-effects models for meta-analysis. *Research Synthesis Methods*, **1**, 97-111.
- Bouchier-Hayes DM, Anderson P, Van AS, et al (2006). KTP laser versus transurethral resection: early results of a randomized trial. *J Endourol*, **20**, 580-5.
- Bouchier-Hayes DM, Appledorn SV, Bugeja P, et al (2010). 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 International*, **105**, 964-9.
- Capitán C, Blázquez C, Martín MD, et al (2011). Greenlight hps 120-w laser vaporization versus transurethral resection of the prostate for the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia: a randomized clinical trial with 2-year follow-up. *Eur Urol*, **60**, 734-9.
- Committee APG (2003). AUA guideline on management of benign prostatic hyperplasia (2003). Chapter 1: Diagnosis and treatment recommendations. *J Urol*, **170**, 530-47.
- Cui D, Sun F, Zhuo J, et al (2013). A randomized trial comparing thulium laser resection to standard transurethral resection of the prostate for symptomatic benign prostatic hyperplasia: four-year follow-up results. *World J Urol*, **32**, 1-7.
- Elmansy H, Baazeem A, Kotb A, et al (2012). Holmium Laser Enucleation Versus Photoselective Vaporization for Prostatic Adenoma Greater than 60 ml: Preliminary Results of a Prospective, Randomized Clinical Trial. *J Urol*, **188**, 216-21.
- Elshal AM, Elkoushy MA, El-Nahas AR, et al (2014). GreenLight™ Laser (XPS) Photoselective Vapo-Enucleation versus Holmium Laser Enucleation of the Prostate for the Treatment of Symptomatic Benign Prostatic Hyperplasia: A Randomized Controlled Study. *J Urol*, **193**, 927-34.
- Elzayat EA, Al MMI (2009). Holmium laser ablation of the prostate versus photoselective vaporization of prostate 60 cc or less: short-term results of a prospective randomized trial. *J Urol*, **182**, 133-8.
- Elzayat EA, Habib EI, Elhilali MM (2005). Holmium laser enucleation of the prostate: A size-independent new "gold standard". *Urol*, **66**, 108-13.
- Geavlete B, Multescu R, Dragutescu M, et al (2010). Transurethral resection (TUR) in saline plasma vaporization of the prostate vs standard TUR of the prostate: "the better choice & rsquo; in benign prostatic hyperplasia? *J Urol*, **106**, 1385.
- Gilling PJ, Mackey M, Cresswell M, et al (1999). Holmium laser versus transurethral resection of the prostate: a randomized prospective trial with 1-year followup. *J Urol*, **162**, 1640-4.
- Higgins, JPT (2008). Cochrane handbook for systematic reviews of interventions version 5.0. 2.
- Higgins JPT, Jackson D, Barrett JK, et al (2012). Consistency and inconsistency in network meta-analysis: concepts and models for multi-arm studies. *Research Synthesis Methods*, **3**, 98-110.
- HIGGINS JPT, Whitehead A (1996). Borrowing strength from external trials in a meta-analysis. *Statistics Med*, **15**, 2733-49.
- Horasanli K, Silay MS, Altay B, et al (2008). Photoselective potassium titanyl phosphate (KTP) laser vaporization versus transurethral resection of the prostate for prostates larger than 70 ml: a short-term prospective randomized trial. *Urol*, **71**, 247-51.
- Jansen JP, Crawford B, Bergman G, et al (2008). Bayesian Meta-Analysis of Multiple Treatment Comparisons: An Introduction to Mixed Treatment Comparisons. *Value in Health*, **11**, 956-64.
- Kuntz RM, Ahyai S, Lehrich K, et al (2004). Transurethral holmium laser enucleation of the prostate versus transurethral electrocautery resection of the prostate: a randomized prospective trial in 200 patients. *J Urol*, **172**, 1012-6.
- Lertakyamane J, Ruksamane EO, Tantiwong A, et al (2002). The risk and effectiveness of transurethral resection of prostate. *J Med Assoc Thailand = Chotmai het thangphaet*, **85**, 1288-95.
- Li S, Zeng XT, Ruan XL, et al (2014). Holmium laser enucleation versus transurethral resection in patients with benign prostatic hyperplasia: an updated systematic review with meta-analysis and trial sequential analysis. *Plos One*, **9**, 101615.
- Lu G, Ades AE (2004). Combination of direct and indirect evidence in mixed treatment comparisons. *Statistics Med*, **23**, 3105-24.
- Mamoulakis C, Rosette JJMCHdI, Ubbink DT (2010). Systematic review and meta-analysis of transurethral resection of the prostate versus minimally invasive procedures for the treatment of benign prostatic obstruction. *Urol*, **75**, 1015-22.
- Mavuduru RM, Mandal AK, Singh SK, et al (2009). Comparison of HoLEP and TURP in terms of efficacy in the early postoperative period and perioperative morbidity. *Urologia Internationalis*, **82**, 130-5.
- Meibust WK, Holtgrewe HL, Cockett ATK, et al (2002). Transurethral prostatectomy: immediate and postoperative complications. A cooperative study of 13 participating institutions evaluating 3,885 patients. *J Urol*, **167**, 999-1003.
