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Collaborative Review – Benign Prostatic Enlargement

Meta-analysis of Functional Outcomes and Complications Following Transurethral Procedures for Lower Urinary Tract Symptoms Resulting from Benign Prostatic Enlargement

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Abstract

Context: There is a continuous decline in the number of transurethral resections of the prostate (TURP) and an increase use of minimally invasive surgical therapy (MIST) for lower urinary tract symptoms resulting from benign prostatic enlargement. Current results from randomised controlled trials (RCT) and methodologically sound prospective studies suggest that some of the proposed procedures have the potential to replace TURP.
Objective: To determine the contemporary status of TURP and of the currently most commonly applied transurethral MISTs: (1) bipolar TURP, (2) bipolar transurethral vaporisation of the prostate (bipolar TUVP), (3) holmium laser enucleation of the prostate (HoLEP), and (4) potassium-titanyl-phosphate (KTP) laser vaporisation of the prostate.
Evidence acquisition: This meta-analysis was based on a systematic Medline search assessing the period 1997–2009. All RCTs comparing TURP and the most commonly discussed ablative treatments were included. The end points of our analyses were functional outcomes and treatment-related adverse events.
Evidence synthesis: Twenty-seven publications involving 23 different RCTs with a total of 2245 patients provided the highest level of evidence available (level 1b) and were fully assessed. Meta-analysis was conducted with SAS v.9.1.3 (SAS Institute, Cary, NC, USA). Forest plots were produced using the R software. Pooled odds ratios and 95% confidence intervals were calculated between various operative techniques versus TURP. Functional results between the specific transurethral procedures versus TURP were summarised as differences in means.
Conclusions: This meta-analysis demonstrates statistically comparable efficacy and overall morbidity for MISTs versus contemporary TURP. Type, category (minor vs major), and the number of complications (safety profile) vary specifically for each of the different transurethral techniques. We feel that the individual patient's clinical profile should be carefully assessed to identify the most appropriate transurethral technique.

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1. Introduction

For many years, transurethral resection of the prostate (TURP) has been considered the standard surgical therapy for lower urinary tract symptoms secondary to benign prostatic enlargement (BPE) [1]. Its high success rate is reflected by substantial improvements in symptom scores, urinary flow rate, postvoid residual urine (PVRU) and a low retreatment rate on long-term follow-up. However, despite innovations and improvements, TURP is still associated with significant morbidity, particularly in patients with larger prostates, indwelling catheters, bleeding disorders, or those who are undergoing anticoagulation therapy [2]. Complications mainly consist of perioperative bleeding requiring blood transfusion or transurethral resection (TUR) syndrome but also prolonged catheterisation and hospital stay as well as urinary incontinence and retrograde ejaculation. Therefore, many endoscopic technologies have been proposed to replace TURP as the new reference standard. As a matter of fact, there has been a continuous decrease in the use of TURP and a rise in the use of minimally invasive surgical therapy (MIST) [3].

This all raises the question whether the trend in decreased use of TURP is based on scientific evidence or is this rather a result of aggressive marketing of novel techniques [4]. Prior to including any new therapy in our clinical armamentarium, such a procedure should document an evidence-based, meaningful advantage over TURP. In the past, numerous new techniques have not fulfilled this objective. Morbidity was often only shifted from the intraoperative period to the postoperative period, and high treatment failure rates became evident during prolonged follow-up [5,6]. Therefore, in addition to promising initial clinical results, long-term follow-up data on MIST are mandatory. Current results from randomised controlled trials (RCT) and methodologically sound prospective studies suggest that some of the proposed procedures have the potential to replace TURP.

The objective of this review was to determine the contemporary status of TURP and of the currently most commonly used transurethral MISTs: (1) bipolar TURP, (2) bipolar transurethral vaporisation of the prostate (bipolar TUVP), (3) holmium laser enucleation of the prostate (HoLEP), and (4) potassium-titanyl-phosphate (KTP) laser vaporisation of the prostate. Treatment-specific efficacy and safety profiles were investigated to improve patient counselling and medical decision making.

2. Evidence acquisition

This meta-analysis was based on a Medline search assessing the period from 1997 to 2009. The Medical Subject Headings (MeSH) database keywords consisted of *randomized controlled trial (RCT); benign prostatic hyperplasia (BPH), enlargement (BPE), and obstruction (BPO); minimal invasive surgery;* and the specific MIST and TURP name. Reference lists of all included studies were scanned for additional reports. All authors of this meta-analysis obtained a list of identified publications to screen title, abstract, and full-text copies of potentially relevant studies. With the consensus of all authors, a selected group of articles was reviewed and systematically analysed, specifically taking into account the latest version of the level of evidence rating system.

All currently available RCTs comparing TURP as a reference procedure and the most commonly used ablative treatments with immediate tissue removal (bipolar techniques, HoLEP, KTP laser) were included (Table 1). The end points of our analyses were (1) functional outcome defined by International Prostate Symptom Score (IPSS), quality of life (QoL), maximum urinary flow rate (Q_{max}), and PVRU and (2) treatment-related adverse events. Details of the methodology, intervention, number and characteristics of participants, and outcomes (primary and secondary) were recorded on a data-extraction form. For trials with updated publications, outcome data were combined to obtain the most complete report and the longest follow-up.

3. Evidence synthesis

3.1. Data

Twenty-seven publications involving 23 different RCTs with 2245 study participants provided the highest level of evidence (level 1b) and were fully assessed (Table 1). Statistical analysis was based on data retrieved exclusively from these studies. Eighty-seven percent (20 of 23) of these randomised trials compared MIST (966 patients) with TURP (954 patients), and 13% (3 of 23) compared MIST (166 patients) with simple open prostatectomy (OP; 159 patients). Fig. 1 depicts the distribution of patients from all RCTs according to the mode of surgical intervention.

3.2. Quantitative data synthesis and statistical analyses

Study design and patients' baseline characteristics are presented in Table 1. Mean operative time, weight of retrieved tissue (if available), mean indwelling catheter time, and postoperative functional results are shown in Table 2.

Descriptive statistics were calculated addressing functional outcomes and complication rates for each procedure. Intraoperative, perioperative, late, and overall treatment related complication rates were calculated by dividing the total number of specific complications by the total number of patients treated by each transurethral procedure. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated between various operative techniques versus TURP. Functional results between the specific transurethral procedures versus TURP were summarised as differences in means. Q-statistic was computed to test for heterogeneity [7]. As we experienced heterogeneity, we decided to calculate random effects models. In the random effects model, the true treatment difference in each trial is itself assumed to be a realisation of a random variable. As a consequence, the standard error of each trial estimate is increased because of the addition of this between-trial variation [8]. Results for the various operative techniques versus TURP are presented as forest plots.

