Original Article
Prostate diseases and male voiding dysfunctions

pISSN: 2287-4208 / eISSN: 2287-4690
World J Mens Health 2022 Jan 40(1): 127-138
https://doi.org/10.5534/wjmh.210115

The World Journal of MEN's HEALTH

Transurethral Microwave Thermotherapy for Benign Prostatic Hyperplasia: An Updated Cochrane Review

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Purpose: To assess the effects of transurethral microwave thermotherapy (TUMT) for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia (BPH).

Materials and Methods: We performed a comprehensive search using multiple databases up to May 2021, with no language or publication status restrictions. We included parallel-group randomized controlled trials of participants with BPH who underwent TUMT. We used standard Cochrane methods, including a GRADE assessment of the certainty of the evidence (CoE).

Results: In this update of a previous Cochrane review, we included 16 trials with 1,919 participants. TUMT probably results in little to no difference in urologic symptom scores at short-term follow-up compared to transurethral resection of the prostate (TURP). There is likely to be little to no difference in the quality of life. TUMT likely results in fewer major adverse events. TUMT, however, probably results in a large increase in the need for retreatment. There may be little to no difference in erectile function between these interventions. However, TUMT may result in fewer cases of ejaculatory dysfunction compared to TURP. The overall CoE was moderate to low.

Conclusions: TUMT provides a similar reduction in urinary symptoms compared to TURP, with fewer major adverse events and fewer cases of ejaculatory dysfunction at short-term follow-up. However, TUMT probably results in a large increase in retreatment rates. Study limitations and imprecision reduced the confidence we can place in these results.

Keywords: Lower urinary tract symptoms; Microwaves; Minimally invasive surgical procedures; Prostatic hyperplasia

INTRODUCTION

Benign prostatic hyperplasia (BPH) may cause prostatic enlargement and subsequently compression of the urethra and obstruction. BPH acquires clinical significance when associated with bothersome lower urinary tract symptoms (LUTS) [1]. BPH can progress and cause serious consequences such as acute urinary retention, urinary tract infection, and upper urinary tract deterioration. Initial evaluation of LUTS sugges-

Received: Jul 4, 2021 **Accepted:** Jul 6, 2021 **Published online** Aug 4, 2021
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tive of BPH includes patient history, physical examination including a digital rectal examination, urinalysis, prostate-specific antigen (PSA) blood test, voiding diary, and International Prostate Symptom Score (IPSS) [2,3]. Measurements of maximum flow rate (Qmax) and postvoid residual are also often used in diagnosis and treatment decisions [2].

Treatment decisions are based on symptoms and the degree of bother noted by the patient. Initial treatment options for BPH include conservative management (watchful waiting and lifestyle modification) and medication (alpha-blockers and 5-alpha reductase inhibitors) [2]. If patients have been refractory to conservative and medical treatment and BPH causes subsequent complications, such as acute urinary retention, recurrent urinary tract infection, bladder stones or diverticula, hematuria, or renal insufficiency, surgical options are considered [2]. Clinical guidelines recommend monopolar or bipolar transurethral resection of the prostate (TURP) as a standard treatment modality for subjective symptom relief and objective improvements in urinary flow, but this procedure is also associated with significant morbidity and long-term complications, including hematuria requiring blood transfusion, urethral stricture, recurrent urinary tract infection, and urinary incontinence [2]. Moreover, men may experience ejaculatory (65%) and erectile dysfunction (10%) related to TURP [4]. Furthermore, BPH is a disease common in older men who have an increased risk of complications for general anaesthesia and the surgery itself [5]. Some alternatives to TURP include laser enucleation, vaporisation, and Aquablation, but they all require spinal anaesthesia [2]. In recent years, the number of men undergoing TURP has steadily declined due to increasing pharmacologic treatments (alpha-blockers and 5-alpha-reductase inhibitors) and minimally-invasive treatments that are usually performed under local anaesthesia [6], such as convective radiofrequency water vapour therapy [7], prostatic urethral lift [8], prostatic arterial embolisation [9] which are covered in current evidence-based guidelines [10].

Transurethral microwave thermotherapy (TUMT) uses microwave-induced heat to ablate prostatic tissue and is designed to have fewer major complications than TURP [11]. The patient is treated in an outpatient setting under local anaesthesia. The treatment catheter is then placed within the urethra, confirmed by the return of sterile water and transabdominal or transrectal ultrasound, and the balloon is inflated. The catheter is composed of a curved tip, a temperature sensor and a microwave unit. The distal port contains the bladder balloon, allowing for urine drainage and cooling. A rectal probe may be inserted to monitor the rectal temperature [12]. TUMT has evolved over the past decades, incorporating urethral cooling, thus allowing higher energy delivery and reducing the procedure time to around 30 minutes and improved outcomes, but the higher energy leads to more significant discomfort during the procedure, in which patients often require sedation and analgesia, with a continued risk of urinary retention [11].

