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Current status of Minimally Invasive Treatment for Benign Prostatic Obstruction

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Abstract

Scientific and technological advances during the last years have challenged the established therapy patterns regarding Benign Prostatic Obstruction (BPO). The aim of this review is to highlight the current status in the field of Minimally Invasive Treatments (MIT) of BPO, including transurethral microwave thermotherapy, transurethral needle ablation, laser treatment (photoselective vaporization and enucleation), transurethral ethanol injection therapy, and water induced thermotherapy. This review mainly focuses on recent publications that have provided interesting data on efficacy and durability of MIT and on the current recommendations of European Association of Urology, American Urological Association, and 6th International Consultation on Prostate Cancer and Prostate Diseases. In general these innovative minimal invasive techniques result in decrease of morbidity but still efficacy of TURP is better compared to MIT. Therefore, minimally invasive therapies should be considered alternatives but not replacements for TURP.

Key words: Benign Prostatic Obstruction, minimally invasive treatment, TUMT, TUNA, laser, WIT, TEAP.

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Introduction

Living in the aging male era, urologists are invited to confront the continuously increasing number of patients suffering from lower urinary tract symptoms due to benign prostatic obstruction (BPO), and seeking for adequate management.

Scientific and technological advances during the last years have challenged the established therapy patterns regarding BPO such as transurethral resection of the prostate (TURP) and open prostatectomy. Various minimally invasive treatments (MIT) have been developed using new techniques including thermal-based therapies, laser therapy and other treatment modalities such as prostatic ethanol injection. The driving forces behind this development of minimally invasive methods were the rather unchanged morbidity of transurethral resection of prostate in terms of early (bleeding, TUR-syndrome) and late complications (particularly relating to sexual dysfunction), as well as the need for anesthesia and hospitalization.

However, it is the destiny of all therapeutic modalities for BPO to be compared to TURP that remains the mainstay. Therefore for the objective evaluation of the MIT efficacy this review will mainly rely on randomized studies that have compared MIT with TURP and avai-

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Table 1: Clinical outcome of the largest TUNA studies

Reference	Pts (n)	Symptom score			Max. Flow Rate (ml/sec)		
		Preop.	Postop.	Change	Preop.	Postop.	Change
Roehrborn et al[6]	130	23,7	11,9	50%	7,8	14,6	68%
Zlotta et al[7]	188	20,9	8,7	58%	8,6	12,1	40%
Campo et al[8]	72	20,8	6,2	67%	8,2	15,9	71%
Ramon et al[9]	68	22,0	7,5	66%	8,4	11,6	33%
Virdi et al[10]	71	22,3	7,4	67%	7,0	14,2	103%
Chapple et al[11]	58	22,0	10,0	54%	8,8	11,5	30%

lable meta-analysis of clinical data. Furthermore, this review will also focus on long-term data and the recommendations of European Association of Urology (EAU)[1], American Urological Association (AUA)[2], and 6th International Consultation on Prostate Cancer and Prostate Diseases[3] in order to delineate the current status of Minimally Invasive Treatment for Benign Prostatic Hyperplasia. Long-term follow-up data have been provided for some minimally invasive therapies, whilst others have been only recently developed, and need more time for evaluation before they can gain general attention. It should also be underlined that prostatic stents are not included in this review, since we have evaluated minimally invasive modalities that "ablate" prostatic tissue.

Transurethral needle ablation (TUNA)

From all the available thermal-based treatments of symptomatic BPH, transurethral needle ablation (TUNA) and transurethral microwave thermotherapy (TUMT) have been the best studied. TUNA therapy uses low-level radiofrequency (RF) energy that is delivered by needles that are placed accurately into the prostate. The monopolar RF signal of 490 kHz allows excellent heat penetration and uniform tissue distribution of heat[4,5] resulting in localized necrotic lesions in the hyperplasic tissue. Temperatures approach 80-100°C while the prostatic urothelium is preserved[4,5]. TUNA can be performed as an outpatient procedure under local anaesthesia and sedation in the vast majority of patients.

A significant number of clinical studies on TUNA have been published with different number of patients in each study and different follow-up period. Most of these studies are open single-arm series. In Table 1 the clinical results of series with more than 50 patients and a 12 month follow-up are presented[6,7,8,9,10,11]. The improvement in symptom score ranged from to 50% to 67% at 1 year while the reported improvement in maximum flow rate (Q_{max}) was in the range of 30% to 103%. These results were significant when compared with baseline.

