Surgical and Minimally Invasive Interventions for LUTS/BPH: Highlights from 2006

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Abstract

Objectives: This manuscript reviews the strengths and weaknesses of alternatives to transurethral resection of the prostate (TURP) to treat lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH).

Methods: The majority of data discussed in this paper were presented at the 2006 annual meetings of the European Association of Urology and the American Urological Association. Data from randomised controlled trials (RCTs) comparing surgical interventions for LUTS/BPH versus TURP, from studies including >100 patients and with at least 1 yr of follow-up were included. The participants' opinions on two representative clinical cases were assessed via interactive voting.

Results: Short-term efficacy of therapy analogues to TURP (bipolar transurethral resection in saline [TURIS], transurethral vaporisation of the prostate [TUVP], and holmium laser resection/enucleation [HoLRP/HoLEP]) seems comparable to TURP, with good safety profiles. Various direct comparative studies show that energy-based ablative techniques (transurethral needle ablation [TUNA], transurethral microwave therapy [TUMT], and photoselective vaporisation of the prostate [PVP]) may be an effective alternative to TURP and are associated with fewer complications. Mechanical stenting seems to be a solution for patients who cannot undergo general anaesthesia. Initial data on the use of botulinum toxin for LUTS/BPH looks promising. However, in all cases, more long-term data (>5 yr of follow-up) are needed to confirm these short-term outcomes.

Conclusions: Accumulating evidence is reported in favour of several alternatives to TURP. However, in all cases, prospective, long-term RCTs are needed to evaluate if these promising short-term outcomes are sustained over time.

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1. Introduction

Lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) are frequently encountered in ageing men. Over the age of 40, about one quarter of men suffer from LUTS/BPH [1]. Treatment options for LUTS/BPH generally fall into three categories, specifically, watchful waiting, pharmacology (primarily \( \alpha_1 \)-adrenoceptor antagonists, 5a-reductase inhibitors), and (minimally invasive) surgery. Surgery is recommended for patients who are moderately to severely bothered by their LUTS and refractory to medical treatment [2]. A minimally invasive procedure is appropriate for patients with moderate and occasionally severe LUTS in whom the prostate is still relatively small [2].

For decades, transurethral resection of the prostate (TURP) has been considered the “gold standard” surgical intervention for patients with LUTS/BPH [3]. Following TURP, 70–85% of patients experience improvement of symptoms [4]. However, TURP can be associated with significant morbidity, including TUR syndrome, intraoperative and postoperative bleeding with need for blood transfusions, and acute myocardial infarction [5–7]. However, recent developments in TURP have significantly decreased the associated morbidity [7,8].

The relatively high incidence of complications traditionally associated with TURP has driven the development of novel surgical/minimally invasive treatments for LUTS/BPH. Here, we discuss several alternatives to TURP, which can be used to treat LUTS/BPH, in particular the TURP analogues such as bipolar transurethral resection in saline (TURIS), transurethral vaporisation of the prostate (TUVP) and holmium laser resection/enucleation (HoLRP/HoLEP), energy-based thermal ablation with transurethral needle ablation (TUNA), transurethral microwave therapy (TUMT) and photoselective laser vapourisation (PVP), botulinum toxin injections, and mechanical intervention with intraprostatic stents. New surgical and minimally invasive treatments for LUTS/BPH should have a comparable efficacy and durability to TURP, but better safety outcomes, such as fewer perioperative and postoperative complications, which reduce the length of hospital stay and allow the patient to return earlier to work or to take up regular activities of daily living. Furthermore, the new techniques should be less costly.

2. Methods

The majority of data discussed in this paper were presented at the 2006 annual meetings of the European Association of Urology (EAU) and the American Urological Association (AUA). Data from randomised controlled trials (RCTs) comparing surgical interventions for LUTS/BPH versus TURP, from studies with >100 patients, and with at least 1 yr of follow-up were included. The data were presented and discussed during the “New Horizons in Urology” meeting in Marbella. The meeting was attended by approximately 135 urologists from countries throughout Europe. Two specific patient cases were introduced to the audience, followed by an interactive voting session where the delegates had to select their preferred treatment option. The subsequent debate with the audience and experts was chaired by Prof. Schulman and Dr. Illing.

3. TURP analogues

3.1. Bipolar TURIS

Using bipolar TURS, coagulation occurs at a much lower peak voltage of 65–120 V compared with monopolar systems of 500–800 V, depending on the system used. It has been suggested that this lower peak volume of energy will cause fewer filling symptoms after resection than standard monopolar TUR systems [9,10]. High-frequency current generated by a bipolar instrument tends to remain superficial. The bipolar resection system makes it possible to use physiologic 0.9% saline as the irrigation fluid, which reduces the risk of TUR syndrome [11].

