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Long-Term Evaluation of Transurethral Needle Ablation of the Prostate (TUNA) for Treatment of Symptomatic Benign Prostatic Hyperplasia: Clinical Outcome up to Five Years from Three Centers

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Abstract

Objective: TUNA has been demonstrated to be a safe and effective therapy for BPH. However the major criticism, as with all alternative treatments for BPH, was the lack of long-term data. We present the clinical outcome of patients treated by TUNA and followed for 5 years.

Methods: 188 consecutive patients with symptomatic BPH treated with TUNA were followed for five years in three different centers. All patients were treated using the TUNA II or TUNA III catheters under local anesthesia only without general or spinal anesthesia. Baseline and 5-year follow-up evaluation included urinary peak flow, International Prostate Symptom Score (IPSS) and post-void residual urine (PVR). The number of patients requiring additional medical or surgical treatment was recorded. Statistics were performed using the *t*-test.

Results: At a mean follow-up of 63 months, mean urinary peak flow rate increased from 8.6 ml/s to 12.1 ml/s ($p < 0.01$, *t*-test), IPSS and PVR decreased from 20.9 and 179 ml to 8.7 and 122 ml, respectively (both $p < 0.001$, *t*-test). The percentage of patients who improved by at least 50% their peak uroflow and IPSS was 24% and 78% respectively. Mean prostate volume and PSA levels did not change significantly (53.9 cc vs. 53.8 cc and 3.3 vs. 3.6 ng/ml, respectively at 5 years, both p values > 0.05, *t*-test). Two patients died of unrelated comorbidities and 10 were lost for follow-up. Medical treatment was given to 12 patients (6.4%), a second TUNA performed in 7 patients (3.7%) and surgery indicated in 22/186 (11.1%). Overall 41/176 patients (188 at start, 2 deaths and 10 lost to follow-up) or 23.3% required additional treatment at 5 years follow-up following the original TUNA procedure.

Conclusions: TUNA is effective and provides good long-term clinical improvement at 5-year follow-up. TUNA treatment stands the test of time at 5-year follow-up with low and acceptable failure rates. More than 75% of the patients do not need additional treatment for BPH on the long run.

Keywords: TUNA; BPH; Minimally invasive therapy

1. Introduction

Transurethral needle ablation of prostate (TUNA) is a minimally invasive procedure for the treatment of benign prostatic hyperplasia using low level radiofrequency energy delivered directly into the prostate in order to create controlled tissue necrosis [1–3]. This procedure is FDA approved and has already undergone extensive evaluation as an outpatient office based treatment for symptomatic BPH. Several studies have demonstrated that it is a safe and effective therapy for BPH that can be performed in outpatient setting and without the need for spinal or general anaesthesia [4,5].

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Prospective studies including one randomized study comparing TUNA and transurethral resection of the prostate (TURP) demonstrated its efficacy in terms of subjective and objective parameters improvement and showed fewer side effects than TURP [6–8]. Urodynamic studies have also shown significant improvements in flow rates and in maximum detrusor pressure and detrusor opening pressures as compared to baseline values [9,10]. However, the major common limitation for a wider acceptance of all new minimally invasive therapies by the urological community and health authorities has been the lack of long-term data concerning efficacy, re-intervention rates and side effects. We present here the long-term data of patients treated with transurethral needle ablation of the prostate for symptomatic BPH with a mean follow-up of 5 years.

2. Material and methods

2.1. Treatment protocol

The TUNA procedure has already been described in details previously [1,2,11]. In this study we used TUNA II and TUNA III generation of catheters with a generator manually monitored [11]. Noteworthy, no visualisation of needles as opposed to the current Pro Vu™ or Precision™ catheters was available with the Tuna II and III devices [11]. Similarly, the system was operator dependent for delivery of thermal energy and monitoring of impedance as opposed to the fully automatic TUNA systems currently in use. Patients were placed in the supine position and 2% intra-urethral lidocaine jelly was instilled at the beginning of the procedure. Patients received intravenous antibiotic prophylaxis (at the discretion of each center) and intravenous sedation with 5 mg valium and 50 mg of pethidine if required. The TUNA catheter was advanced and positioned in the prostate using direct fiber-optic vision. After rotating the shaft for the deploying needles toward the selected prostatic area, both lateral lobes were treated in 2–3 planes, beginning at 1 cm from the bladder neck to 1 cm proximal to the verum montanum. The required length of the needles and deployment of the shield were pre-determined with measurement of the transverse diameter of the prostate obtained by transrectal ultrasound of the prostate. Needle deployment was calculated as 6 mm less than the distance from the urethra to the capsule. Shielding varied from 4 to 6 mm with a needle deployment from 10 to 20 mm. One pair of lesions was produced for each 20 mg of prostate. Each treatment was scheduled to last 5 minutes. Total power was manually controlled and temperature increased with a preset threshold temperatures of the tip of the needles for each minute of treatment. No suprapubic catheter was placed after treatment. However, if patients were unable to urinate before hospital discharge, a suprapubic tube was inserted.