While TUMT was once the most widely-used procedure for minimally-invasive surgical therapies among the USA's Medicare population [13], its use has declined since its peak in 2006 [14]. A recent study in Australia highlighted that TUMT currently constitutes only 0.26% of all procedures performed for BPH [15].

This is an abridged version of an updated Cochrane review focusing on comparing TUMT *versus* TURP. This review aimed to assess the effects of TUMT to treat LUTS in men with BPH. The full review details the methods and additional results and analyses [16].

MATERIALS AND METHODS

1. Inclusion criteria

We updated the methods of this review based on the protocol of a suite of reviews on minimally invasive treatments for LUTS [7-9]. We included parallel-group RCTs regardless of their publication status or language. We included men over the age of 40 with a prostate volume of 20 mL or greater with LUTS as determined by IPSS of eight or over, and a Qmax <15 mL/s, as measured by non-invasive uroflowmetry, invasive pressure flow studies, or both. We excluded studies of men with active urinary tract infection, bacterial prostatitis, chronic renal failure, untreated bladder calculi or large diverticula, prostate cancer, and urethral stricture disease, as well as those who had undergone prior prostate, bladder neck, or urethral surgery. We also exclude studies of people with other conditions that affect urinary symptoms, such as neurogenic bladder due to spinal cord injury, multiple sclerosis, or central nervous system disease.

Our comparison included TUMT *versus* TURP, other minimally invasive treatments, or sham. We did not

use the measurement of the outcomes assessed in this review as an eligibility criterion. Our primary outcomes included urologic symptom scores, quality of life, and major adverse events. Our secondary outcomes were retreatment, erectile function, ejaculatory function, minor adverse events, acute urinary retention, and indwelling urinary catheter. We considered the clinically important differences for the review outcome measures to rate the overall certainty of evidence [17]. We considered outcomes measured up to and including 12 months after randomisation as short-term and later than 12 months as long-term for urologic symptom scores, quality of life, major adverse events, retreatment, erectile function, ejaculatory function, minor adverse events, and acute urinary retention. We assessed retreatment, indwelling urinary catheter and hospital stay as short-term only.

2. Search methods

We performed a comprehensive search with no restrictions by date, by the language of publication or publication status. We searched the following sources on May 31st 2021: CENTRAL (Cochrane Central Register of Controlled Trials); MEDLINE (Ovid); Embase (Elsevier); LILACS (Bireme); CINAHL; Scopus; Web of Science (Clarivate analytics); ClinicalTrials.gov; World Health Organization International Clinical Trials Registry Platform. We also performed searches in additional resources.

3. Data collection and analysis

We used Covidence software (Veritas Health Innovation, Melbourne, Australia) to identify and remove potential duplicate records. Two review authors (JVAF, LG) independently screened articles for eligibility and independently extracted data [18]. We presented a PRISMA 2020 flow diagram showing the process of