Statistical tests were performed using SPSS v.13.0 (SPSS, Chicago, IL, USA) and SAS v.9.1.3 (SAS Institute, Cary, NC,

Table 1 – Summary of (mean) baseline characteristics from included randomised trials comparing minimally invasive therapies with transurethral resection of the prostate

Comparator	Authors	Publication yr	No. of patients	Max. follow-up, yr	Age, yr	TRUS, cm^3	IPSS	QoL	Q_{max}, ml/sec	PVRU, ml
Bipolar TURP	Yang et al	2004	58; 59	0.3	N/A	46; 49	20.9; 21.6	3.7; 4.0	10.4; 10.9	99.0; 150
Bipolar TURP	Singh et al	2005	30; 30	0.3	68.9; 67.9	24.1; 27.9	20.5; 21.6	4.6; 4.4	5.8; 5.1	124.0; 136.0
Bipolar TURP	Seckiner et al	2005	24; 24	1.0	61.2; 63.9	49.4; 41.4	24.1; 23.2	4.4; 4.7	8.5; 8.3	88.0; 138.0
Bipolar TURP	Fung et al	2005	21; 30	0.3	72.5; 73.0	N/A	15.8; 19.4	3.6; 3.6	N/A	N/A
Bipolar TURP	Patankar et al	2006	53; 51	0.1	64.0; 62.0	51.3; 52.3	23.3; 23.7	N/A	5.9; 6.4	N/A
Bipolar TURP	Nuhoglu et al	2006	27; 30	1.0	64.6; 65.2	47.0; 49.0	17.6; 17.3	N/A	6.9; 7.3	96.0; 88.0
Bipolar TURP	Michielsen et al	2007	118; 120	1.5	73.8; 73.1	N/A	N/A	N/A	N/A	N/A
Bipolar TURP	De Sio/Autorino et al	2006; 2007	35; 35	3.0	59.0; 61.0	51.6; 47.5	24.2; 24.3	4.2; 3.9	7.1; 6.9	80.0; 75.0
Bipolar TURP	Ho et al	2007	48; 52	1.0	66.6; 66.5	56.5; 54.8	22.6; 24.6	N/A	6.8; 6.5	N/A
Bipolar TURP	Iori et al	2008	26; 25	1.0	65.0; 63.0	49.0; 48.0	21.0; 20.0	3.0; 3.6	7.0; 8.7	99.0; 96.0
Bipolar TUVP	Dunsumir et al	2003	30; 21	1.0	63.0; 60.0	36.0; 42.0	24.0; 17.0	N/A	9.6; 10.4	112.0; 96.0
Bipolar TUVP	Tefekli et al	2005	51; 50	1.0	68.7; 69.4	50.1; 50.4	21.3; 20.4	N/A	7.8; 8.3	N/A
Bipolar TUVP	Hon et al	2006	81; 79	0.7	66.1; 68.1	38.0; 40.0	21.3; 20.6	4.2; 4.3	12.0; 11.9	147.0; 182.0
Bipolar TUVP	Kaya et al	2007	25; 15	3.0	67.2; 66.0	50.0; 51.0	21.0; 22.0	N/A	6.0; 6.0	N/A
HoLEP vs open	Kuntz et al	2002; 2008	60; 60	5.0	69.2; 71.2	114.6; 113.0	22.1; 21.0	N/A	3.8; 3.6	280.0
HoLEP	Kuntz/Ahyai et al	2004; 2007	100; 100	3.0	68.0; 68.7	53.5; 49.9	22.1; 21.4	N/A	45.9; 5.9	238.0; 216.0
HoLEP	Montorsi et al	2004	52; 48	1.0	65.1; 64.5	70.3; 56.2	21.6; 21.9	4.6; 4.7	8.2; 7.8	N/A
HoLEP	Gupta et al	2006	50; 50	1.0	65.8; 65.7	57.9; 59.8	23.4; 23.3	N/A	5.2; 4.5	112.0; 84.0
HoLEP	Tan/Wilson et al	2006	30; 30	2.0	71.7; 70.3	77.8; 70.0	26.0; 23.7	4.8; 4.7	8.4; 8.3	N/A
HoLEP vs open	Naspro et al	2006	41; 39	2.0	66.3; 67.3	113.3; 124.2	20.1; 21.6	4.1; 4.4	7.8; 8.3	N/A
KTP	Bouchiers-Hayes et al	2006	38; 38	1.0	65.2; 66.2	42.4; 33.2	N/A	N/A	N/A	147.0; 119.0
KTP	Horasanli et al	2008	39; 37	0.5	69.2; 68.3	86; 88	18.9; 20.2	N/A	8.6; 9.2	183.0; 176.9
KTP vs open	Alivizatos et al	2008	65; 60	1.0	74.0; 67.5	93.0; 96.0	20.0; 21.0	3.0; 3.0	8.6; 8.0	97.0; 89.0

TRUS = transrectal ultrasound; IPSS = International Prostate Symptom Score; QoL = quality of life; Q_{max} = maximum flow rate; PVRU = postvoid residual volume urine; TURP = transurethral resection of the prostate; N/A = not available; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate.

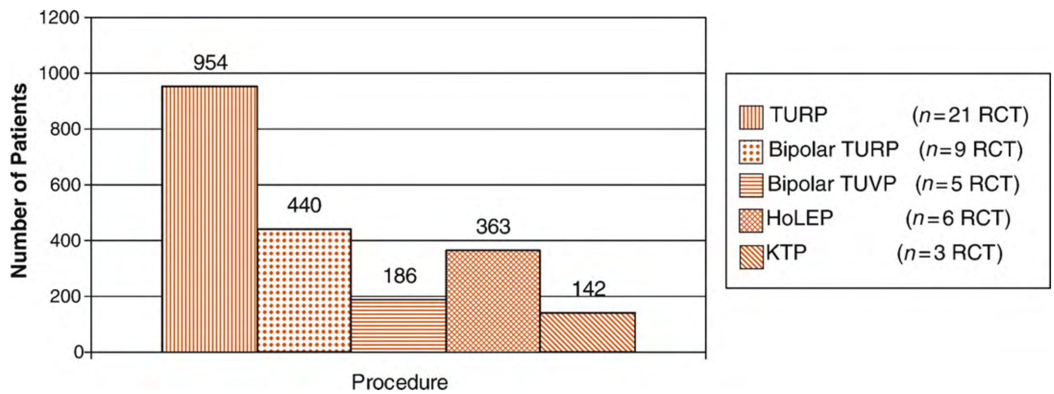

Fig. 1 – Distribution and total number of randomised patients differentiated to transurethral procedure.
TURP = transurethral resection of the prostate; RCT = randomised controlled trial; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate.