2.2. Patients and inclusion criteria

188 consecutive patients who fulfilled the inclusion criteria with symptomatic BPH from 3 different centers (51 in Belgium, 115 in Greece and 22 in Norway) were included in the study (January 1994 to June 1997). All patients underwent transrectal ultrasonography of the prostate. Patients had to fulfil the following inclusion and exclusion criteria:

- peak flow rate less than 15 ml/s, >5.0 ml/s,
- prostate volume less than 90 cc,
- IPSS $\geq$ 18,
- QoL $\geq$ 3.

Patients with a post-void volume of more than 250 ml as measured by transabdominal ultrasound, patients with an elevated PSA (>10 ng/ml) and patients with large median lobes were excluded.

2.3. Outcome and efficacy evaluation

Maximum peak flow rate, IPSS, QoL, serum PSA measurement, prostate volume estimation by transrectal ultrasonography and residual volume measured by abdominal ultrasound were assessed before treatment and at follow-up. No pressure-flow studies were performed. Statistical analysis of the efficacy parameters included the Student *t*-test. The mean follow-up was 63 months. During the follow-up period, 10 patients were lost for data analysis (6.1%) and 2 died of unrelated comorbidities (1.2%). All patients (except 10 who were followed for 4 years) were followed for a minimum of 5 years. In total, apart of the 12 patients lost for follow-up or dead of unrelated comorbidities, long-term follow-up was available in all patients unless additional therapies (41 patients) were required.

3. Results

Table 1 summarizes the baseline data for the 188 patients. There were no statistically significant differences between the three centers ($p > 0.05$, data not shown).

Table 1 also presents the comparison of pre-treatment and long-term follow-up of treated patients in whom follow-up was available (131). 131 patients data were used for comparison as data from the 41 patients, who underwent other treatments or were put on medical

Table 1

	Baseline	Long-term follow-up	p value
N patients	188	131*	
Q_{max}			
Mean (ml/s)	8.6	12.1	<0.001
SD	2.7	2.9	
Range	5.0–14.9	6.5–19.2	
Res Vol			
Mean	179 cc	121 cc	<0.001
SD	82	51	
Range	0–250	0–250	
IPSS			
Mean	20.9	8.7	<0.001
SD	4.0	2.2	
Range	18–26	2–20	
Quality of life			
Mean	4.9	2.2	<0.001
SD	1.3	(1.3)	
Range	3–6	0–3	

* 131 patients were used for comparison as the data of the 41 patients who underwent surgery or other treatments or received medical therapy before the long-term follow-up term could not be included. Among the 131 patients, 10 had a 4-year follow-up while 121 had 5-year data.

Table 2
Percentage of patients improved after TUNA by 50% at the long-term follow-up compared to baseline values ($n = 131$)[a]

Parameter	Improvement by 50%
Q_{max} (ml/s)	24%
Mean residual volume (ml)	72%
IPSS	78%
QoL	77%

[a] Patients treated surgically or medically during follow-up are not included because they did not reach 5-year follow-up. Among the 131 patients, 10 had a 4-year follow-up while 121 had 5-year data.

therapy before 5-year follow-up, could not be included. These 131 available patients had not been treated either surgically or with drugs after the TUNA treatment. 121 patients had 5-year follow-up, 10 patients had 4-year follow-up. Analyzing separately the 121 patients at 5-years did not change results in a significant manner (data not shown). As compared to baseline values, peak flow rate, mean residual volume, IPSS and QoL improved significantly (all $p < 0.05$). Table 2 presents data in terms of percentage of patients achieving a 50% improvement as compared to pre-treatment values. At 5 years follow-up, 24% of patients had a 50% improvement in Q_{max} as compared to baseline, 72% of patients had an improvement of 50% in mean residual volume, 77% in terms of QoL and 78% in terms of IPSS (all $p < 0.05$ as compared to pre-treatment values). Regarding Q_{max}, 97/131 (74.0%) had a $Q_{max} > 10.0$ ml/s at the long-term follow-up visit whereas 23/131 (17.5%) achieved a $Q_{max} > 15.0$ ml/s. Figs. 1 and 2 present the long-term follow-up outcomes in terms of mean peak flow rate and symptom score.