Terrone et al. [12] performed a bipolar resection in 50 patients with randomised allocation to either TURP or bipolar treatment. There were no statistically significant differences in the mean duration of the procedure (TURIS vs. TURP: 53.4 vs. 51.6 min), mean amount of tissue resected (TURIS vs. TURP: 31.3 vs. 25.2 g), and mean postoperative plasma sodium concentration (TURIS vs. TURP: 139.9 mmol/l vs. 139.5 mmol/l). Improvement in maximum urinary flow rate (\( Q_{\max} \)) was similar between the groups (TURIS vs. TURP: 22.2 vs. 20.9 mL/s) with a trend to a quicker improvement of voiding symptoms in the bipolar group. The mean catheterisation time was lower in the bipolar group (TURIS vs. TURP: 2.6 d vs. 3.4 d, \( p = 0.06 \)). Outcomes of this trial show that bipolar TURS has a comparable efficacy to TURP. These data were confirmed in another RCT including 100 patients with LUTS/BPH; the study found no statistically significant differences in efficacy and safety outcomes between bipolar TURIS and TURP [13]. TUR syndrome did not occur in any group. Ho et al. [14] presented the outcomes of a single-blind, prospective RCT comparing bipolar TURIS and monopolar TURP, including 48 and 52 patients, respectively. TUR syndrome did not occur in the TURIS group compared to two patients from the TURP group...
group. This might be due to the smaller decline in postoperative plasma sodium concentration in the TURIS group compared to the TURP group ($p < 0.05$). Recatheterisation (TURIS vs. TURP: 10.4% vs. 7.7%) and reoperation for bleeding (TURIS vs. TURP: 6.2% vs. 3.8%) were comparable in the groups. The mean improvement rate in terms of $Q_{\text{max}}$, postvoid residual (PVR) and International Prostate Symptom Score (IPSS), assessed 1, 3, 6, and 12 mo postoperatively, was similar in both groups.

Tan et al [15] demonstrated in a prospective study the use of GYRUS Loop TURP versus conventional TURP. LUTS/BPH patients in the GYRUS arm enjoyed a shorter length of hospital stay and a shorter catheter time with fewer bladder washouts (Table 1). Erectile dysfunction and TUR syndrome complications were not reported in the GYRUS group, compared to three and one patient, respectively, in the TURP group. Follow-up at 3, 6, 12, 18, and 24 mo noted similar reduction in IPSS and increase in $Q_{\text{max}}$ in both groups. The GYRUS Loop TURP has the advantage that it allows the surgeon to collect tissue for histopathologic examination, unlike standard prostate vaporisation techniques.

### 3.2. TUVP

TUVP (or TVP) is done by a special, grooved, roller electrode (usually shaped like a cylinder), which, inserted through a resectoscope, delivers a strong electric current [16]. The roller electrode is rolled over the tissue, vaporising the top 1–3 mm of tissue. In this way, TUVP is comparable to laser vaporisation techniques. Unfortunately, with each pass of the roller, the layer below the vaporised tissue becomes more solid or coagulated. This coagulated tissue is harder to vaporise, a drawback that makes the procedure more tedious and time-consuming. For this reason, TUVP is best limited to men with small or medium-sized prostates.

A prospective, randomised study with a 5-yr follow-up was conducted to compare TURP to TUVP using Plasmainetic$^\text{TM}$ energy [17]. This study enrolled 51 patients in the TUVP arm and 25 in the TURP arm. Already 6 mo postoperatively, there was a significant reduction in IPSS in both groups (TUVP vs. TURP: 75.4% vs. 71.1%), which was sustained up to 5 yr of follow-up (TUVP vs. TURP: 78.9% vs. 71.5%). Operative duration and improvements in $Q_{\text{max}}$ and quality of life (QoL) scores were also similar between the two groups. Interestingly, TUVP seems to be associated with less intraoperative bleeding, that is, mean blood loss was 251 ml in the TUVP group and 497 ml in the TURP group.

### 3.3. HoLRP/HoLEP

Some recent review papers on HoLEP concluded that this technique is at least as effective as TURP in improving LUTS/BPH. Moreover, HoLEP has the advantage that prostates of all sizes can be operated on, which also makes it a valuable alternative to open prostatectomy for patients with large prostates [3,18]. However, no follow-up data for >5 yr exist, which makes it impossible to evaluate its long-term durability [18,19].