On the other hand there is only a minority of randomized studies comparing TUNA to TURP. Bruskewitz et al compared TUNA to TURP[4] in a randomized clinical trial with a 1-year follow up. A total of 65 patients were treated with TUNA and 56 with TURP. The symptom score markedly improved from 24.7 to 11.1 in the TUNA group against 23.3 to 8.3 in the TURP group. The maximum urinary flow rate significantly improved from 8.7 to 15.0 ml/sec and from 8.4 to 20.8 ml/sec in the TUNA and TURP group, respectively. The treatment was found to be effective and safe. Another clinical trial comparing TUNA with TURP randomized 59 patients[12]. Improvements in Q_{max}, post voiding residual volume (PVR), IPSS and the quality of life (QoL) score were statistically significant for both groups at 3 and 18 months of follow-up. The effect of TUNA therapy on Q_{max} was smaller than that of TURP, whereas no significant differences were found between the two groups regarding improvements in IPSS and QoL scores.

Although studies with short-term data are able to provide evidence of the initial efficacy and safety of the method, studies with long-term follow-up are essential for the evaluation of durability of the obtained results. Re-treatment rate represents an important parameter for the evaluation of treatment durability. Zlotta et al. reported the long-term results of 188 men treated with TUNA therapy (follow-up up to 5 years). The mean IPSS decreased at 5 years (when 131 men were evaluable). Overall, 41 of the 176 patients (23%) after a mean 63 months follow-up required additional BPH therapy. Interesting long-term follow-up results at 5 years were obtained from a randomized multicentric clinical trial comparing TUNA to standard TURP[13]. A total of 121 men were enrolled in this study and adverse events were significantly fewer in the TUNA group. The overall improvement was superior in the TURP group, and in addition 14% of patients treated with TUNA eventually required re-treatment, compared with 2% of the TURP group who received additional treatment.

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A strong body of data is provided by a recent meta-analysis[14]. Boyle et al analyzed the results from two randomized trials, two non-randomized protocols and 10 single-arm studies conducted on TUNA. The meta-analysis was based on the changes in the mean score at the end of the study from that at baseline. TUNA achieved a 50% decrease of the mean IPSS from baseline at 1 year after treatment and this improvement remained durable up to 5 years despite a slight deterioration. Maximum urinary flow rate (Q_{max}) improved by 70% from baseline to 1 year, representing a 15 ml/s increase in mean Q_{max}. Although there was a tendency for the Q_{max} to decline slightly over time, however the mean Q_{max} 5 years after treatment was more than 50% improved over baseline. When only the two randomized trials are considered, the mean decline in IPSS was 11.6 after TUNA and 15.7 after TURP (difference statistically significant). Similarly, improvement in mean Q_{max} after TUNA (7.0ml/sec) was less than that after TURP (11.6 ml/sec). Again this difference of 4.6ml/sec was statistically significant[14]. This meta-analysis showed that TUNA is an effective and safe minimally invasive treatment for men with even severe symptoms who do not wish to undergo long-term medical therapy, or are poor candidates for surgery or are concerned about the side-effects of TURP[14].

The excellent side-effect and safety profile of TUNA has been well documented in several short- and long-term studies. The most common post-treatment complication reported after TUNA is urinary retention, ranging from 13.3% to 41.6%. The retention is transient (12-48 hours) in the majority of patients[5,15]. A mild degree of transient macroscopic hematuria is noted in most patients for a period of 24 hours and does not require specific treatment. Postoperative urinary infection and epididymitis occur rarely (0% to 3.1%). Urethral strictures may occur in 0% to 1.5% of patients and are related to instrumentation of the urethra. The risk of urethral stricture is smaller than after standard TURP[15].Sexual dysfunction is rare after TUNA and urinary incontinence was not reported in any series[5,15]. Sexual function was reported as being better preserved in the TUNA group, where only 3.1% of patients referred erectile dysfunction compared with 21% in the TURP group.