Finally, Table 3 presents the evolution in prostate volume and PSA as compared to baseline. No statistically significant differences were found when comparing pre- and post-TUNA data.

No significant differences neither were observed in terms of pre-TUNA parameters as peak flow rates, residual volume or symptoms between these who responded to therapy and those who underwent other procedures during follow-up (all $p > 0.05$, Student t-test, data not shown).

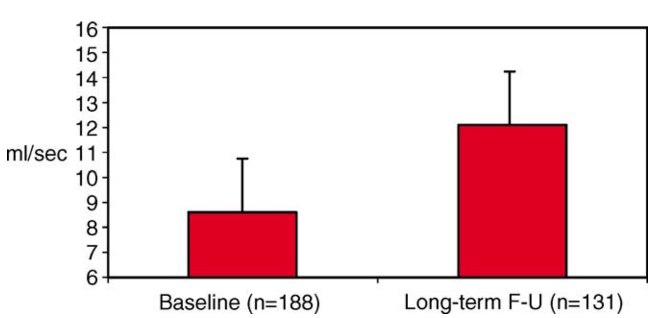

Fig. 1. TUNA peak flow/long-term follow-up. 10 patients had 4-year follow-up, 121 had 5-year follow-up.

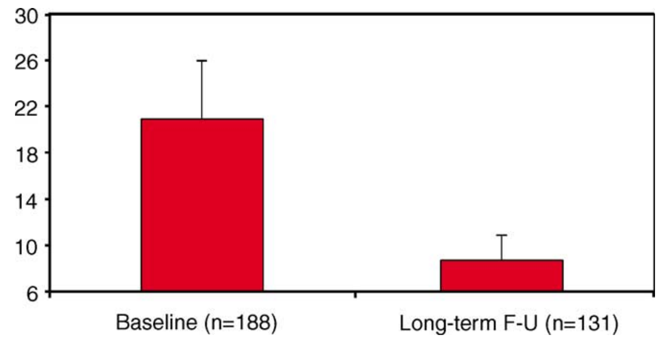

Fig. 2. TUNA IPSS/long-term follow-up. 10 patients had 4-year follow-up, 121 had 5-year follow-up.

Table 3
PSA and prostate volume

	Baseline	Long-term follow-up[a]	p value
N	188	131	
Prostate volume			
Mean	53.8 cc	55.7 cc	NS
SD	17.9	20.5	
Range	25–90	15–95	
PSA			
Mean	3.6 ng/ml	3.3 ng/ml	NS
SD	2.2	2.3	
Range	0.3–10.0	0.4–16.5	

[a] Among the 131 patients, 10 had a 4-year follow-up while 121 had 5-year data.

3.1. Re-treatment rates and need for additional therapies

With 188 patients at the beginning of the study, 10 lost for follow-up and 2 dead of unrelated comorbidities, 176 patients were available for assessment of the re-treatment rates and need for additional therapies. Additional medical therapy (alpha-blockers in all cases) because of patient's dissatisfaction was needed in 12 out of 176 patients (6.8%). Seven patients (3.9%) were re-treated with TUNA and 22 were operated. In total 41 out of 176 patients (23.3%) required additional therapy after TUNA at 5 years (27 patients within the first 3 years, 14 at 4-year follow-up, none at 5 years).

Sexual function was not assessed specifically neither long-term side effects.

