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A review of the effects of transurethral microwave thermotherapy (TUMT) for lower urinary tract symptoms (LUTS) in men with benign prostate hyperplasia

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ABSTRACT

In the last decade of the new millennium, it can be seen that the number of transurethral microwave thermotherapy (TUMT) treatments has decreased significantly. Investigating the reasons for this trend, it was decided to review the literature data on TUMT. This review mainly focuses on the effectiveness of TUMT on lower urinary tract symptoms (LUTS) and the impact on erectile function (EF). The reference method was transurethral resection of the prostate (TURP). MEDLINE, EMBASE, Scopus and Cochrane Library databases between 1991–2021 were searched to identify studies on TUMT. The review included both randomized controlled trials and non-randomized trials; 55 items were selected for further analysis. They included 13 randomized reports, 1 non-randomized report and 8 reviews. Surprisingly, data analysis shows that TUMT is almost as effective in reducing LUTS as TURP. However, significant differences in complication profiles were noted. Transurethral microwave thermotherapy showed negligible morbidity and no serious complications compared to TURP. Transurethral microwave thermotherapy is also characterized by a slight influence on erectile dysfunction and retrograde ejaculation in contrast to TURP. Two facts of TUMT draw attention: the lack of precise qualification criteria and too few randomized controlled trials. Despite the critical attitude of some researchers to TUMT, it seems to be a valuable method and a suitable alternative to TURP. However, further research is needed with an increasing number of randomized controlled trials. This review aims to discuss the effects on EF of TUMT for LUTS in men with benign prostate hyperplasia.

Keywords: erectile dysfunction; transurethral microwave thermotherapy; TUMT; lower urinary tract symptoms; LUTS; benign prostate hyperplasia; complications, review.

INTRODUCTION

While studying the literature, it was noticed that despite many positive reports on transurethral microwave thermotherapy (TUMT), common opinion tends to contest it as a valuable treatment for benign prostate hyperplasia (BPH) [1, 2, 3, 4].

As a result, from the last decade of the new millennium, it can be seen that the number of TUMT treatments has decreased significantly [3, 4]. Treatment of BPH is always elective surgery and therefore it is sometimes difficult for the patient to accept a method with a high risk of serious complications, such as transurethral resection of the prostate (TURP) [5].

This review aims to discuss the effects on erectile function (EF) of TUMT for lower urinary tract symptoms (LUTS) in men with BPH.

CURRENT MANAGEMENT OF BENIGN PROSTATE HYPERPLASIA AND LOWER URINARY TRACT SYMPTOMS

Current management of LUTS due to BPH still include dominantly conservative treatment or minimally invasive procedures [5, 6]. Nowadays, open surgery is almost completely abandoned [4].

Among minimally invasive procedures it seems that TURP is currently considered to be the reference standard. But significant morbidity and serious complications like bleeding, transurethral resection (TUR) syndrome, urethral stenosis, bladder neck contractures or sexual dysfunction and the fact that only about 5–10% of cases actually require TURP, has caused a slow shift downwards in its position on the treatment options panel [5, 6, 7, 8, 9, 10].

For these reasons, other less invasive techniques have been advocated. They include TUMT, transurethral needle ablation, and laser prostatectomy (including holmium laser enucleation of the prostate – HoLEP) and potassium titanyl phosphate, high intensity focused ultrasound, transurethral water vapor therapy: the Rezum system, mechanical devices like prostatic stents represent the best studied and most accepted minimally invasive procedures [2, 11, 12, 13, 14].

The fractionation of prostatic tissue should be mentioned but this novel concept is only just being developed. It is based on new technologies able to deliver enough high intensity energy to cause tissue emulsification without thermal effects. Two cutting edge technologies are under development, and are considered as experimental treatments under investigation, i.e., histotripsy and aquablation [15, 16].

As a result, many urologists and their patients started looking for better alternatives. It seemed such an alternative could be TUMT [12, 17, 18, 19, 20, 21, 22].

Yerushalami et al. first introduced TUMT into urological practice [22]. Transurethral microwave thermotherapy heats

the prostate gland above the temperature of protein denaturation. This activates the coagulation process locally, denervates α receptors, which reduces smooth muscle tone and finally induces cell apoptosis [21, 22, 23]. Unlike TURP, the clinical effects of TUMT treatment are not immediate. Full therapeutic success is usually achieved after at least 3–6 months [6, 12, 19, 23]. Despite minor complications and many advantages, such as outpatient surgery or local anesthesia, interest in this method is declining. This is also noticeable in the decline in the number of scientific reports regarding this treatment [4, 12, 17, 24, 25]. It is difficult to find an unambiguous answer and it is completely incomprehensible why, despite some optimistic reports on TUMT, its gradual withdrawal from routine practice is observed [17, 19, 24].