Table 2 – Summary of (mean) outcome data from included randomised studies comparing minimally invasive surgical therapies with transurethral resection of the prostate

Comparator	Authors	Operating time, min	Resected tissue, g	Length of catheter use, d	Incidental PCa, %	IPSS	IPSS QoL	Q_{max}, ml/sec	PVRU, ml
Bipolar TURP	Yang et al	46.0; 55.0	N/A	2.7; 3.2	N/A	10.8; 11.1	2.1; 2.2	17.1; 14.8	13.9; 34.5
Bipolar TURP	Singh et al	39.3; 36.9	24.0; 27.6	2.5; 3.4	N/A	5.3; 6.2	1.1; 1.0	19.0; 17.8	N/A
Bipolar TURP	Seckiner et al	52.9; 52.9	36.6; 31.9	3.1; 3.1	N/A	8.7; 8.3	1.8; 2.0	18.8; 15.7	N/A
Bipolar TURP	Fung et al	36.6; 32.9	18.6; 25.1	1.1; 1.2	N/A	7.0; 9.7	N/A	16.6; 14.7	N/A
Bipolar TURP	Patankar et al	50.0; 57.9	N/A	0.8; 1.8	N/A	6.1; 7.7	N/A	19.2; 20.7	N/A
Bipolar TURP	Nuhoglu et al	55.0; 52.0	N/A	1.8; 3.2	N/A	5.4; 4.7	N/A	17.1; 17.9	N/A
Bipolar TURP	Michielsen et al	56.0; 44.0	21.0; 21.3	4.0; 4.5	21.2; 20.0	N/A	N/A	N/A	N/A
Bipolar TURP	De Sio/Autorino et al	49.0; 53.0	20.0; 24.0	3.0; 4.2	N/A	6.8; 6.2	1.0; 0.8	20.5; 21.5	25.0; 20.0
Bipolar TURP	Ho et al	59.0; 58.0	29.8; 30.6	N/A	N/A	N/A	N/A	18.0; 18.0	6.0; 6.0
Bipolar TURP	Iori et al	39.1; 31.7	N/A	1.0; 1.3	N/A	7.0; 6.7	1.0; 1.0	24.2; 23.2	20.0; 27.0
Bipolar TUVP	Dunsumir et al	33.0; 26.0	0.0; 8.0	0.8; 0.7	N/A	6.0; 5.0	N/A	18.0; 16.0	90.0; 80.0
Bipolar TUVP	Tefekli et al	40.3; 57.8	N/A	2.3; 3.8	N/A	7.9; 7.3	N/A	17.2; 16.9	N/A
Bipolar TUVP	Hon et al	32.6; 28.5	0.0; 21.5	N/A	10.1; 0.0	7.7; 6.9	1.7; 1.5	25.6; 23.5	64.0; 69.0
Bipolar TUVP	Kaya et al	N/A	N/A	N/A	N/A	7.6; 14.4	N/A	5.7; 21.8	N/A
HoLEP vs open	Kuntz et al	135.9; 90.6	93.7; 96.4	1.3; 8.1	5.0; 10.0	3.0; 3.2	N/A	24.3; 24.4	10.6; 5.3
HoLEP	Kuntz/Ahyai et al	94.6.; 73.8	35.9; 37.2	1.0; 2.0	3; 10	3.0; 10.0	N/A	29.0; 27.5	8; 20
HoLEP	Montorsi et al	74.0; 57.0	36.1; 25.4	1.3; 2.4	11.5; 8.3	4.1; 3.9	1.4; 0.8	25.1; 24.7	N/A
HoLEP	Gupta et al	75.4; 62.6	17.2; 24.2	1.2; 2.0	N/A	5.2; 5.6	N/A	25.1; 23.7	20.0; 20.0
HoLEP	Tan/Wilson et al	62.1; 33.1	40.4; 24.7	0.7; 1.9	N/A	6.1; 5.2	1.25; 1.3	21.0; 19.0	33.7; 51.8
HoLEP vs open	Naspro et al	72.1; 58.3	59.3; 87.9	1.5; 4.1	4.8; 7.6	7.9; 8.1	1.5; 1.66	19.2; 20.1	N/A
KTP	Bouchiers-Hayes et al	31.3; 30.2	N/A	0.51; 1.9	N/A	12.0; 12.4	N/A	17.9; 20.6	37; 27
KTP	Horasanli et al	87; 51	N/A	1.7; 3.9	N/A	13.1; 6.4	N/A	13.3; 20.7	79; 23
KTP vs open	Alivizatos et al	80.0; 50.0	0.0; 73.5	1.0; 5.0	N/A	9.0; 8.0	1.0; 1.0	16.0; 15.1	17; 12

PCa = prostate cancer; IPSS = International Prostate Symptom Score; QoL = quality of life; Q_{max} = maximum flow rate; PVRU = postvoid residual volume urine; N/A = not available; TURP = transurethral resection of the prostate; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate.

USA). Forest plots were produced using the R software. All tests were two-sided, with a significance level of 0.05.

4. Results: minimally invasive surgical techniques compared to transurethral resection of the prostate

4.1. *Meta-analysis of functional outcomes*

4.1.1. *International Prostate Symptom Score*

Fig. 2 demonstrates that the most prominent change in symptom score from baseline is noted for HoLEP, being that this is the only procedure with a statistically significantly higher IPSS reduction ($p = 0.005$) compared to TURP. The remaining MISTs led to statistically comparable changes in IPSS as TURP.

4.1.2. *Quality of life*

Fig. 3 shows that the reduction in the IPSS QoL index following either bipolar TURP and bipolar TUVP or HoLEP is similar to TURP ($p > 0.3$). Because of the lack of standard deviations, KTP laser QoL data could not be pooled and analysed.

4.1.3. *Peak urinary flow rate*

All procedures improve Q_{max} in a statistically significant manner compared to their baseline data. Fig. 4 shows that of

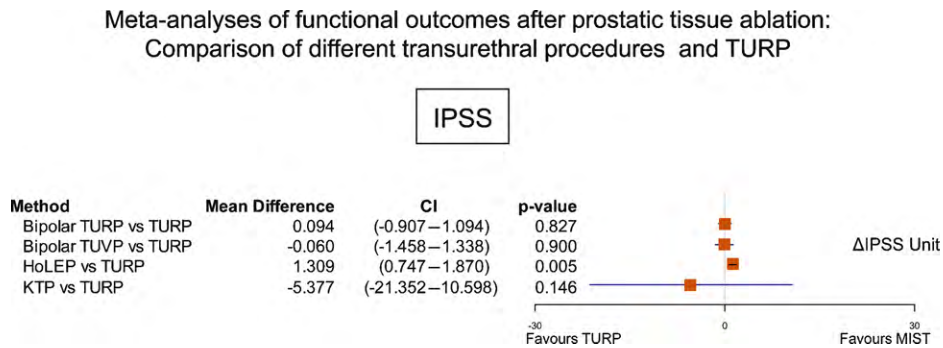

Fig. 2 – Forest plot for International Prostate Symptom Score.
CI = confidence interval; TURP = transurethral resection of the prostate; IPSS = International Prostate Symptom Score; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate; MIST = minimally invasive surgical technique.

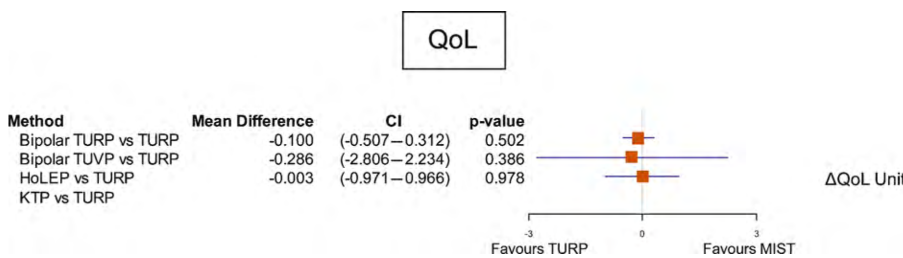

Fig. 3 – Forest plot for quality of life (question 8 of the International Prostate Symptom Score).
QoL = quality of life; CI = confidence interval; TURP = transurethral resection of the prostate; IPSS = International Prostate Symptom Score; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate; MIST = minimally invasive surgical technique.