Wilson et al [20] recently compared the efficacy and safety of HoLEP with TURP among patients with LUTS/BPH with a prostate size of 40–200 g. HoLEP was superior to TURP with respect to catheter time, hospital stay, and volume of tissue resected but the procedure took longer. There were no significant differences between the two surgical groups at 2 yr of follow-up with respect to total IPSS, IPSS QoL, and $Q_{\text{max}}$ (Fig. 1). The safety profile was comparable between both groups; five patients in the HoLEP group needed recatheterisation compared to four

| Table 1 – Results of TURP versus GYRUS Loop TURP |
|-----------------|-----------------|
| TURP (n = 51)   | GYRUS (n = 103) |
| **Hospitalisation, d** | 3.7            | 1.1            |
| **Catheter removal, h** | 71.6           | 13.6           |
| **Continuous bladder washout time, h** | 56.3           | 12.5           |
| **TUR syndrome, n** | 1              | 0              |

TUR = transurethral resection of the prostate.

Patients treated with GYRUS Loop TURP had a shorter hospitalisation and a shorter catheter time with less continuous bladder washout time than patients treated with TURP [15].

![Fig. 1 – Surgical treatment of lower urinary tract symptoms/benign prostatic hyperplasia (LUTS/BPH) with holmium laser enucleation (HoLEP) versus transurethral resection of the prostate (TURP) [20]. Improvements in total International Prostate Symptom Score (IPSS), quality of life (QoL), and maximum flow rate ($Q_{\text{max}}$) were comparable between both groups at 2 yr of follow-up.](image-url)
patients undergoing TURP. None of the patients in the HoLEP group needed a reoperation or blood transfusion during the 2-yr follow-up compared to, respectively, two and one in the TURP group. In conclusion, prostate resection can be done with comparable efficacy to TURP with adapted electrosurgical procedures (TURIS, GYRUS Loop, or TUVP) or laser treatment (HoLEP). Instead of the conventional thin resection loop, thick loops and roller electrodes provide more effective tissue coagulation by increasing the contact surface. Major advantages include a faster recovery, reduced bleeding, and a lower incidence of TUR syndrome. There is substantial evidence that a whole prostate resection can be done by HoLEP, though the prolonged learning curve and high costs of HoLEP instruments are frequently cited as drawbacks of this technique.

4. Energy-based thermal ablation

4.1. TUMT

TUMT is a nonsurgical treatment that uses microwave heating to destroy excess tissue in the prostate. The heat is delivered to the prostate by means of insertion of a catheter in the urethra. The procedure takes about 1 h and can be performed on an outpatient basis without general anaesthesia [21]. Mattiasson et al [22,23] recently published the outcomes of a prospective randomised multicentre study with a 5-yr follow-up. A total of 154 patients with LUTS/BPH were randomised to TUMT or TURP in a 2:1 ratio. Patients were followed up at 3, 6, 12, 24, 36, 48, and 60 mo after treatment; 66% of all patients completed the 60 mo of follow-up. Total IPSS already decreased 3 mo postoperatively from 21 to 8 (61.9%) in the TUMT group and from 20 to 7 (65.0%) in the TURP group, which was sustained over 5 yr. $Q_{\text{max}}$ and IPSS QoL were comparable between the two groups. The frequency of severe adverse advents was 5% in the TUMT group compared to 17% in the TURP group. In the TURP group, 10% of patients needed additional treatment versus 4.3% in the TURP group.

Harik et al [24] presented data from a multicentre, European pooled analysis of 614 patients treated with high-energy TUMT who were followed for 2–8 yr. Fig. 2 shows the percentage of patients who had a >50% improvement in IPSS, IPSS QoL, and $Q_{\text{max}}$ at 2, 3, 6, and 8 yr of follow-up. The frequency of retreatment was defined as postoperative surgical intervention, not including additional drug treatment. In the majority of patients, the retreatment rate was 20.5% at 3 yr and 33.2% at 8 yr. Risk factors for retreatment included transitional zone volumes <20 ml or >50 ml, prostate-specific antigen (PSA) values <1.8 ng/ml, and the presence of an endove-sical lobe >0.5 cm.