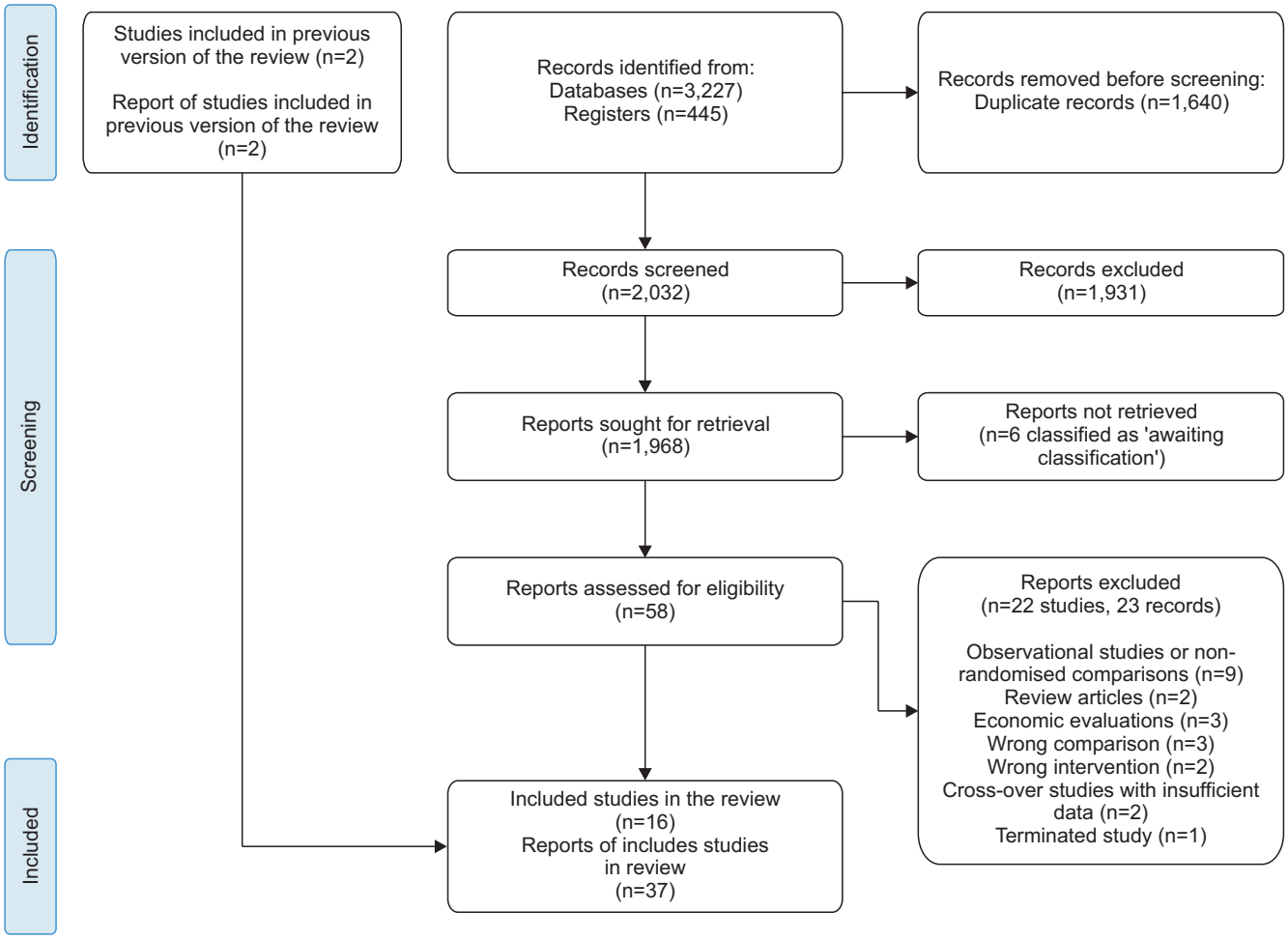

Fig. 1. PRISMA flow diagram.