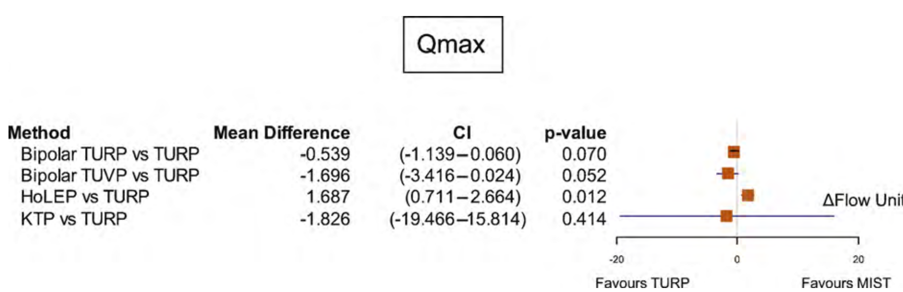

Fig. 4 – Forest plot for maximum flow rate.
Q_{max} = maximum flow rate; CI = confidence interval; TURP = transurethral resection of the prostate; IPSS = International Prostate Symptom Score; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate; MIST = minimally invasive surgical technique.

all MISTs, only HoLEP achieves a statistically significant higher increase of Q_{max} compared to TURP ($p = 0.012$). Bipolar TURP, bipolar TUVP, and KTP laser show no statistically significant differences of Q_{max} compared to TURP ($p > 0.052$; Fig. 4).

4.1.4. Postvoid residual urine

Fig. 5 compares PVRU reduction and demonstrates no statistically significant differences between TURP and any of the MISTs.

4.2. Descriptive and meta-analysis of complications

For statistical analyses, complications were categorically stratified into intraoperative, perioperative, and late adverse events. Additional stratification of complications into minor or major was omitted because of inconsistent definitions in the literature.

Tables 3–5 provide an overview of the type and frequency of intraoperative, perioperative, and late complications for the respective transurethral procedures. In

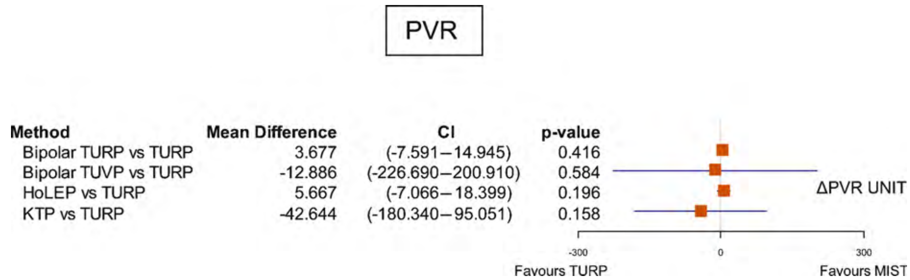

Fig. 5 – Forest plot for postvoid residual volume urine.
PVRU = postvoid residual volume urine; CI = confidence interval; TURP = transurethral resection of the prostate; IPSS = International Prostate Symptom Score; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate; MIST = minimally invasive surgical technique.

Table 3 – Treatment-specific intraoperative complications

Procedure	Bleeding	Capsular perforation	Conversion to TURP	Injury of the mucosa	Transfusion	TUR syndrome	Total
TURP, % (range)	0.3 (0–7.7)	0.1 (0–2.7)	0.0	0.0	2.0 (0–9)	0.8 (0–5)	3.2
Bipolar TURP, % (range)	0.0	0.0	0.0	0.0	1.9 (0–3.7)	0.0	1.9
Bipolar TUVP, % (range)	0.0	0.0	0.0	0.0	0.5 (0–2)	0.0	0.5
HoLEP, % (range)	0.0	0.2 (0–2)	0.0	3.3 (0.0–18.2)	0.0	0.0	3.5
KTP, % (range)	0.0	0.0	3.5 (0–8)	0.0	0.0	0.0	3.5

TURP = transurethral resection of the prostate; TUR = transurethral resection; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate.

Table 4 – Treatment-specific perioperative complications

Procedure	AUR, recatheterisation	Clot retention	Secondary apical resection	Secondary coagulation revision	Secondary haemorrhage	Episodes of haematuria	Urosepsis	UTI, fever	Total
TURP, % (range)	4.5 (0.0–13.3)	4.9 (0–39)	0.1 (0.0–3.3)	1.0 (0.0–14.3)	0.5 (0–8)	3.5 (0–100)	0.1 (0.0–3.3)	4.1 (0–22)	18.7
Bipolar TURP, % (range)	3.6 (0.0–10.4)	4.3 (0–16)	0.0	0.0	0.5 (0–8)	1.0 (0–58)	0.0	2.6 (0.0–11.5)	12.0
Bipolar TUVP, % (range)	8.2 (0–30)	5.3 (0–14)	0.0	0.0	0.5 (0–1)	0.0	0.0	0.0	14.0
HoLEP, % (range)	5.9 (0.0–16.6)	0.0	0.5 (0.0–3.3)	1.4 (0–5)	0.0	0.0	0.0	0.9 (0.0–4.9)	8.8
KTP, % (range)	9.9 (7.7–15.3)	0.0	2.1 (0.0–5.2)	0.0	0.7 (0–3)	0.0	0.0	12.0 (0–17)	24.7

AUR = acute urinary retention; UTI = urinary tract infection; TURP = transurethral resection of the prostate; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate.

Table 5 – Treatment-specific late complications

Procedure	Bladder neck stenosis	Urethral stricture	Reintervention due to BPE	Secondary treatment	Transient dysuria	Urgency	Stress UI	Total
TURP, % (range)	2 (0–21)	4.1 (0–21)	0.5 (0–7)	0.1 (0–4.3)	0.8 (0–22)	2.2 (0–38)	0.6 (0–5)	10.5
Bipolar TURP, % (range)	0.5 (0–4)	2.4 (0–8)	0.2 (0–3)	0.2 (0–2.9)	0	0.2 (0–2)	0	3.5
Bipolar TUVP, % (range)	0.5 (0–1)	1.9 (0–6)	2.4 (0–12)	0	2.9 (0–12)	0	0	7.7
HoLEP, % (range)	1.2 (0–3)	4.4 (2–8)	0	0	1.2 (0–10)	5.6 (0–44)	0.9 (0–3)	13.3
KTP, % (range)	5.0 (0–13)	6.3 (3–10)	5.6 (0–18)	0	8.5 (0–22)	0	0	25.4

BPE = benign prostatic enlargement; UI = urinary incontinence; TURP = transurethral resection of the prostate; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate.

total, six main intraoperative, eight perioperative, and seven late complications were recorded. It becomes apparent that each surgical procedure has its own specific risk and safety profile. The distribution of intraoperative, perioperative, late, and overall complications is displayed in Fig. 6. Independent of the surgical procedure, intraoperative complications occur less frequently than in the perioperative or late postoperative phases.