Currently, TUMT has been withdrawn from The European University Association (EUA) recommendations [24]. An optimistic outlook for TUMT, still a recommended option in the American Association of Urology (AUA) guidelines [26, 27, 28, 29].

STUDIES ON THE EFFECTIVENESS OF TREATMENTS FOR BENIGN PROSTATE HYPERPLASIA

The main purpose of this review was to evaluate the effectiveness of TUMT in the treatment of BPH and its impact on EF of the treated patients. The reference method in the review was TURP.

Searching databases in MEDLINE, EMBASE, Scopus and Cochrane Library 1991–2021 allowed to identify several studies on TUMT. The review included both randomized controlled trials, nonrandomized trials as well as meta-analyses or reviews. Fifty five items were selected for the final analysis, including 13 randomized reports, 1 non-randomized review and 8 reviews [2, 3, 4, 8, 12, 19, 21, 22, 25, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39]. This review included over 5,000 patients who were treated with TUMT. However, this appears to be a rather small number of patients in comparison with TURP.

The effectiveness of BPH treatment can be expressed by subjective parameters such as various types of questionnaires, for example Internationale Prostate Symptoms Score (IPSS) or objective parameters like urodynamic or ultrasound examination [5, 6, 7, 34, 35, 36]. There are several objective urodynamic variables which include maximum urinary flow (Qmax), post-urinary retention (PVR), detrusor pressure (Pdet max), and minimum urethral opening pressure (Pmuo) [10, 17, 24, 40]. Ultrasound examination provides details of prostate size and the amount of post-voiding urine retention [5, 10, 24].

There are 5 objective variables that describe the effectiveness of BPH treatment. They include Qmax, PVR, Pdet max, prostate volume determined by ultrasound examination, and Pmuo [5, 18, 24, 18, 38]. Table 1 shows the randomized and non-randomized control trials and review articles about TUMT. The table compares the effects on LUTS and the ratio of postoperative complications between patients after TUMT and TURP. The effect on sexual function is shown separately. When searching the literature, it can be noticed that there is a significant decrease in the number of publications on TUMT, especially in the last decade of this millennium. Surprisingly, negative opinions about TUMT did not dominate, and many of them were rather positive. Many authors have highlighted certain clinical limitations, such as prostate size and the presence of a 3rd lobe, or even inappropriate qualification. Many authors pointed out that the observation period was too short and lasted on average about 6 months, which does not seem to allow for fully objective conclusions to be drawn.

This review appears some few authors who attribute TUMT significantly worse results in improving LUTS compared to TURP [4, 10, 24]. But Madersbacher et al. [5] and Madersbacher and Marberger [6] and Ekstrand et al. [38] showed significantly improved IPSS scores in patients after TUMT. Moreover, they did not observe any serious complications compared to TURP [5, 6, 38]. There are also other authors who found an improvement in urodynamic parameters [19, 27, 37]. Nawrocki et al. showed a definite advantage of TUMT over sham therapy or watchful waiting [37]. The authors evaluated about 120 symptomatic patients at the period of 6 months. They applied a protocol which included a questionnaire with symptom scores according to AUA and some parameters of urodynamics like peak Qmax, PVR, Pmuo and Pdet max. The examined parameters only changed statistically significantly in the TUMT group [37]. Similarly, Aagaard et al. described a group of patients after TUMT. Within 6 months after thermotherapy, almost 77% of patients were able to deflate without a catheter, and over 79% reported an improvement in quality of life (QoL). The authors reported an improvement in Qmax and a reduction in PVR. Mild complications such as transient haematuria or a short-term increase in body temperature were encountered after treatment [19]. There are other authors who also found TUMT a good alternative to TURP. They reached this conclusion by observing patients who had been qualified for TUMT due to contraindications to TURP. Many of them achieved a satisfactory improvement in urination [2, 3, 20, 36, 39, 41].

Another valuable work on TUMT was carried out by Franco et al. The authors concluded that TUMT provides a similar reduction in LUTS compared to the standard treatment (TURP) with fewer major adverse events. However, TUMT probably results in a large increase in retreatment rates [30].