https://doi.org/10.5534/wjmh.210115

Table 1. Characteristics of the included studies

Study name	Trial period	Setting/country	Description of participants	Duration of follow-up (mo)	Intervention and comparator	Age (y)	IPSS	Prostate volume (mL)
Abbou et al, 1995 [21]	N/A	France	Men ≥50 years with symptoms >3 months, prostate 30–80 g, PFR <15 mL/s, PVR <300 mL	12	TUMT (Thermex II, Prostcare, BSD-50)	65±8	N/A	45±15 g
					Sham	66±7	N/A	44±11 g
Ahmed et al, 1997 [22]	N/A	UK	Men ≥55 years with AUA score >12, >1 year, prostate 25–100 mL, PFR <15 mL/s, and a PVR <300 mL	6	TUMT (Prostatron)	69.36	18.5	36.6
					TURP	69.45	18.4	46.1
Albala et al, 2002 [23]	N/A	USA	Men 50–80 years, AUA index >13 and a bother score >11, PFR <12 mL/s, and PVR >125 mL; prostate 30–100 mL without a significant intravesical middle lobe	12	TUMT (TMx-2000)	65.2±7.3	22.2±5.0	50.5±18.6
					Sham	64.6±7.1	22.7±5.7	47.1±17.9
Bdesha et al, 1994 [24]	N/A	UK	Men with prostatism (WHO score >14), PVR >50 mL, and PFR <15 mL/s	3	TUMT (LEO Microthermer)	63.7	19.2	N/A
					Sham	62.6	18.8	N/A
Blute et al, 1996 [25]	N/A	USA	Men suffering from urinary symptoms (Madsen Symptom score >8), PVR 10,000 mL, PFR <10 mL/s, and prostate length 30–50 mm	12	TUMT (Prostatron)	66.9±7.8	19.9±7.2	37.4±14.2
					Sham	66.9±7.1	20.8±6.7	36.1±13.4
Brehmer et al, 1999 [26]	N/A	Sweden	Men suffering from lower urinary tract symptoms and with an enlarged prostate	12	TUMT (30' - 60' - ECP system)	70.4	N/A	N/A
					Sham			
D'Ancona et al, 1998 [28]	1994–1995	Netherlands	Men ≥45 years with Madsen score >8 months, prostate 2.5–5 cm/30–100 mL, PFR <15 mL/s, and PRV <350 mL	24	TUMT (Prostatron)	69.6±8.5	16.7±5.6	45±15
					TURP	69.3±5.9	18.3±6.3	43±12
Dahlstrand et al, 1995 [27]	N/A	Sweden	Men ≥45 years with Madsen score >8 months, prostate 3.5–5 cm, PFR <15 mL/s, and PRV >150 mL	24	TUMT (Prostatron)	68	N/A	33
					TURP	79	N/A	37
De Wildt et al, 1996 [29]	1991–1992	Netherlands/UK	Men ≥45 years with Madsen score >8 months, PFR <15 mL/s, and PRV >150 mL	12	TUMT (Prostatron)	63.3±8.1	N/A	48.6±16.6
					Sham	66.9±6.0	N/A	49.0±20.0
Floratos et al, 2001 [30]	1996–1997	Netherlands	Men ≥45 years, prostate ≥30 cm3, prostatic urethral length ≥25 mm, a Madsen symptom score ≥8, PFR ≤15 mL/s, and PVR ≤350 mL	36	TUMT (Prostatron)	68	21	42
					TURP	66	20	48
Larson et al, 1998 [31]	1994–1996	USA	Men ≥45 years with AUA score >9, enlarged prostate (3–5 cm TRUS), and PFR <12 mL/s without a significantly enlarged middle lobe	12	TUMT (Targis)	66	20.8	38.1
					Sham	65.9	21.3	44.7
Nawrocki et al, 1997 [32]	N/A	UK	Men with a Madsen symptom score ≥8, PFR ≤15 mL/s, PVR >150 mL, and detrusor pressure >70 cmH2O	6	TUMT (Prostatron)	70	19	41.2±14.6
					Sham		17.5	46.7±16.8
Nørby et al, 2002 [33]	1996–1997	Denmark	Men ≥50 years, IPSS ≥7, and PFR ≤12 mL/s	6	TUMT (Prostatron)	66±7	20.5±5.7	43
					TURP/TUIP	68±7	21.3±6.6	44
Roehrborn et al, 1998 [34]	N/A	USA	Men ≥55 years, AUA-SI ≥13, PFR ≤12 mL/s, and prostate volume 25–100 mL	6	TUMT (Dornier)	66.3±6.5	23.6±5.6	48.1±16.2
					Sham	66.0±5.8	23.9±5.6	50.5±18.1

Table 1. Continued

Study name	Trial period	Setting/country	Description of participants	Duration of follow-up (mo)	Intervention and comparator	Age (y)	IPSS	Prostate volume (mL)
Venn et al, 1995 [35]	N/A	UK	Men with a Madsen symptom score ≥8 and PVR <250 mL	6	TUMT (Microwave Engineering Designs)	70.5	19.2	40.4
					Sham	68	20.1	40.6
Wagrell et al, 2002 [36]	1998–1999	Scandinavia/USA	Men IPSS ≥13, PFR ≤13 mL/s, and prostate volume 30–100 mL	5 years	TUMT (ProstaLund Feedback)	67±8	21.0±5.4	48.9±15.8
					TURP	69±8	20.4±5.9	52.7±17.3

Values are presented as mean±standard deviation or mean only.
IPSS: International Prostate Symptom Score, N/A: not available, PFR: peak flow rate, PVR: postvoid residual, TUMT: transurethral microwave thermotherapy, AUA: American Urological Association, TURP: transurethral resection of the prostate, WHO: World Health Organization, LEO: laser electro optics, TUIP: transurethral incision of the prostate, AUA-SI: American Urological Association Symptom Index.

study selection [19]. Two review authors (JVAF, LG) authors independently extracted data and assessed the risk of bias of the included studies using the Cochrane risk-of-bias tool for randomized trials [20]. We summarized data using a random-effects model. We planned to assess heterogeneity statistically with the I^2 statistic >50% were considered to indicate substantial heterogeneity. We planned to test for publication bias by assessing funnel plot asymmetry, but the number of trials per comparison was insufficient. We used Review Manager 5 software (Cochrane Collaboration, Copenhagen, Denmark) to perform the statistical analyses. When possible, we explored the effect of bias in the effect estimates and performed pre-defined subgroup analysis. We intended to explore the effect of bias in the results, but all studies were at a high or unclear risk of bias. We included a 'Summary of findings' table reporting the primary outcomes using the GRADE approach.