4.2.1. *Intraoperative complications*

Intraoperative complications are highest for TURP (3.2%) and HoLEP (3.5%). However, TURP dominates the variance of

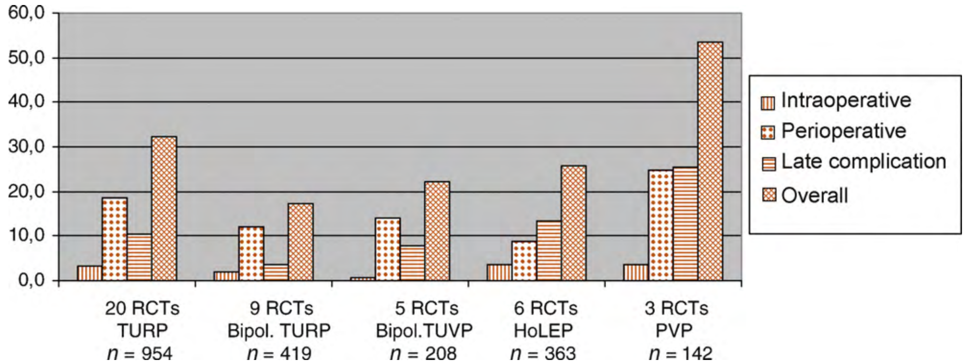

Fig. 6 – Treatment-specific distribution of intraoperative, perioperative, late, and overall complication (in percentage).
RCT = randomised controlled trial; TURP = transurethral resection of the prostate; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; PVP = photoselective vaporisation of the prostate.

intraoperative complications, including bleeding, capsular perforation, the need for blood transfusion, and TUR syndrome. Blood transfusions could not be entirely prevented in bipolar TURP and bipolar TUVP. Capsular perforation also occurred in HoLEP. Additionally, HoLEP carries the specific risk of bladder injury caused during morcellation of the enucleated tissue. Conversion to TURP, if considered as an intraoperative complication, is reported for the KTP laser. MISTs do not harbour the risk of TUR syndrome.

Table 3 shows that except for HoLEP, all other MISTs have numerically fewer intraoperative complications compared to TURP. The KTP laser even shows statistically significantly less intraoperative complications compared to TURP ($p = 0.002$; Fig. 7).

4.2.2. Perioperative complications

Acute urinary retention (AUR), clot retention, recurrent haematuria, and urinary tract infections (UTI) or fever are the most frequently reported adverse events after TURP (Table 4). To a lesser extent, the same profile is apparent after bipolar TURP. Of note for bipolar TUVP, a relatively high rate of AUR (8.2%) is recorded, clot retention being the most frequent cause. The lowest cumulative perioperative complication rates (<10%) have been demonstrated for HoLEP (5.9% AUR and 1.4% reoperation rate resulting from postoperative bleeding). KTP laser is associated with the highest perioperative complication rates, however, mainly consisting of AUR and UTI.

Fig. 8 demonstrates our meta-analysis of perioperative complications, indicating that MISTs in general have numerically less intraoperative complications compared to TURP. When bipolar TURP and TUVP were considered, this difference reached statistical significance ($p = 0.03$).

4.2.3. Late complications

The most important late complications for TURP consist of bladder neck strictures (BNS; 2%), urethral strictures (4.1%), and persistent urgency (2.2%; Table 5). Bipolar techniques have a similar adverse event profile. The lowest cumulative late complication rates are recorded for bipolar TURP and bipolar TUVP. However, bipolar TUVP has a trend towards higher retreatment rates (2.4%). Furthermore, transient dysuria ranging up to 8.3% seems a typical adverse event after bipolar TUVP. Late complications after HoLEP are comparable to TURP. KTP laser shows the highest cumulative late complications, consisting of BNS, urethral stricture, surgical reintervention, and transient dysuria. Fig. 9 shows that except for some trends, yet no statistical significant differences of late complications between MIST and TURP are found.

4.2.4. Overall morbidity

Fig. 10 demonstrates that despite the different risk and safety profiles, there is no statistical difference in the overall morbidity between the investigated MIST and TURP.

5. Discussion

5.1. *Conventional transurethral resection of the prostate*

In this review, 20 contemporary RCTs published between 2005 and 2009 with an overall sample size of 954 TURP patients and a maximum follow-up of 5 yr [9] were analysed. According to our analysis, TURP resulted in a substantial improvement of mean Q_{max} (+162%) and a significant reduction of mean IPSS (−70%), mean QoL scores (−69%), and mean PVRU (−77%). This is explained by true tissue removal with subsequent resolution of bladder outlet obstruction (BOO), indirectly shown by a 45–65% prostate-specific antigen (PSA) reduction [10,11] and by comparing preoperative and postoperative pressure flow studies (PFS) [10,12,13]. However, MISTs in general and bipolar TURP and HoLEP specifically seem to challenge the gold standard of efficacy (Figs. 2–5).

Major drawbacks of contemporary TURP remain intraoperative and perioperative complications. The current analyses demonstrate that the diversity of possible complications after TURP leads to an increased cumulative risk of adverse events. Most relevant complications include bleeding requiring blood transfusion (2%; range: 0–9), TUR syndrome (0.8%; range: 0–5), AUR (4.5%; range: 0–13.3), clot retention (4.9%; range: 0–39), and UTI (4.1%; range: 0–22). These findings are in agreement with the results of a recent prospective multicentre evaluation of 10 654 patients [2,14,15]. Indeed, in our comparative analysis, TURP was associated with the highest risk of bleeding with subsequent need for blood transfusion and remains the only procedure still harbouring the risk of documented TUR syndrome. The wide range of severe complications suggests that TURP-related adverse events are multifactorial, with prostate size and surgical experience probably having the greatest impact. In contrast, our analysis demonstrates that the overall morbidity of TURP is not statistically significantly different compared to minimally invasive procedures. This could be explained by the few late complications and the low long-term failure rate of TURP. In a nationwide analysis of 20 671 patients undergoing TURP, Madersbacher et al reported on a cumulative incidence of secondary TURP procedures of 2.9%, 5.8%, and 7.4% at 1, 5, and 8 yr, respectively, following the procedure [16].

Overall, functional results of TURP are satisfactorily but no longer necessarily superior to other MISTs. It has to be kept in mind that catheter time following TURP is the longest (mean: 2.84 d), and overall intraoperative and perioperative (major) complications remain not negligible. However, considering the limited long-term follow-up of MISTs and the low rate of late complication associated with TURP, the durability of TURP outcomes continues to be unsurpassed [1].

5.2. *Bipolar transurethral resection of the prostate*

The data from 10 RCTs comparing bipolar TURP (440 patients) and conventional TURP (450 patients) were analysed. Bipolar TURP is one of the most recent innovations in transurethral surgery, and all trials were published within the last 6 yr (2004–2008). Michielsen et al reported on the largest RCT (118 bipolar TURP vs 120 TURP patients) [17]. The longest follow-up data are derived from Autorino et al, who published a 3-yr update in 2007 [18]. A limitation of our analysis is that all eligible trials were assessed together, regardless of the different types of bipolar devices [19] applied.