The EAU Clinical Research Office together with Medtronic Sàrl set up a Registry for patients with BPH to obtain information on real life long-term clinical outcomes and economics of TUNA Therapy. The aim is to evaluate 300 patients for 5 years in terms of International Prostate Symptom Score (IPSS), quality of life, International Index of Erectile Function, uroflow data and adverse events. Participating centres upload patient data to a central server that is EAU property. In February 2004, 146 patients (mean age 67 years) have been enrolled (142 evaluated, 86 with 6 months follow-up), with a median baseline IPSS of 20 and Q_{max} of 8.5ml/s[16]. A significant improvement in symptoms of 60% was found at 6-month follow up and of 70% for maximum flow rate. Peri- and post-operative complications were observed in 19% and 27% of patients respectively. Almost 90% of patients received a Foley catheter after the TUNA, but required in only 5% for urinary retention. During the following 6 months, 8% required indwelling catheter. The study is still in progress[16].

TUNA is considered to be effective in partially relieving symptoms of BPH according to the EAU and AUA Guidelines[1,2]. TUNA is not recommended as a first line treatment for the average patient, yet is indicated in high-risk patients unfit for surgery. The 6th International Consultation on New Developments in Prostate Cancer and Prostate Diseases recommends TUNA as an option when instrumental treatment is indicated (except when absolute indication for surgery exists)[3].

Transurethral microwave thermotherapy TUMT

TUMT uses a special transurethral catheter with a microwave antenna that transmits heat into the prostate with the eventual goal of destroying tissue by achieving temperatures that exceed the cytotoxic threshold (> 45°C and inducing cell death (coagulation necrosis). The extent of the necrosis is governed by two physical variables: intraprostatic temperature and duration of heat exposure.[17] It has also been suggested that TUMT causes denervation of alpha-receptors, thereby decreasing the smooth muscle tone of the prostatic urethra of the smooth muscle cells[18].

During the last decade, numerous studies have been published presenting the clinical results from the application of TUMT for the treatment of LUTS associated with BPO. These studies have used different devices with different technical specifications and treatment protocols, have had different follow-up periods and response criteria, and have differed in patient selection. Short-term subjective and objective improvement with various microwave devices has been proven by all these studies. In an interesting review, de la Rosette et al reported that the maximum improvement in urinary flow rate is achieved 3 months after TUMT.[19] Q_{max} baseline values were at average 9-10ml/s, while 3 months following TUMT. Q_{max} improved approximately 5-6ml/s. It remained stable at 6 and 12 months follow-up thus

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Table 2: Clinical outcome of TUMT systematic review and pooled data of PLF Treatment

		Symptom score				Max. Flow Rate (ml/sec)		
Reference	Treatment	Pts (n)	Preop.	Postop.	Change	Preop.	Postop.	Change
Hoffman[20]	TUMT	322	19.4	6.7	65%	7.9	13.5	70%
	TURP	218	19.6	4.5	77%	8.6	18.7	119%
Gravas[21]	TUMT	183	20.9	6.4	69%	7.7	16.1	109%
	TURP	65	20.7	7.1	66%	7.5	18.6	148%

representing an average 50-60% increase, but some deterioration was noted with time. The average IPSS improvement after high-energy thermotherapy, is approximately 60%. The maximum reduction is obtained 3 months after treatment, with a slight but insignificant further improvement at the 6 and 12-month visit.

Hoffman et al[20] performed an excellent systematic review of all available randomized controlled trials evaluating the efficacy and safety of microwave thermotherapy in treating men with LUTS and BPO, in order to quantify the therapeutic efficacy. Treatment was offered by different TUMT devices and software including Prostatron (Prostatsoft 2.0 and 2.5) and ProstaLund Feedback. TUMT was somewhat less effective than TURP in reducing LUTS. Weighted Mean Differences (WMD) were calculated with 95%CI for the between treatment differences in pooled means. WMD for the symptom score at the follow-up for all six studies was –1.83 (–3.09 to –0.58), favouring TURP. It was also found that the mean urinary symptom scores for TUMT patients almost always decreased from the moderate-to-severe symptom range to the mildly symptomatic range. TURP led to greater improvement in Q_{max} than TUMT, with a WMD for Q_{max} at the follow-up of 5.37 (4.22–6.51) mL/s. The mean Q_{max} after TUMT was usually < 15mL/s, since only two studies reported a mean post TUMT Q_{max} greater than 15mL/s. In contrast, five studies reported that TURP achieved a mean Q_{max} > 15ml/s. Clinical outcomes of this systematic review are listed in Table 2.