RESULTS

We identified 3,227 records from electronic databases, including 445 records from trial registers. After removing duplicates, we screened the titles and abstracts and then full texts, finally including 16 randomized controlled trials (37 reports) in this review (see Fig. 1 for PRISMA flow chart and Table 1 for a summary of the study's characteristics) [21-36]. The list of excluded studies is available in the full version of the review [16]. All studies were at an overall high or unclear risk of bias (see Fig. 2). In this abridged version of the review, we summarize the findings of the six studies with 632 randomized participants in the main comparison of TUMT *versus* TURP [22,27,28,30,33,36]. Most studies did not report their funding sources; three studies were funded by their manufacturers [31,34,36], two by public institutions [32,33], and one by a combination of manufacturers and public funders [21]. See Table 2 for a summary of the main results.

1. Urologic symptom scores

Based on four studies with 306 participants, TUMT probably results in little to no difference in urologic symptom scores measured by IPSS scores when compared to TURP at 6 to 12 months follow-up (mean difference [MD], 1.00; 95% confidence interval [CI], -0.03 to 2.03) [22,28,33,36]. In two studies with 108 participants

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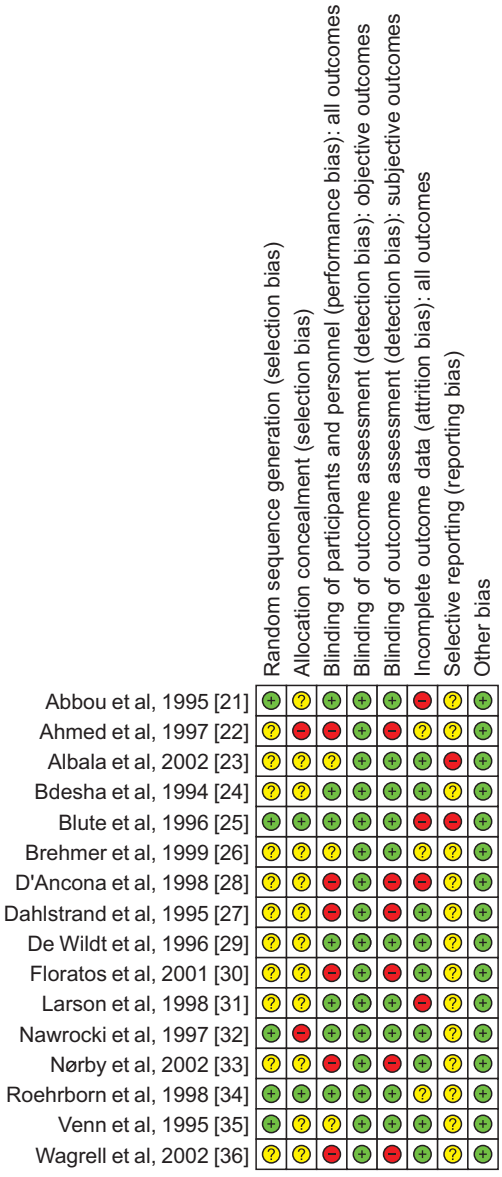

Fig. 2. Risk of bias of the included studies.

that assessed this outcome with the Madsen-Iversen score (range 0 to 28), a small difference was found favouring TURP (MD, 1.59; 95% CI, 0.69–2.48; 2 studies, 108 participants; I^2=0%) [27,28]. The certainty of the evidence is moderate due to an overall high risk of bias. As for long-term data, three studies with 187 participants reported long-term data, and we are uncertain of the effect of TUMT on urologic symptom scores when compared to TURP at 2- to 5-year follow-up (standardized MD, 0.32; 95% CI, 0.03–0.62; I^2=0%) [27,28,36]. Another study with 155 participants was not incorporated in meta-analysis due to missing data and reported that the TUMT group had a reduction in IPSS scores from 20 to 12 at three years, whereas the TURP group had a reduction from 20 to 3 in the same period (p<0.001) [30]. The certainty of the evidence is very low due to an overall high risk of bias (severe attrition at long-term follow-up) and imprecision.