As surgical technique and amount of resected tissue are not statistically significantly different from TURP [17,20–24], it is not surprising that functional results of bipolar TURP are similar to those of TURP (Figs. 2–6). Comparing monopolar and bipolar treatment in an RCT, Iori et al showed an equal resolution of obstruction by repeat PFS at 12 mo after the procedure [25]. In our analysis, the length of catheter time (mean: 2.7 d) after bipolar TURP appeared slightly shorter compared to monopolar TURP. Interestingly, the risk of blood transfusion in both techniques is comparable, suggesting a similar blood loss for monopolar and bipolar TURP. Blood transfusion represents the only reported intraoperative complication of bipolar TURP. None of the trials mentioned TUR syndrome as an adverse event of bipolar TURP. However, operation time was always <1 h, and resection weight did not exceed 37 g [23].

The perioperative complications are the same for monopolar and bipolar TURP (AUR, clot retention, and UTI). However, it is important to note that these complications are significantly less common in bipolar compared to monopolar TURP (Forest plot 2).

Of five RCTs with a minimum follow-up of 1 yr, three noted a higher incidence of stricture formation in the bipolar TURP arm [23,24,26], and two noted an equal distribution between bipolar and monopolar TURP [17,18].

Taken together, functional results of bipolar TURP are comparable to TURP. At the same time, the risk of TUR syndrome during bipolar TURP seems to be negligible in small to midsized prostates. Conversely, results for large prostates with longer operation times are pending. According to our analysis, the advantages of bipolar over monopolar TURP include less frequent complications and overall morbidity. These findings are in agreement with the very detailed meta-analysis of Mamoulakis et al [27]. The authors concluded that bipolar TURP is preferable because of its more favourable profile. However, more medium- and long-term follow-up data are needed to analyse the durability and late complications of bipolar TURP, specifically regarding the urethral stricture rates according to the different devices.

5.3. *Bipolar transurethral vaporisation of the prostate*

Evidence is derived from four RCTs, including a total of 187 patients undergoing bipolar TUVP [28–31]. These trials

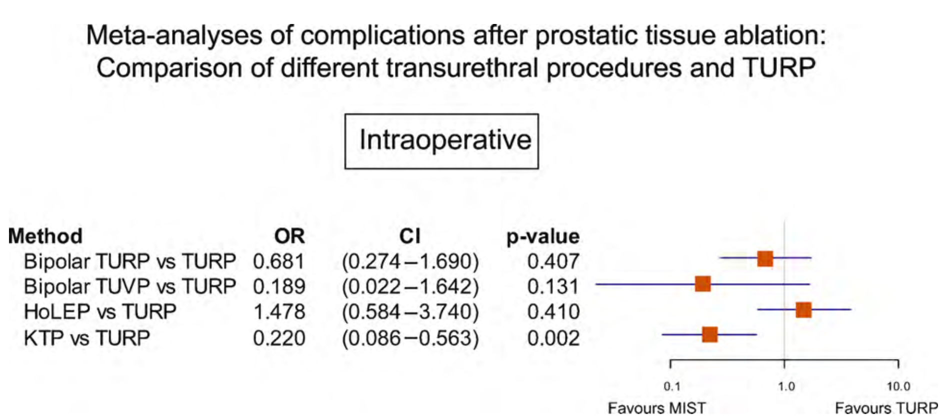

Fig. 7 – Forest plot of intraoperative complications.
TURP = transurethral resection of the prostate; OR = odds ratio; CI = confidence interval; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate; MIST = minimally invasive surgical technique.

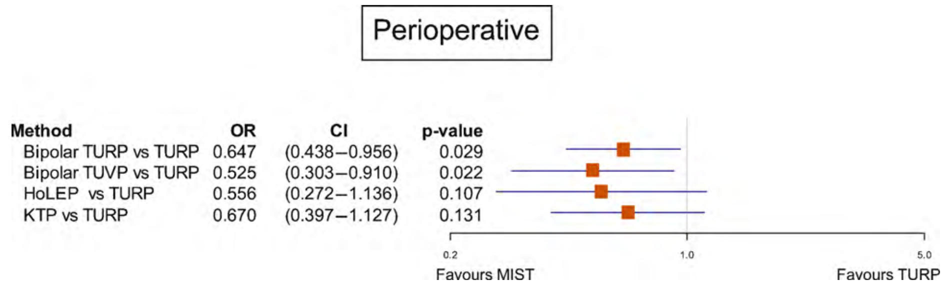

Fig. 8 – Forest plot of perioperative complications.
OR = odds ratio; CI = confidence interval; TURP = transurethral resection of the prostate; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate; MIST = minimally invasive surgical technique.

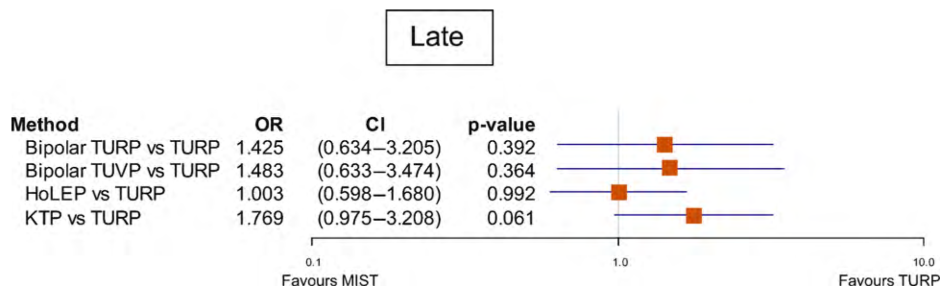

Fig. 9 – Forest plot of late complications.
OR = odds ratio; CI = confidence interval; TURP = transurethral resection of the prostate; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate; MIST = minimally invasive surgical technique.

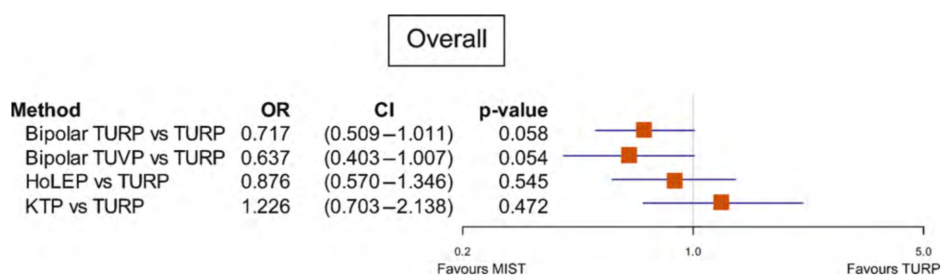

Fig. 10 – Forest plot of overall complications.
OR = odds ratio; CI = confidence interval; TURP = transurethral resection of the prostate; TUVP = transurethral vaporisation of the prostate; HoLEP = holmium laser enucleation of the prostate; KTP = potassium-titanyl-phosphate; MIST = minimally invasive surgical technique.

were published between 2003 and 2007. The maximum follow-up available is 3 yr. Our analyses demonstrate that after bipolar TUVP, the change in IPSS, QoL, and PVRU seem to be comparable to TURP. On the contrary, improvements of Q_{max} are borderline statistically significant ($p = 0.05$) in favour of TURP. Unfortunately, PFS to further clarify the impact of surgical technique (bipolar TUVP vs TURP) on BOO are lacking.