Gravas et al performed a pooled analysis of 3 studies of ProstaLund Feedback TUMT with 12-month follow--up.[21] Two randomized studies comparing PLFT to TURP and an open label study with no comparative group were combined. The responder rate was 85.3% and 85.9% in the PLFT and TURP group, respectively. One-sided 95% CI analysis showed noninferiority of PLFT as compared to TURP. Responder was defined as a patient that following treatment had an IPSS of 7 or less, and/or 50% or greater improvement in IPSS from baseline, and/or Q_{max} of 15ml/s or more, and/or 50% or greater improvement in Q_{max} from baseline. In Table 2 detailed pooled data of IPSS and Q_{max} improvement are presented.

Djavan et al conducted a randomized prospective study to evaluate targeted TUMT against terazocin[22]. It was demonstrated that the clinical outcomes of TUMT were significantly greater than those achieved by terazosin. The mean IPSS improved significantly from baseline by 6 months in both groups, with a greater improvement in patients after TUMT, where the IPSS was 38% lower than that in the terazosin group. Q_{max} also increased significantly from baseline in both groups by 6 months and remained stable thereafter; it was 19.8% higher after microwaves treatment than with terazosin. These patients have been followed-up for 18 months.[23] The subjective and objective improvement observed at 6 months was maintained at 18 months, and it was significantly greater in the TUMT group compared to the terazosin group. Furthermore, the actuarial rate of treatment failure at 18 months in the terazosin group (41%) significantly exceeded that of the TUMT group (5.9%).

Re-treatment rate represents an important parameter for the evaluation of treatment durability. Retreatment of TUMT is related to treatment failure whereas retreatment of TURP is related to complications of resection. Reported re-treatment rates after TUMT range from 19.8% to 29.3% but with different mean follow-up durations (from 30 to 60 months).[24,25,26,27] In the randomized study comparing TUMT to TURP, the results of 36 months of follow-up were presented.[24] The level of improvement was found to be durable up to 3 years. The cumulative risk of retreatment for TUMT Prostasoft 2.5 and TURP was 19.8% and 12.9%, respectively. Similarly, d' Ancona et al found a retreatment rate of 26% and 4.7 % for TUMT and TURP in their randomised study with a mean follow-up of 30 months[25]. The relatively longer-term outcomes still favoured TURP in both of these studies. In a recent multicenter trial by Miller et al evaluated the durability of the Targis 60-minute treatment on 150 patients during a 5-year period. They reported that 29.3% of the patients (44/150) underwent additional BPH treatment at some

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Table 3: Morbidity following TUMT and TURP (pooled data of randomized controlled studies)

	de la Rosette[19]		Walmsley[34]		Hoffman[20]	
Variables	**TUMT**	**TURP**	**TUMT**	**TURP**	**TUMT**	**TURP**
Hospitalization time in days	0	4 (3.9-4.1)	0	2.8 (1.0-4.1)		
Catheterization time in days	13.7 (12.7-14)	3.6 (3-4.1)				
Urinary Tract Infections %	14.6 (3.3-18)	13.1 (4-20)	9 (3-19)	6 (5-9)	17.7 (43/244)	13.9 (21/151)
Dysuria %			51 (12-99)	15 (9-23)	31.2 (53/170)	13.1 (14/107)
Retention %			15 (1-33)	5 (4-8)	23.9 (51/213)	6.9 (9/130)
Transfusions %			1.5 (0-9)	8 (5-11)	0 (0/144)	5.7 (6/105)
TURsyndrom%					0 (0/176)	6.1 (6/98)
Erectile Dysfunction %	4.4 (0-6)	9.3 (0-21)	8.7 (0-8)	10 (7-13)	5.7 (8/140)	13.9 (10/72)
Retrograde ejaculation %	19.8 (0-33)	63 (50-80)	20 (2-49)	65 (56-72)	22.2 (10/45)	57.6 (19/33)
Strictures-meatal / bladder neck stenosis	0.7 (0-2.8)	9.6 (4.8-15.6)	2 (0-9)	7 (5-8)	0.6/100 (2/320)	5.8/100 (15/256.5)
Treatment failure	18 (10.8-25.8)	2.6 (0-4.8)	18 (10.8-25.8)	2.6 (0-4.8)	7.5/100 (30/398)	1.0/100 (3/284.5)

point before 5 years, while they estimated that the cumulative Kaplan-Meier re-treatment risk was 33.9% at 5 years.[27] In a study by Gravas et al, 213 patients with or without retention were treated using the TUMT 3.5 protocol and were followed for up to 5 years. 28.6% of patients without urinary retention required additional treatment while treatment failure was 37.8% in the retention group, but the cumulative risk at 5 years was 42.3% and 58.8%, respectively[28].