2. Quality of life

Based on one study with 136 participants, TUMT likely results in little to no difference in the quality of life compared to TURP at 12-month follow-up (MD, -0.10; 95% CI -0.67 to 0.47) [36]. Another study with 66 participants reported similar scores in quality of life in the TUMT group (median, 2; interquartile range [IQR] 1–3) and in the TURP group (median, 1; IQR, 1–2) at six-month follow-up (p=0.64 from a three-arm comparison with interstitial laser coagulation) [33]. The certainty of the evidence is moderate due to an overall high risk of bias. As for long-term data, TUMT may result in little to no difference in the quality of life compared to TURP at 60-month follow-up (MD, 0.00; 95% CI, -0.46 to 0.46) [36]. Another study with 155 participants reported that quality-of-life scores decreased from 4 to 2 at three years in the TUMT group and from 4 to 1 in the TURP group (p<0.001) [30].

3. Major adverse events

Based on six studies with 525 participants, TUMT probably results in significantly fewer major adverse events when compared to TURP at 6- to 12-month follow-up (risk ratio [RR], 0.20; 95% CI, 0.09–0.43; I^2=0%) [22,27,28,30,33,36]. Based on 168 cases per 1,000 men in the TURP group, this corresponds to 135 fewer (153 to 96 fewer) per 1,000 men in the TUMT group. These events primarily included: hospitalization due to bleeding, clot retention, serious infection, TURP syndrome, urethral stricture (requiring another surgical intervention). The certainty of the evidence is moderate due to an overall high risk of bias.

4. Retreatment

Based on five studies with 463 participants, TUMT probably results in a large increase in the need for retreatment at 6- to 36-month follow-up (RR, 7.07; 95% CI, 1.94–25.82; I^2=0%) [27,28,30,33,36]. Retreatment was usually TURP, TUMT, or TUMT and then TURP. Based on no cases per 1,000 men in the TURP group, this corresponds to 90 more (40 to 150 more) per 1,000 men in the TUMT group. The certainty of the evidence is

Table 2. TUMT compared to TURP for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia

Outcome	No. of participants (studies) Follow-up	Certainty of the evidence (GRADE[b])	Relative effect (95% CI)	Anticipated absolute effects[a] (95% CI)	
				Risk with TURP	Risk difference with TUMT
Urologic symptom scores Assessed with: IPSS Scale from 0 (best: not at all) to 35 (worst: almost always) Follow-up: 6–12 months	306 (4 RCTs)	⨁⨁⨁⊖ MODERATE[c]	-	The mean urologic symptoms score (IPSS) was 5.63	Mean differences 1.00 higher (0.03 lower to 2.03 higher)
Quality of life Assessed with: IPSS-QoL Scale from 0 (best: delighted) to 6 (worst: terrible) Follow-up: 12 months	136 (1 RCT)	⨁⨁⨁⊖ MODERATE[c]	-	The mean quality of life was 1.5	Mean differences 0.10 lower (0.67 lower to 0.47 higher)
Major adverse events Assessed with: Clavien–Dindo classification system (Grade III, IV, and V complications) Follow-up: 6–12 months	525 (6 RCTs)	⨁⨁⨁⊖ MODERATE[c]	RR 0.20 (0.09–0.43)	168 per 1,000	Study population 135 fewer per 1,000 (153 fewer to 96 fewer)
Retreatment Participants requiring additional procedures or surgery Follow-up: 6–12 months	463 (5 RCTs)	⨁⨁⨁⊖ MODERATE[c,d]	RR 7.07 (1.94–25.82)	0 per 1,000	Study population 90 more per 1,000 (40 more to 150 more)
Erectile function (sexually active men only) Assessed with: issues related to erectile function Follow-up: 6–12 months	337 (5 RCTs)	⨁⨁⊖⊖ LOW[c,e]	RR 0.63 (0.24–1.63)	129 per 1,000	Study population 48 fewer per 1,000 (98 fewer to 82 more)
Ejaculatory function (sexually-active men only) Assessed with: issues related to ejaculatory function Follow-up: 6–12 months	241 (4 RCTs)	⨁⨁⊖⊖ LOW[c,e]	RR 0.36 (0.24–0.53)	523 per 1,000	Study population 335 fewer per 1,000 (397 fewer to 246 fewer)

Patient or population: men with lower urinary tract symptoms due to benign prostatic hyperplasia. Setting: outpatient (TUMT)/inpatient (TURP)-UK, Netherlands, Scandinavia, USA. Intervention: TUMT. Comparison: TURP.

TUMT: transurethral microwave thermotherapy, TURP: transurethral resection of the prostate, CI: confidence interval, RCT: randomized controlled trial, IPSS: International Prostate Symptom Score, IPSS-QoL: IPSS-quality of life, RR: risk ratio.

[a]The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]GRADE Working Group grades of evidence: (1) High certainty: We are very confident that the true effect lies close to that of the estimate of the effect. (2) Moderate certainty: We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. (3) Low certainty: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect. (4) Very low certainty: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

[c]Downgraded by one level for study limitations: studies at an overall high risk of bias.