- Montorsi F, Naspro R, Salonia A, et al (2004). Holmium laser enucleation versus transurethral resection of the prostate: results from a 2-center, prospective, randomized trial in patients with obstructive benign prostatic hyperplasia. *J Urol*, **172**, 1926-9.
- Oesterling JE (1995). Benign prostatic hyperplasia. Medical and minimally invasive treatment options. *New England J Med*, **332**, 99-109.
- PhD PHCM, Chen CH, Kang CH, et al (2010). GreenLight HPS laser 120-W versus diode laser 200-W vaporization of the prostate: Comparative clinical experience. *Lasers Surgery Med*, **42**, 624-9.
- Rassweiler J, Teber D, Kuntz R, et al (2006). Complications of Transurethral Resection of the Prostate (TURP)—Incidence, Management, and Prevention. *Eur Urol*, **50**, 969-80.
- Razzaghi MR, Mazloomfard MM, Mokhtarpour H, et al (2014). Diode laser (980nm) vaporization in comparison with transurethral resection of the prostate for benign prostatic hyperplasia: randomized clinical trial with 2-year follow-up. *Urol*, **84**, 526-32.
- Rij SV, Gilling PJ (2012). In 2013, holmium laser enucleation of the prostate (HoLEP) may be the new 'gold standard'.

- Roberts RO, Jacobsen SJ, Jacobson DJ, et al (1998). Natural history of prostatism: high American Urological Association Symptom scores among community-dwelling men and women with urinary incontinence. *Urol*, **51**, 213-9.
- Roehrborn CG, McConnell J, Bonilla J, et al (2000). Serum prostate specific antigen is a strong predictor of future prostate growth in men with benign prostatic hyperplasia. PROSCAR long-term efficacy and safety study. *J Urol*, **163**, 13-20.
- Salanti G, Ades AE, Ioannidis JPA (2011). Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *J Clin Epidemiol*, **64**, 163-71.
- Salanti G, Higgins JP, Ades AE, et al (2008). Evaluation of networks of randomized trials. *Statistical Methods Med Res*, **17**, 279-301.
- Schmid, Stewart CH, Rothstein GB, et al (2013). Software for Statistical Meta-analysis : Handbook of Meta-analysis in Ecology and Evolution.
- Shingleton WB, Terrell F, Renfro DL, et al (1999). A randomized prospective study of laser ablation of the prostate versus transurethral resection of the prostate in men with benign prostatic hyperplasia. *Urol*, **54**, 1017-21.
- Sun N, Fu Y, Tian T, et al (2014). Holmium laser enucleation of the prostate versus transurethral resection of the prostate: a randomized clinical trial. *Int Urol Nephrol*, **46**, 1277-82.
- Tan A, Liao C, Mo Z, et al (2007). Meta-analysis of holmium laser enucleation versus transurethral resection of the prostate for symptomatic prostatic obstruction. *British Journal of Surgery*, **94**, 1201-8.
- Tan AHH, Gilling PJ, Kennett KM, et al (2003). A randomized trial comparing holmium laser enucleation of the prostate with transurethral resection of the prostate for the treatment of bladder outlet obstruction secondary to benign prostatic hyperplasia in large glands (40 to 200 Grams). *J Urol*, **170**, 1270-4.
- Thangasamy IA, Chalasani V, Bachmann A, et al (2012). 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*, **62**, 315-23.
- Tugcu V, Tasci AI, Sahin S, et al (2008). Comparison of photoselective vaporization of the prostate and transurethral resection of the prostate: a prospective nonrandomized bicenter trial with 2-year follow-up. *J Endourol*, **22**, 1519-25.
- Westenberg A, Gilling P, Kennett K, et al (2004). Holmium laser resection of the prostate versus transurethral resection of the prostate: results of a randomized trial with 4-year minimum long-term followup. *J Urol*, **172**, 616-9.
- Xia SJ, Zhuo J, Sun XW, et al (2008). Thulium Laser versus Standard Transurethral Resection of the Prostate: A Randomized Prospective Trial. *Eur Urol*, **53**, 382-89.
- Xue B, Zang Y, Zhang Y, et al (2013). GreenLight HPS 120-W laser vaporization versus transurethral resection of the prostate for treatment of benign prostatic hyperplasia: A prospective randomized trial. *J X-Ray Sci Technol*, **21**, 125-32.
- Yan H, Ou TW, Chen L, et al (2013). Thulium laser vaporesction versus standard transurethral resection of the prostate: A randomized trial with transpulmonary thermodilution hemodynamic monitoring. *Int J Urol*, **20**, 507-12.
- Yang SS, Hsieh CH, Lee YS, et al (2012). Diode laser (980 nm) enucleation of the prostate: a promising alternative to transurethral resection of the prostate. *Lasers Med Science*, **28**, 353-60.
- Zhang F, Shao Q, Herrmann TRW, et al (2012). Thulium laser versus holmium laser transurethral enucleation of the prostate: 18-month follow-up data of a single center. *Urol*, **79**, 869-74.
- Zhao CB, Ju-Cong LI, Yuan PQ, et al (2011). A meta-analysis of holmium laser enucleation of the prostate for benign prostatic hyperplasia. *Zhonghua Nan Ke Xue = National J Andrology*, **17**, 1112-20.