4. Discussion

The relative scepticism concerning the efficacy of minimally invasive treatments for BPH is due to the lack of long-term data [12,13]. There is little doubt that TUNA treatment produces objective effects on BPH parameters, improves symptoms and helps patients at least in the short term [1,5,9,12]. However, long-term data to convince the urological community that their place in the urologist's armamentarium is legitimate was still lacking. Our five-year long-term follow-up data show that TUNA therapy stands the test of time and is a low-morbidity and anaesthesia-free procedure that is an attractive alternative for treatment of patients with symptomatic BPH. Objective and subjective improvement after TUNA was in the range of several other studies [1,4–8,10]. Overall, 75% of patients did not require additional therapy on the long term (5 years). To the best of our knowledge, our series represents the largest long-term follow-up series on the use of TUNA for symptomatic BPH. Our data also provide objective figures not on one single center but from 3 centers in various regions of Europe. The potential mechanism of the long-term results achieved with TUNA could putatively be related in part to a long-term alpha-blockade [2]. Schulman et al. have shown an improved efficacy sustained during 4 years of follow-up with tamsulosin itself [13].

Although medical therapy is certainly chosen by a majority of urologists (and patients) as the first line treatment for BPH, there is definitely a niche for alternative minimally invasive therapies. Medical therapy does not work for all patients and many are tired from taking ‘‘a pill’’ on a daily basis for years. They certainly do not provide better peak flow improvements than TUNA and have some draw-backs including the price [12]. Other long-term studies on minimally invasive therapies have shown that many of the high-energy devices stand the test of time with low and acceptable re-treatment rates [12,14]. Two of the most important aspects in evaluating surgical treatment options for LUTS are the need to use anaesthesia, early and late morbidity and long-term re-treatment rates. Too often and maybe inappropriately minimally invasive therapies for BPH have been compared with surgery only. The advantage of these therapies in terms of morbidity should be balanced with the fact that they do not necessarily have to reach the same levels of efficacy as TURP. Indeed patients are more often interested in improving their symptoms and quality of life. The prospective multi-centre one-year study and the randomized study against TURP demonstrated that TUNA was associated with fewer side effects than TURP although it could not reach the same high peak flow rates in the same extent as TURP did but was equally effective in enhancing QoL and symptoms score [6]. When addressing the issue of re-treatment rates after TURP, percentages vary substantially. Floratos et al. found that at 3 years, the cumulative retreatment rate was 12.9% [14]. Nowadays, it would probably be appropriate to compare minimally alternative treatments with pharmacological therapies for BPH. These have to be taken life-long, are costly and only marginally reduce the later incidents of surgery. Djavan et al. compared directly the efficacy, safety and durability of TUMT with the alpha-blockers during the follow-up of 18 months [15]. By 18 months, medical therapy had failed in 7 times more patients than the microwave group did. Re-treatment rates with TUMT using higher energy were on average 20% at 3- or 4-year follow-up [12,16]. The re-treatment rates with high-energy TUMT is thus in the same range as TUNA although, because high-energy TUMT was introduced more recently, 5-year data are still expected.

Floratos et al. also reported on the long-term follow-up after laser therapy. They followed 190 patients treated with laser therapy for BPH, 107 with visual laser ablation (VLAP), 30 with contact laser vaporization and 53 with interstitial coagulation. With a mean follow-up of 4 years, re-treatment rates were 14% for both VLAP and contact laser against 41% at 3 years for interstitial coagulation [17].

One of the potential limitations of our study is that patients with a median lobe or hypertrophied bladder neck or very large prostates (>90 cc) were excluded from the trial. However, recent data have shown that clinical efficacy with TUNA can be obtained even in patients with a median lobe or large prostates [18]. In addition, we did not perform pressure-flow studies to ascertain that patients became unobstructed after TUNA. Another limitation was the use of initial generations of TUNA devices and catheters. There was no reading of the temperature at the tip of the needle (which was only estimated roughly based on previous pathological and thermo-mapping studies) [2]. Needles could not be seen when introduced in the lateral lobes and the bladder neck or median lobe could not be treated. Power delivery was adapted manually which also prevented from having uniform treatment procedures. With the new generation of TUNA catheters and generators where power, impedance and temperature are fully computer monitored and lesions can be produced extensively in only 3 minutes (including the bladder neck), these limitations might possibly be overcome.

In conclusion, our multicenter study using the first generation of TUNA devices supports that this procedure is effective at 5-year follow-up, both in terms of subjective and objective parameters. Three quarters of the patients do not require any additional therapy on the long run. These results support the place of TUNA as a minimally invasive anaesthesia-free procedure for treatment of symptomatic BPH in the urologists' armamentarium. In the near future, even better results might be anticipated with the new generation of devices.

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