One of the commonly used arguments for the application of TUMT as an alternative to TURP treatment for BPH is its low morbidity. Data regarding morbidity coming from the systematic analysis of published randomized studies comparing TUMT to TURP confirm this standpoint.[24,25,29,30,31,32,33] In addition, Wagrell et al found that the number of serious adverse events (i.e. bleeding) was significantly higher in TURP group (17%) compared to TUMT group (2%).[33] The impact of TUMT on sexual function in terms of erectile dysfunction and retrograde ejaculation has also been studied in comparison to TURP, with pooled data to be in favour of TUMT.[34] Table 3 presents pooled data of randomized controlled studies on morbidity following TUMT and TURP. The reported low morbidity and the absence of any anesthesia (spinal or general) needs, make TUMT a true outpatient procedure representing an excellent option for patients in high operative risk (American Society of Anaesthiologists classification 3 and 4) who are unsuitable for an invasive treatment.[35]

EAU Guidelines state that TUMT is considered as the most attractive interventional modality alternative to TURP, and should be reserved for patients who want to avoid surgery or who do not respond favorably to medication.[1] According to the AUA Guidelines TUMT is effective in partially relieving symptoms in BPH patients, whereas there is no evidence of superiority of one device over another.[2] The 6th International Consultation on New Developments in Prostate Cancer and Prostate Diseases concludes that TUMT has good clinical outcomes that seem durable and low morbidity and represents an option when instrumental treatment is indicated (except when absolute indication for surgery exists)[3].

Water –induced thermotherapy (WIT)

WIT is another thermal-based therapy for BPO that aims to produce heat-induced coagulative necrosis and secondary ablation of the obstructing hyperplastic tis-

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Table 4: Clinical outcome of WIT studies

Reference	Pts. (n)	FU (m)	Symptom score		Q_{max} (ml/sec)	
			Preop.	Postop.	Preop.	Postop.
Muschter[36-38]	125	12	24	12.0	8.7	15.7
		24.0		11.0		16.3
		36		11.2		16.0
Breda[39]	9	15	R	6.3*	R	11.5*
60°/ 50F	3		18.6	7	11.7	17.1
	2		23.5	19.4	8.7	9.5
Breda[39]	15	8	R	10.7†	R	10.7†
62°/ 60F	11		20.8	8.0	9.3	18.3
	3		21.5	19.5	9.1	8.9

R: retention

* 8 patients catheter-free

† 11 patients catheter-free

sue. The source of thermal energy is heated water circulated in a proprietary closed-loop system, which includes a specially designed catheter.

Currently limited data on WIT efficacy and morbidity are available. A single prospective, international, uncontrolled, multicenter trial has contributed to the evaluation of WIT efficacy, having demonstrated symptom reduction and safety. In this study[36] and its subsequent updates[37,38], 125 patients were included and evaluated at 3, 6, 12, 24 and 36 months. In addition a single-center has reported the results[39] from the use of two different WIT protocols in terms of temperature setting and balloon inflation. Clinical outcome of WIT is presented in Table 4.

No significant morbidity has been reported. Adverse events included prolonged or excessive dysuria (11.2%); epididymitis (3.2%); prolonged and excessive hematuria (22.4%); transient impotence (1.6%); transient urinary urge incontinence (2.4%); culture-confirmed bacteriuria or urinary tract infection (32.8%); urethral pain (4.8%); proctitis (0.8%); and urinary retention subsequent to the post-treatment catheterization period (12.0%).[36] No patient suffered from newly occurring permanent erectile dysfunction or retrograde ejaculation. Interest in sex, sexual activity, and other measures were not affected or were slightly improved by WIT[40].

Data regarding durability are also preliminary[36-38]. A re-treatment rate of WIT (requiring subsequent TURP) of 5.6%, 9.6% and 11.2% was found after 12, 24 and 36 months, respectively. On an intention-to-treat basis, the treatment failure rates were higher: 10.4% after 12 months, 23.2% after 24 months and 36% after 36 months.