The catheter is removed earlier after bipolar TUVP compared to TURP (mean: 1.3 d vs 2.8 d). In our analysis, mean operation time for TUVP was 36 min, being thereby the shortest for all MISTs. Whether the absence of TUR syndrome is related to the short operative time or to the technique itself remains unclear. Nevertheless, intra-operative adverse events during bipolar TUVP appear to be minimal and are perioperatively statistically significantly less frequent compared to TURP. Tefekli et al were the only researchers who noted the need for blood transfusion in one patient undergoing this procedure using a hybrid technique (ie, vaporising the middle and lateral lobes but performing final apical resection with the resection loop) [31]. According to our analyses, the mean risk of postoperative AUR after bipolar TURP is 8.2% and seems relatively high compared to TURP. Dunsumir et al and Fung et al reported AUR rates following bipolar TUVP of 30% and 19%, respectively [20,28]. Clot retention in the bipolar TUVP arm was reported by Hon et al in only 11% (vs $n = 30$ patients for TURP) [29–31].

In 2007, Kaya and co-workers updated their 1-yr results to a further 2 and 3 yr of follow-up, respectively [30,32]. They demonstrated that improvement in IPSS and Q_{max} were significantly better and that the need for secondary surgery was significantly lower after TURP (6.6%) compared to bipolar TUVP (12%; $p < 0{,}05$). However, their small-sized study included only 25 bipolar TUVP and 15 TURP patients [30]. Tissue ablation using bipolar TUVP seems to be particularly difficult in the apical region of the prostate. Therefore, Kaya et al recommend using a bipolar resection loop around the verumontanum and apex. In agreement with Tefekli et al, they demonstrated a functional outcome comparable to TURP at a mean follow-up of 1.5 yr. However, postoperative severe storage symptoms, AUR with a need for recatheterisation, and urethral stricture formation were higher compared to conventional TURP [31].

In conclusion, the promising initial efficacy and safety profile of bipolar TUVP might be compromised by inferior clinical outcomes at midterm follow-up. Longer follow-up is needed to evaluate the efficacy of bipolar TUVP.

5.4. *Holmium enucleation of the prostate*

To determine outcomes and complications of HoLEP, data from four RCTs comparing HoLEP and TURP [10,12,13,33–36] and two additional RCTs comparing HoLEP and OP [37,38] were analysed in detail. HoLEP represents one of the first proposed MISTs, and recently, data on long-term follow-up ($\geq$5 yr) became available [39,40]. Functional results are at least as good as for TURP. In fact, according to our meta-analysis, the reduction in IPSS and the increase in Q_{max} are significantly more pronounced after HoLEP than after TURP (Figs. 2 and 4). As a consequence, HoLEP is the only endoscopic procedure to date with proven superior efficacy compared to TURP. This result is probably related to the surgical technique of HoLEP, which achieves prostatic cavities similar to those seen after simple OP [41]. Thus, if performed properly, a maximum amount of tissue is removed, resulting in complete resolution of obstruction as shown by PFS in a number of studies [10,12,13,42,43]. Furthermore, the substantial PSA reduction of >80% after HoLEP is an indirect sign of its ablative capabilities [10].

That said, operation time is significantly longer compared to TURP. Interestingly, when comparing mean tissue retrieval rates (grams per minute) of HoLEP and TURP within the analysed studies, there was no significant difference (0.52 g/min vs 0.57 g/min), suggesting that the two procedures are equally (time) efficient. Mean duration of indwelling catheter time is 1.13 d and shorter than after TURP.

Potential intraoperative complications consist of capsular perforation (as the laser fibre cuts along the surgical capsule), injury to the bladder mucosa (caused by the morcellator blades) [13,38,44–46], or (rarely) postponed morcellation (resulting from technical defects of the morcellator) [44,47]. HoLEP is prostate-size independent [48] and can be used as an alternative surgical approach to OP in large prostates [37,44]. Thus far, TUR syndrome after HoLEP has never been reported, even in very large prostates. The risk of relevant bleeding and the need for blood transfusion are also minimal (Tables 3–5). None of the RCTs reports the need for blood transfusion, but some of the prospective trials do in 1–1.7% of cases [44,47,49]. Perioperative and late adverse events are similar to TURP, including AUR secondary to blood clot formation, UTI, and BNS or urethral stricture formation (Table 5). Overall, postoperative urgency seems to be slightly higher in HoLEP patients and occurs in 5.6% and 2.2% of cases after HoLEP and TURP, respectively. Of note, in contradiction to the majority of comparative RCTs, more early and transient dysuria and urgency after HoLEP compared to TURP or OP may be encountered [13,38]. Stress urinary incontinence is $\leq$1% and seems to occur in a similar frequency as in TURP [50].

In summary, HoLEP is at least as effective as TURP. Despite no statistically significant differences in overall morbidity, complications are less frequent after HoLEP compared to TURP. In addition, long-term follow up of HoLEP shows durability of the excellent postoperative results. These findings, plus the fact that the HoLEP procedure is prostate-size independent, in contrast to TURP, makes HoLEP a strong competitor for the new reference standard in transurethral surgery for symptomatic BPE.

5.5. *Potassium-titanyl-phosphate laser*

Currently, three RCTs with limited follow-up (up to 1 yr) are available: two comparing KTP laser to TURP [11,51] and one KTP laser to OP [52]. Although photoselective laser vaporisation of the prostate performed with the KTP laser (80 W) at 532 nm was initially proposed for the treatment of high-risk anticoagulated patients [53], it rapidly achieved broader clinical use. Most of the evidence of midterm efficacy and safety comes from prospective but not randomised trials [54–56]. Functional results of the three available RCTs suggests comparable efficacy to TURP. Horasanli et al and Alivizatos et al evaluated the use of the KTP laser in larger-sized prostates and reported that IPSS values remained higher at 6 and 12 mo of follow-up compared to TURP or OP [11,52]. However, for small to midsize prostates, a comparable symptom score reduction for KTP laser and TURP was achieved [57].

Recently, Hamann et al published the first prospective study on KTP laser vaporisation of the prostate, demonstrating equip-effective resolution of obstruction for small to midsized prostates by repeat PFS [55]. In their study cohort, the mean PSA reduction was 37.1% at 12 mo after KTP laser. Similarly, Ruszat et al were able to demonstrate a significant average PSA decrease of 49% in the so-far largest prospective non-RCT series of 500 GreenLight laser patients. However, they noted a significantly lower relative decrease of total PSA with increasing prostate size, potentially indicating less vaporisation. In summary, for small to midsized prostates, the available data demonstrate that the KTP laser may be equivalent to TURP. For larger prostates, however, further prospective studies are warranted. It is not unlikely that these studies incorporating the 120-W lithium triborate (LBO) laser could potentially tackle larger prostates more efficiently and overcome the currently significantly longer operating times of the KTP laser. It has been a universal finding of all trials that catheter time independent of prostate size is significantly shorter after KTP laser vaporisation (mean: 1.08 d) compared to TURP.