[d]We did not downgrade for imprecision since we used a minimally conceptualized approach: although the confidence interval is wide, there are no concerns about whether the effect results in a moderate to a large increase in the retreatment rate.

[e]Downgraded by one level for imprecision: the incidence is mostly reported in a subset of sexually active participants.

moderate due to an overall high risk of bias.

5. Erectile function

Based on five studies with 337 participants, TUMT may result in little or no difference in erectile function when compared to TURP at 6- to 12-month follow-up (RR, 0.63; 95% CI, 0.24–1.63; I^2=35%) [22,27,30,33,36]. The certainty of the evidence is low due to an overall high risk of bias and imprecision (the incidence is mostly reported in a subset of sexually active participants). As for long-term data, one study reported five-year data on erectile dysfunction with an incidence of 7.5% in the TUMT group and 15.4% in the TURP group (data were available for 119/154 randomized participants) [36]. The certainty of the evidence is very low due to an overall high risk of bias and imprecision (the incidence is mostly reported in a subset of sexually active participants with high attrition).

6. Ejaculatory function

Based on four studies with 241 participants, TUMT may result in fewer cases of retrograde ejaculation when compared to TURP at 6- to 12-month follow-up (RR, 0.36; 95% CI, 0.24–0.53; I^2=0%) [22,27,30,33]. The certainty of the evidence is low due to an overall high risk of bias and imprecision (the incidence mostly reported in a subset of sexually active participants).

7. Minor adverse events

Based on five studies with 397 participants, TUMT may result in little to no difference in the incidence of minor adverse events when compared to TURP at 6- to 12-month follow-up (RR, 1.27; 95% CI, 0.75–2.15; I^2=0%) [22,27,28,33,36]. These events primarily included urinary tract infections. The certainty of the evidence is low due to an overall high risk of bias and imprecision.

8. Acute urinary retention

Based on four studies with 343 participants, TUMT may result in an increased incidence of acute urinary retention when compared to TURP at 6- to 12-month follow-up (RR, 2.61; 95% CI, 1.05–6.47; I^2=40%) [22,28,33,36]. The certainty of the evidence is low due to an overall high risk of bias and imprecision (the incidence mostly reported in a subset of sexually active participants). In many cases, we highlight that participants undergoing TURP were routinely catheterised after surgery and for shorter periods than TUMT (see below).

9. Indwelling urinary catheter

The evidence is very uncertain about the effect of TUMT on the duration of catheterisation compared to TURP. This outcome was not adequately reported across the included studies.

DISCUSSION

Based on data from six studies with 414 participants, when compared to TURP, TUMT probably results in little to no difference in urologic symptom scores in the short term, but due to the lack of any eligible study with follow-up longer than 12 months, we are uncertain about the long-term effects. There may be little to no difference in minor adverse events, quality of life or erectile function between these interventions. TUMT likely results in significantly fewer major adverse events and less ejaculatory dysfunction compared to TURP. TUMT, however, likely results in a large increase in the need for retreatment (usually by repeated TUMT or TURP) and acute urinary retention. The duration of indwelling catheterization was not adequately reported across studies.

The studies did not consistently define or report on adverse events, particularly dysuria, hematuria, and sexual dysfunction, and our estimates for these complications may be unreliable. In addition, few studies evaluated the quality of life. Although studies usually reported the occurrence of urinary retention, they did not consistently or uniformly indicate its duration or the use of catheterization. One important complication that was not reported in the clinical trial literature was thermal injury. On 11 October 2000, the U. S. Food and Drug Administration (FDA) published a Public Health Notification because they had received 16 reports of severe thermal injury associated with TUMT, including ten resulting in fistula formation and six resulting in tissue damage to the penis or urethra [37]. The FDA noted that the injuries could take hours or days to develop. Although the FDA recommended several corrective measures for physicians, they considered TUMT to be safe and effective based on the performance of over 25,000 procedures.

The current American Urological Association guidelines for the management of LUTS considered TUMT to be an appropriate alternative for treating men with

LUTS with small- to average-size prostate [10], with the warning that patients should be advised that surgical retreatment rates are higher compared to TURP, which corresponds with the findings of our review. The Canadian guidelines considered TUMT an optional treatment for men with moderate symptoms, with similar considerations about retreatment [38]. The European Association of Urology does not list TUMT as one of their alternatives for managing LUTS [2].