TRANSURETHRAL MICROWAVE THERMOTHERAPY AND THE EFFECTS ON ERECTILE FUNCTION

The analysis of sexual function after TUMT is definitely more positive compared to TURP [18, 31, 42, 43, 44, 45, 46]. Generally, the majority of reports confirm the negative correlation of TURP with sexual dysfunction. TUMT is definitely indicated as a much more favorable option in this matter [2, 3, 4, 39]. However, there are reports that somewhat elude TURP's negative opinion on sexual function, but these are in the minority [47]. Another comprehensive retrospective meta-analysis on the effects of TUMT on LUTS and sexual dysfunction was carried out by Hoffman et al. In this review, which is based on many

TABLE 1. The effect of transurethral microwave therapy of prostate and transurethral resection of prostate on lower urinary tract syndrom and sexual function and ratio of complications

Authors and study year	Study design	Erectile function		Ejaculatory function		LUTS		Complications	
		TUMT	TURP	TUMT	TURP	TUMT	TURP	TUMT	TURP
Walmsley and Kaplan (2004) [3]	Rev					↑	↑	↓	
Frieben et al. (2010) [43]	Rev		↓		↓				
Madersbacher and Marberger (1999) [6], Madersbacher et al. (1994) [7]	Rev	=	↓	=	↓	↑	↑	↓	↑
Reich et al. (2008) [10]	RTC		↓			=	↑		↑
Tabatabaei and Zangi (2015) [17]	Rev					↑	↑	↓	↑
Hoffman et al. (2012) [4]	Rev	=	↓		↓	↑	↑	↓	
Aagaard et al. (2014) [19]	Rev					↑		↓	
Tzortzis et al. (2009) [12]	Rev	=	↓	=	↓	↑	↑	↓	↑
Wilhelm (2018) [25]	Rev	=		=		↑		↓	
Ekstrand et al. (2002) [38]	RTC					↑			
Ahmed et al. (1997) [26]	RTC	=	↓	=		=	↑		↑
Nawrocki et al. (1997) [37]	RTC					↑			
Nørby et al. (2002) [8]	RTC	=	↓	=		↑		↓	↑
Saitz et al. (2019) [41]	nRTC					↑		↓	
de la Rosette et al. (1994, 2003) [2, 39]	RTC	=	↓			↑		↓	
Wasson et al. (1995) [47]	RTC		=	=		↑	↑		↑
Oka et al. (2019) [48]	RTC	=	↓	=		↑	↑		
Mattiasson et al. (2007) [34]	RTC					↑	↑	↓	↑
D'Ancona et al. (1997) [33]	RTC	=	↓			↑	↑	↓	↑
Dahlstrand et al. (1993) [35]	RTC		↓			↑	↑	↓	↑
Franco et al. (2021) [30]	RTC	=		=	↓	↑		↓	

LUTS – lower urinary tract symptoms; TUMT – transurethral microwave thermotherapy; TURP – transurethral resection of the prostate; RTC – randomized control trial; nRTC – non randomized control trial; Rev – review for erectile function, ejaculatory function and LUTS: ↓ – deterioration; ↑ – an improvement; = – without of changes; empty – no data for ratio of complications; ↓ – decreased of number; ↑ – an increased of number

randomized studies, the authors found that, in general, the IPSS questionnaire improved by 65% and 77% and Qmax by 70% and 119%, respectively, for TUMT and TURP. Another important conclusion from this review was that sham therapy turned out to be significantly less effective than TUMT. Finally, they found that TUMT had significantly less negative effects on sexual function compared to pharmacological treatment or TURP [4]. Nørby et al. observed significantly fewer complications after TUMT compared to TURP. They emphasized differences in complication profiles. Transurethral microwave thermotherapy showed negligible morbidity and had no negative effect on sexual function, unlike TURP [8]. Objective variables of BPH treatment were tested by Ahmed et al. All variables improved after both TURP and TUMT, however the negative impact of TURP on the EF of the patients was much more profound [26]. The above observations were also confirmed by Dahlstrand et al. [35] and Oka et al. [48]. Some authors reported a short-term effectiveness of TUMT [4, 8, 24]. But Mattiasson et al. followed a group of patients after TUMT for 5 years. They compared the effectiveness and safety of TUMT with TURP. The overall conclusion was that both TUMT and TURP showed similar significant improvement in all objective parameters. However, in the TUMT group, approx. 10% required additional interventions, as opposed to 4.3% for TURP. The authors conclude that the clinical outcome after 5 years was comparable to the results observed after TURP, but the safety of the procedure was definitely in favor of TUMT [34]. Another valuable work regarding TUMT is a report by D'Ancona et al. The authors compared the results of treatment with TURP and high energy microwave thermotherapy. Patients were assessed using the Madsen questionnaire, some chosen voiding parameters, transrectal ultrasound of prostate gland and cystometry. All tests were repeated at 12-month intervals. In both groups, a significant relief of bladder outlet obstruction was observed. After 1 year, this improvement was still over 78% and 68% for TURP and TUMT, respectively. No serious complications occurred in either group. The authors conclude that a high-energy TUMT can be rated highly in BPH treatment options [33]. A more positive effect of TUMT on erectile and ejaculatory function compared to TURP was observed by Franco et al. [30].