It is obvious that randomized studies against one of the standard treatments are required, thus WIT remains investigational

Laser treatments

The laser technology has been applied to treat LUTS secondary to BPO 15 years ago. The laser techniques include coagulation, vaporization, resection and dissection depending on the wavelength, power, and type of emission (continuous or pulsed). Four types of laser have been used for treatment of symptomatic BPH; Neodymium: Yttrium Aluminum Garnet (Nd:YAG), the Holmium: YAG (Ho:YAG), the Potassium Titanyl Phosphate: YAG (KTP:YAG) and the diode laser. Described surgical techniques include Visual Laser Ablation of the Prostate (VLAP), Interstitial Laser Coagulation (ILC) of the prostate, Photoselective Vaporization of the Prostate (PVP), Holmium Laser Bladder Neck Incision, Holmium Laser Resection of the Prostate (HoLRP), Holmium Laser Ablation of the Prostate (HoLAP), and Holmium Laser Enucleation of the Prostate (HoLEP). Ho:YAG laser has excellent incisional, ablative and haemostatic properties[41] and has been used for bladder neck incision, ablation (HoLAP), resection (HoLRP) and enucleation of the prostate (HoLEP). HoLEP represents the most recent step in the evolution of holmium laser prostatectomy due to the refinement of the holmium laser technique and development of an efficient tissue morcellator that allow the true anatomic enucleation of a prostatic adenoma of any size.

The long catheterization time and severe storage symptoms with delayed improvement resulted in abandoning VLAP as a treatment option. Furthermore, EAU

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Table 5: Clinical outcome of PVP studies

Reference	Pts (n)	Symptom score			Max. Flow Rate (ml/sec)		
		Preop.	Postop.	Change	Preop.	Postop.	Change
Te[44]	139	23.9	4.3	82%	7.8	22.6	189%
Sulser[45]	57	18.9	7.8*	59%	7.8	18.5*	137%
Sandhu[46]	64	18.4	6.7	64%	7.9	18.9	139%
Bachmann[47]	64	18.1	5.2†	71%	6.9	18.1†	162%
Sarica[48]	240	22.6	3.7	84%	7.9	27.9	253%

* At 3 months †At 6 months

Table 6: Clinical outcome of recent HoLEP studies

Reference	Pts (n)	Symptom score			Max. Flow Rate (ml/sec)		
		Preop.	Postop.	Change	Preop.	Postop.	Change
Hurle[50]	155	26.5	2.0	92%	9.3	22.5	141%
Tan[51]	31	26.0	5.0	81%	8.4	21.8	159%
Kuntz[52]	100	22.1	1.7	92%	4.9	27.9	469%
Vavassori[53]	196	26.2	2.0	92%	9.3	22.5	148%
Elzayat[54]	225	18.7	3.9	79%	8.0	26.2	227%

and AUA guidelines suggest that contact laser should not be considered as first line treatments of BPO and should be only used in high-risk patients. The relatively high re-treatment rate, delayed improvement and longer catheterization time are the main reasons that led AUA to not recommend ILC as a treatment option, while the EAU guidelines recommend the use of ILC only in the treatment of high-risk patients.[1,2]

This review will mainly focus on photoselective vaporization of the prostate that has demonstrated promising results and holmium laser enucleation that challenges both open prostatectomy and TURP.

Photoselective Vaporization of the prostate (PVP)

The high-power potassium-titanyl-phosphate (KTP) laser has been recently introduced This system vaporizes obstructive prostatic tissue and seals blood vessels using a high power 80-watt KTP laser (i.e., a potassium-titanyl phosphate crystal laser) and a fiberoptic delivery system inserted through a standard cystoscope. The procedure is performed on an outpatient basis in a hospital or surgical center and may be performed under local, spinal, or general anesthesia.

Hai and Malek[42] reported the first pilot study of 10 patients who underwent 80 W KTP laser vaporization of the prostate. Te et al[43] reported the first multicenter study of 139 patients with a mean prostate volume of 54.6 cc, who underwent 80 W KTP laser vaporization of the prostate with 12 months follow-up. The postoperative complications included dysuria (9.4%), transient hematuria (8.6%), transient urge incontinence (6.5%) recatheterization (5%), retrograde ejaculation (36%) bladder neck contracture (1.4%) and urethral stricture (0.7%). Clinical results from studies on PVP[44,45,46,47,48] are listed in Table 5.