The certainty of the evidence was primarily affected by: (1) high risk of bias across studies: most studies did not report the randomization process adequately, and for the TUMT *versus* TURP comparison, none of the included studies was blinded; (2) imprecision: details on ejaculatory and erectile function were only reported as binary outcomes in a subset of sexually-active participants; (3) our interpretation of the retreatment data was cautious since this was not consistently reported across studies; in some cases, it was described in the initial flow of participants across the studies, in some studies as a comment about follow-up, and in other cases within adverse events.

Considering that review methods have improved over time, including the details of the search strategy, we decided to run our searches from inception using the original inclusion criteria of the previous version of the review but excluding the comparison to alpha-blockers. We identified the citations of some additional reports of the included studies, including long-term data on one of the studies, but we were unable to retrieve some of the full text through different means. Finally, reporting on some of the outcomes was scattered and not thoroughly detailed. For some outcomes, including adverse events, retreatment, acute urinary retention, ejaculatory and erectile function, we had to interpret the data available in the flow of participants and the section describing "complications". It is unclear whether the studies reported all events or only those they considered relevant, especially with a lack of a prespecified protocol.

The previous version of this Cochrane Review yielded similar results for the global effects of TUMT in relation to sham and TURP [39]. The main difference from the previous version of the review is that we pooled the data for more outcomes in each comparison, with additional critical outcomes in the summary of findings tables. This provided us with a greater understanding of the differences between TURP and TUMT. In this version, we favour an interpretation of similar urinary symptoms scores at short-term follow-up, considering that long-term data from selected studies provided very low-certainty evidence to highlight substantial differences between these interventions. We also found important differences in the incidence of major adverse events and the incidence of retrograde ejaculation between these interventions, favouring TUMT.

We found a few additional systematic reviews on this topic. A health technology assessment from Sweden assessed the average IPSS score and concluded that TUMT was inferior to TURP in improving symptoms, which does not consider the confidence interval and minimally important differences [40]. Furthermore, the authors stated that they could not determine the differences in major adverse events, as we found in our review, which could be explained by the lack of grouping of serious events. Nevertheless, the findings related to retreatment were similar. Another systematic review reported similar results for urinary symptoms and retreatment but highlighted the lower incidence of serious adverse events with TURP than TUMT [41]. They state that the retreatment rate for TUMT may vary from 20% to 80% (focusing on observational data) but simultaneously highlight that the rate of retreatment is lower in long-term randomised trials such as the one included in our review [36]. Finally, two systematic reviews focusing on sexual outcomes reported a lower incidence of sexual adverse events (especially retrograde ejaculation) for men undergoing TUMT compared to TURP, which agrees with our findings [42,43]. None of these studies followed Cochrane methods for high-quality reviews.

CONCLUSIONS

TUMT provides a similar reduction in urinary symptoms compared to the standard treatment (TURP), with fewer major adverse events and fewer cases of ejaculatory dysfunction at short-term follow-up. However, TUMT probably results in a large increase in retreatment rates. Most of the evidence is short-term and from studies with a high risk of bias. Patients' values and preferences, their comorbidities and the effects of other available minimally-invasive procedures, among other factors, can guide clinicians when choosing the optimal treatment for this condition.

ACKNOWLEDGEMENTS

Juan Víctor Ariel Franco is a PhD candidate in the Programme of Methodology of Biomedical Research and Public Health, Universitat Autònoma de Barcelona (Spain). The authors acknowledge the previous authors and contributors to the first versions of the review: Richard M. Homan, Manoj Monga, Sean P. Elliott, Roderick MacDonald, Jens Langsjoen, James Tacklind, and Timothy J. Wilt. The authors also acknowledge the support of the Cochrane Review Group throughout the editorial process. This article is based on a Cochrane Review published in the Cochrane Database of Systematic Reviews (CDSR) 2021, Issue 6, DOI: 10.1002/14651858.CD004135.pub4 (see www.cochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and the CDSR should be consulted for the most recent version of the review.

Conflict of Interest

JVAF: none declared. LG: none declared. CMEL: none declared. MB: Boston Scientific (consultant for endourology and stone management), Auris Health (consultant for robotic surgery and endourology). PD: none declared.

Author Contribution

JVAF: conceived, designed, and wrote the protocol and full review, and performed all aspects of the data abstraction, analysis, risk of bias assessment and certainty of evidence ratings. LG: performed all aspects of the data abstraction, analysis, risk of bias assessment and certainty of evidence ratings, and drafted the review. CMEL: designed and ran the electronic searches, drafting the full review. MB: reviewed critical content, and gave final approval for the draft of the review. PD: conceived, designed and wrote the protocol for the update, reviewed the methods and the critical content, and gave final approval for the draft of the review.

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