CONTROVERSIES IN THE TREATMENT OF BENIGN PROSTATE HYPERPLASIA

Most studies were performed over 20 years ago so there are some study limitations and imprecisions which reduce the confidence we can place in these results [30].

Different opinions about TUMT appear in the literature data varying from very positive to less satisfying. But nowhere is TUMT described as an inappropriate method for LUTS. Analyzing these less satisfactory opinions, the inappropriate qualification of patients for this method draws attention. Overall, many authors emphasized that if the patient had a significant size or 3rd lobe of the prostate, he may need retreatment. But in fact, this is not a failure because the Transurethral microwave thermotherapy method includes a risk of retreatment. Unfortunately, many authors notice it as a failure of TUMT and immediately qualified the patients to other methods [2, 5, 6, 33, 49, 50, 51]. However, from many benefits for patients like: good efficacy, the absence of serious complications, or the treatment of BPH on an outpatient without an anaesthetist's assistance, the interest in TUMT remains consistently low [5, 6, 24, 33, 49, 51]. It should be trusted that despite the withdrawal of TUMT procedures from the EUA recommendations, it will not discourage urologists from further research on this very valuable method. Fortunately, there is still a small group of TUMT supporters, and their commitment reminds others of this method [3, 12, 18, 19, 32]. Given the emergence of newer minimally-invasive treatments, high-quality head-to-head trials with longer follow-up are needed to clarify their relative effectiveness. 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 [30, 32, 40]. Further research and technical improvements can prevent TUMT from being completely forgotten [32, 40].

CURRENT GUIDELINES ON THE MANAGEMENT OF LOWER URINARY TRACT SYMPTOMS DUE TO BENIGN PROSTATE HYPERPLASIA

In both the EUA and AUA guidelines TURP has been the gold-standard treatment for alleviating urinary symptoms and improving urinary flow in men with symptomatic benign prostatic hyperplasia [24, 28, 29]. According to EAU guidelines, the surgical treatment options for LUTS/BPH are now divided into the following 5 sections: resection, enucleation, vaporisation, alternative ablative techniques, and non-ablative techniques. The resection of the prostate – both monopolar (M-TURP) or bipolar (B-TURP) – resulted in a substantial mean Qmax improvement (+162%), a significant reduction in IPSS (–70%), QoL score (–69%) and PVR (–77%) [52, 53]. Enucleation – open prostatectomy reduces LUTS by 63–86% (12.5–23.3 IPSS points), improves QoL score by 60–87%, increases mean Qmax by up to 375% (+16.5–20.2 mL/s), and reduces PVR by 86–98% [54]. Holmium laser enucleation of the prostate – an initial meta-analysis reported no significant differences in short-term efficacy (Qmax) and re-intervention rates (4.3% vs. 8.8%) between HoLEP and M-TURP [55]. Transurethral microwave thermotherapy has been withdrawn from the EUA's recommendations [53]. According to AUA guidelines, TUMT may be offered as a treatment option to patients with LUTS/BPH. It is a conditional recommendation with evidence level: grade C [24, 28, 29, 31].

CONCLUSION

This review of recent clinical studies and clinical trials, and evidence from systematic review and meta-analysis, supports the use of TUMT for LUTS in men with BPH. Transurethral microwave thermotherapy has advantages when compared with TURP, with reduced postoperative complications that include EF. However, because there is still some controversy regarding the use of TUMT, further clinical trials are awaited to provide the evidence required for future management guidelines.

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