Photoselective Vaporization of the prostate seems to be a safe and efficacious modality for treating BPH. However, data are still early and insufficient for definitive conclusions.

Additional high quality, randomized controlled trials would strengthen the evidence base for this laser procedures.

Holmium Laser Enucleation of the Prostate (HoLEP)

Gillling et al[49] subsequently reported their preliminary experience with 64 patients who have undergone HoLEP combined with intravesical morcellation. Since then several clinical studies have shown the efficacy and safety of HoLEP[50,51,52,53,54] (Table 6). However, the main criticism of HoLEP includes a significant learning curve and the difficulty in tissue removal.

Another advantage of HoLEP is that it has no size limitation, with significant improvement of the symp-

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toms and flow rate regardless of the size of the prostate.

Holmium laser enucleation of the adenoma has been proposed for larger prostates (>200 g) that have traditionally been treated by open prostatectomy[55]. The main evident advantages are reduced blood loss, quicker catheter removal and shorter hospital stay. A randomized study comparing HoLEP and transvesical prostatectomy found that both procedures are equally effective with less perioperative morbidity in the HoLEP group[56]. The blood transfusion rate was 13% in open prostatectomy group and none in the HoLEP group. Matlaga et al reported the largest series (86 patients) with the largest mean prostate size (170cc, from 125 to 309cc). Clinical data indicated that HoLEP might be the ideal treatment for patients that required open prostatectomy[57].

Tooher et al reviewed literature on holmium laser prostatectomy[58]. For laser enucleation, three randomized controlled studies and one comparative trial were available. Published data demonstrated that holmium laser prostatectomy seems to be at least as effective as TURP in short term, with a mean difference of 3.4ml/sec at Q_{max} between the two procedures in favour of laser, but this difference was not statistically significant.[58] However, long-term efficacy and durability still cannot be determined due to insufficient data. Safety of HoLEP appears to be superior to TURP in terms of a number of key indicators, including transfusion rates, postoperative bladder irrigation, duration of catheterization and length of hospital stay. The authors underlined that definite conclusions could not be reached due to a lack of high quality and long-term data.[58]

Recently, Gilling et al performed a meta-analysis of 4 RCTs comparing HoLEP and TURP.[59] They found that urodynamic relief of obstruction (PdetQ$_{max}$ and Schaffer grade) was superior with HoLEP compared with TURP but only when prostate volumes were >50g.

Adverse events and disadvantages are more similar to those found after TURP than those reported with other minimally invasive techniques. In particular, HoLEP is also superior to TURP with less bleeding, amount of tissue removed, decreased catheter time and hospital stay.[60,61] There was no blood transfusion needed in the HoLEP group in contrast to the TURP group where the transfusion rate was 3.3%. Kuo et al reviewed the complications of their 206 HoLEP and found that transfusion, clot retention episodes, urethral stricture, and bladder contractures occurred in 1%, 2.4%, 2.4%, and 3.9% of the patients, respectively[62]. In another study Montorsi et el found that HoLEP and TURP were equally effective with similar rate of complications at 1 year follow-up.[63] There was no TUR syndrome in the HoLEP group, versus 2.2% of patients in the TURP group. Transient urge incontinence was reported in 44% and 38% of the HoLEP and TURP groups, respectively. This complication is usually short term and self-limiting. Urethral stricture occurred in 1.7% in HoLEP group and 7.4% in the TURP group. The impact on erectile dysfunction and retrograde ejaculation is very similar between the two groups. The erectile function did not show a decrease from baseline in either group. In addition Kuntz et al reported that 74% of sexually active patients in the HoLEP group and 70.3% in the TURP group had retrograde ejaculation.[55]

The 6th Intenational Consultation on Prostate Cancer and Prostate Diseases suggest that HoLEP is equivalent to TURP/Adenomectomy with low morbidity but with the disadvantage of a long learning curve.[3]

Transurethral Ethanol Ablation of the Prostate (TEAP)

Is defined as a minimally invasive transurethral procedure to effectively treat patients with symptomatic BPO, by injecting anhydrous ethanol into the prostate under continuous urethroscopic irrigation.