Conversion to TURP because of impaired visibility caused by bleeding is the only documented intraoperative adverse event of KTP laser vaporisation. In patients with large prostates, Alivizatos et al reported that in 7.7% of the patients, electrocoagulation was briefly used to achieve adequate haemostasis [58]. Ruszat et al experienced intraoperative bleeding in 3.6% of cases, which led to a conversion to TURP in 1.4% of patients undergoing KTP laser vaporisation [56]. However, the good haemostatic properties of the KTP laser and its use with saline irrigation avoid the risk of blood transfusion and TUR syndrome, even in patients with ongoing anticoagulation and longer operation times [53]. In our analysis, intraoperative complications with the KTP laser were statistically significantly lower compared to TURP (Fig. 7). The majority of studies, irrespective of their design, mention AUR and UTI as the most frequent perioperative complications. These adverse events range from 0–15% (Table 3). Compared to TURP, prolonged postoperative storage symptoms after KTP laser are not uncommon. Most of the reviewed trials report a mean rate of 10% (range: 10–22) for transient dysuria [51,54,56,58–62]. Surgical experience, previous treatment with finasteride, total laser energy used, and the degree of laser fibre degradation are potential explanations for this phenomenon [63,64].

So far, comparative trials of KTP laser vaporisation of the prostate and TURP report similar rates of BNS and urethral strictures. Still, there is a need for more medium- and long-term FU specifically to evaluate the risk for reintervention because of persisting or recurrent BOO. Our pooled results, pointing at an average reintervention rate of 5.6% per year, may be biased by the Horasanli trial, in which large prostates (mean of 86 ml in transrectal ultrasound [TRUS]) were treated. The authors reported a remarkably high reintervention rate of 18% at 6 mo. Still, referring to a recently published updated cohort study, the rate of reintervention (repeat KTP laser/TURP) was 6.7% for the KTP laser versus 3.9% for TURP, which was statistically significant at 2 yr of follow-up [54]. In contrast, the most extended non-RCT follow-up data (with some patients completing up to 5 yr following KTP laser vaporisation of the prostate) demonstrated a TURP-like reintervention rate of 6.9% [56,65].

Overall, in small to midsized prostates, the KTP laser shows promising results with (so far) comparable efficacy to TURP. In large prostates, these results are controversial, which further stresses the need for evidence-based guidelines on indications for vaporisation techniques, specifically with respect to prostate size.

In KTP laser vaporisation of the prostate, intraoperative complications are generally rare (even in patients with ongoing anticoagulation). Instead, complications seem to increase postoperatively. However, the overall complication rate is statistically significantly not different compared to TURP ($p = 0.472$). More RCTs with medium- to long-term follow-up are needed to determine the durability of KTP laser vaporisation of the prostate.

6. Other new procedures

Reich et al [66] most recently published initial clinical results of bipolar plasma vaporisation of the prostate with a mushroom-like electrode. The rational for this bicentre feasibility study was based on the introduction of a new vaporisation device with a similar safety and efficacy profile as the GreenLight laser but at substantially lower costs. Despite the promising results, the authors concluded that RCTs are needed, as their prospective study on 30 patients was not comparative and had only 6 mo of follow-up. In addition, ablation of the prostate using the diode laser at different wavelengths and power might be of interest [67–69]. However, again there is not a single RCT. And the latest case control study comparing the 120-W LBO laser and a 980-nm high-intensity diode laser demonstrated statistically significantly higher rates of BNS, retreatment, and stress UI for the diode laser already in the short-term outcome [70].

At present, there is one RCT with 1-yr follow-up and four nonrandomised feasibility studies on the thulium laser for prostate tissue ablation [71–75]. Because the body of evidence for the thulium laser is still limited, a detailed comparative meta-analysis is not feasible yet. Still, the efficacy and safety profile of the 52 thulium laser vaporesection results from the RCT published by Xia et al [71] seems promising, as it parallels the results of holmium laser resection of the prostate presented by Gilling et al 10 yr ago [12]. Bach et al [75] recently demonstrated the feasibility of thulium:yttrium aluminium garnet laser enucleation of the prostate in 88 men mimicking HoLEP. Independent of the surgical technique, all studies using the thulium laser reported a significant improvement in functional results after a mean catheter time of 1–2 d. Xia et al [71] reported only three types of complications after thulium laser vaporesection of the prostate: UTI (3.9%), transient urgency (23.1%), and urethral stricture (1.9%). Based on the data derived from non-RCTs, other potential complications after thulium laser consist of intraoperative bleeding (3.4%), blood transfusion (0.7–3.6%), AUR (3.6–7.7%), secondary apical resection shortly after the initial procedure (2.2–7.2%), secondary haematuria (1–3%), BNC (1.8%), and reintervention because of a recurrence of symptoms or tissue (2.3–3%) [72–75]. Obviously, the latter information from non-RCTs dilutes the published safety profile of thulium laser vaporesection of the prostate by Xia et al [72]. This underlines the necessity for further well-designed RCTs to evaluate the future role of the thulium laser for prostatic tissue ablation.

7. Conclusions

This meta-analysis demonstrates statistically comparable efficacy and overall morbidity for MISTs versus contemporary TURP, although only a limited number of RCTs and few long-term data are available. However, type, category (minor vs major), and the number of complications (safety profile) vary specifically for each of the different transurethral techniques used for the treatment of clinical BPE.

This might be a meaningful advantage over TURP in selected patients. Hence, TURP seems to loose its monopoly.

We feel that after considering the patient's performance status, medication, prostate size, and personal expectations, the selection of the most appropriate transurethral technique for the individual patient must be of the utmost importance. Still, more evidence in terms of RCTs and longer follow-up is desirable for bipolar TUVP and GreenLight laser and essential for the very recently introduced techniques (eg, thulium laser ablation or enucleation of the prostate). Innovative techniques need to be performed as part of randomised studies; otherwise, our urologic armamentarium might be changed by an "early-adopter bias" of aggressive marketing of novel techniques. Bipolar TURP and HoLEP passed the phase of feasibility. For bipolar TURP, further long-term data are still warranted to define its place in contemporary BPE management. For HoLEP, the next step is its broader clinical application outside of experienced centres, ideally, under the mentorship of established HoLEP surgeons to generally shorten the learning curve.

Author contributions: Sascha A. Ahyai 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: Ahyai, Gilling, Kaplan, Kuntz, Madersbacher, Montorsi, Speakman, Stief.
Acquisition of data: Ahyai, Gilling, Kaplan, Kuntz, Madersbacher, Montorsi, Speakman, Stief.
Analysis and interpretation of data: Ahyai, Gilling, Kaplan, Kuntz, Madersbacher, Montorsi, Speakman, Stief.
Drafting of the manuscript: Ahyai, Gilling, Kaplan, Kuntz, Madersbacher, Montorsi, Speakman, Stief.
Critical revision of the manuscript for important intellectual content: Ahyai, Gilling, Kaplan, Kuntz, Madersbacher, Montorsi, Speakman, Stief.
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