Based on the available studies, it seems that IPSS and Q_{max} were improved significantly at 3 months after TEAP, and these results were sustained at 12 months.[64,65,66,67,68] A mean improvement of 53% and 34% was reported for IPSS and Q_{max}, respectively (Table 7). However, long-term studies are limited. Goya et al followed 17 patients for longer than 3 years (median follow-up for 4.3 years).[68] IPSS and Q_{max} improved after TEAP and were stable at 3-year follow-up without any major complications associated with the procedure. However, durable improvement was reported in only 59% of patients.

Plante et al reviewed the complications of TEAP among 200 patients from 15 countries.[69] Overall more than 90 % of patients were able to void 96 hours after TEAP. The most commonly reported adverse events were storage symptoms (21.5%), urinary retention (17.5%), urinary tract infection, and hematuria (13%), most of which resolved without intervention by one month post TEAP. Urinary incontinence, erectile dysfunction and retrograde ejaculation occurred in less than 5% of the patients. The most serious complication was ethanol-induced bladder necrosis that occurred in three cases.

The reported re-intervention rate ranged from 7% by one year to 26% by 3 years after TEAP.[67-68] TEAP conversion to TURP within 6 months was reported in 10 % of the deep injection group and 15% in superficial injection group.[70] If the reported case series are continuously

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Table 7: Clinical outcome of TEAP studies

Reference	Pts (n)	Symptom score			Max. Flow Rate (ml/sec)		
		Preop.	Postop.	Change	Preop.	Postop.	Change
Plante[64]	5	23.4	13.8	41%	9.9	13.1	32%
Ditrolio[65]	13	22.4	5.9	74%	5.7	11.9	108%
Gutierrez[66]	118	21.2	10.7	50%	9.3	13.7	47%
Grise[67]	93	20.6	10.3	50%	9.9	13.4	35%
Goya[68]	34	21.8	9.6	56%	8.3	13.6	63%

observed for another 4 years, the re-treatment rate may be anticipated.

TEAP seems to be effective, at least for one year, and might be a suitable option in patients with co--morbidities who are unfit to undergo TURP. Further randomized studies comparing this procedure with other minimally invasive procedures or with TURP are warranted. Therefore, ethanol injection therapy of the prostate remains to be established and long-term outcome is required to define its potential role for the management of BPO.[3]

Discussion

It is obvious that the range of therapeutic options for the management of BPO continues to widen. Increased choice creates the increased need for clarity in selection and application of these various treatment options. Living in the era of evidence-based medicine, high quality data are required for the evaluation of MIT and further elucidation of the role of those therapies in the management of symptomatic BPO.

Minimally invasive therapies can be positioned between medical therapy and surgical treatment. Surgical treatment remains the procedure with the best results but is associated with significant morbidity. On the other hand, medical therapy requires a strict medication schedule, is associated with long-term costs, side effects and compliance problems. MIT is associated with reduced risk compared to TURP and has a reliable efficacy, even if it is less effective than TURP. In addition, MIT offers a one-time therapy while efficacy of medication seems to be lower than for MIT but the latter may have a higher morbidity.

In that view TUNA and TUMT are closer to medical management while lasers are coming close to TURP/ adenomectomy and maybe even overpower the latter. However, caution should be regarded for the green light laser since we need more durable data

At present WIT and TEAP are both investigational and should not to be recommended for general clinical use.

The current trend is to compare minimally invasive therapies to medical therapy. The Minimally Invasive Surgical Therapy Trial compares combination medical therapy with either microwave therapy versus transurethral needle ablation. The results of this trial are expected with interest and will have great clinical relevance.

It should also be underlined that 'improved' TURP techniques have been introduced namely bipolar resection of the prostate. Advantages of these newer resection techniques include the ability to use isotonic saline (avoidance of TUR-syndrome), reduced blood loss and less heat damage to the surrounding tissue. Therefore, bipolar resection may further improve TURP and the advantages of laser may be less that indicated at present. Studies on bipolar resection are on their way.

Consequently, one needs to balance on the one hand the clinical outcomes, morbidity and technical improvement of these technologies. On the other hand there are obvious patient's preferences as well as doctors preferences that may guide the eventual choice of therapy.

Conclusion

In general, efficacy of TURP is better compared to MIT. Innovative minimal invasive techniques result in decrease of morbidity and hospitalization time. Thus, these therapies are particularly useful in those patients who are in high operative risk. Although TURP is challenged by some of these treatments, still it cannot be replaced by them until their long-term durability of efficacy is well documented.

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