4.1.1. Real-life practice with TUMT, an illustrative case study

The case of a 65-yr-old patient who had a catheter in situ for urinary retention (PVR 1.2 l) was discussed. The patient had borderline hypertension and diabetes. He previously had a myocardial infarction and was currently on aspirin medication. The patient was moderately overweight, had a blood pressure of 150/95 mm Hg, and had a soft abdomen. Digital rectal examination revealed a very large, benign-feeling prostate. Transrectal ultrasound (TRUS) showed a prostate of 70 ml. The patient was at moderate risk, ASA score 3. It was considered safe for him to undergo a procedure under general anaesthesia. The patient wished to be catheter-free. Based on this information, the attendees from the closed meeting were asked to select the next step in the management of this patient. The outcomes of the interactive voting clearly showed that this was a complex case (Fig. 3). One third of the group would recommend TURP, nearly a third would do an open prostatectomy, and another third chose a minimally invasive treatment (TUNA, PVP, or TUMT). During the subsequent debate, the participants discussed that intermittent catheterisation may be warranted before considering any surgical intervention. One also has to be aware that aspirin is known to cause increased bleeding during prostatectomy. This case was taken from a Swedish group who has a great deal of experience with TUMT in patients with LUTS/BPH. The procedure was performed in an outpatient setting and took only 45 min with a maximum prostate temperature of 60 °C. The procedure was well tolerated and the outcome
was good. The patient left the hospital the same day with no bleeding. The catheter was left for 14 d and the patient successfully passed a trial without catheter in a day case unit. His PVR returned below 100 ml, he had a Q\textsubscript{max} of 13 ml/s at 3 and 12 mo, and an IPSS score of 6 at 12 mo. The patient was pleased with the procedure. The successful outcome of the TUMT, frequently applied in Swedish centres, was heavily criticised by the audience because of lack of efficacy and potential selection bias.

4.2. TUNA

TUNA generates a necrosis by heat application (70–110 °C) via interstitial application of two needles through which energy is applied by radiofrequency electromagnetic pulses, which induces necrosis in the prostatic tissue, and consequently reduces prostate size. TUNA can be performed under local anaesthesia in an outpatient setting [25].

Boyle et al [26] concluded from a systematic review that TUNA is an effective treatment for men with LUTS/BPH, even in case of severe symptoms (IPSS reduction by 12.1 points and Q\textsubscript{max} increase by ~70%). TUNA may be a durable (at least 5 yr of follow-up) therapy. This conclusion was confirmed by Bouza et al, but they pointed out that TUNA is less effective and less durable than TURP. Sexual function (especially ejaculation disorders) is better preserved than with TURP, but the retreatment rate following TUNA was significantly higher than with TURP (10% vs. 1%) [27].

During the EAU 2006, the outcomes of the TUNA electronic real-life data registry set-up by the EAU in November 2003 were presented [28]. By September 2005, 230 patients, with a mean age of 67 yr, had undergone the procedure in 20 centres among nine European countries. After 6 mo of follow-up, the mean total IPSS, IPSS QoL, and Q\textsubscript{max} improved significantly compared to baseline (Table 2). Postoperative complications occurred in 31% of patients, including 17 patients (13%) who developed acute urinary retention. Sixteen patients (12%) were classified as treatment failures.

4.3. PVP

By means of PVP, a high-powered GreenLight laser (532 nm) combines low optical tissue penetration (0.8 mm) with selective absorption in tissues with a high oxyhaemoglobin content, such as the vascularised prostate [18,29]. Therefore, a superficial tissue layer can be vaporised rapidly and haemostatically at the temperature threshold of 100 °C by high-power (60–120 W), high-density laser energy. Heat-induced coagulation allows the creation of an almost bloodless cavity, giving the potential of even

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<th>Table 2 – The 6-mo follow-up data from the multicentre, real-life, data registry on TUNA</th>
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TUNA = transurethral needle ablation; IPSS = International Prostate Symptom Score; QoL = quality of life; Q\textsubscript{max} = maximum flow rate; IEFF = International Index of Erectile Function.

LUTS/BPH patients (n = 130) who underwent TUNA have a significant improvement from baseline in total IPSS, QoL, Q\textsubscript{max}, and the IEFF-5 [28].
patients on anticoagulation therapy the prospect of catheter-free discharge. The learning curve of the technique is short. However, the vaporisation can be time-consuming and less tissue is removed than with standard TURP. The efficacy is similar to TURP and the perioperative morbidity is reported to be less than that of conventional TURP [18,29].

Sustained improvement in flow rate and symptoms with minor complications were reported at the 5-yr follow-up by Malek et al [30]. Ruszat et al [31] evaluated the efficacy and feasibility of PVP in a 2-yr follow-up study in 70 patients with refractory urinary retention secondary to LUTS/BPH. PVP seems to be a safe and effective treatment for these patients.

In a prospective, double-centre study with 12 mo of follow-up, 147 patients were treated with PVP and 87 patients with TURP [32]. The efficacy was comparable at 1 yr of follow-up with superior intraoperative safety of PVP compared to TURP. The transurethral catheter could be removed 1.8 d after PVP compared to 2.9 d after TURP. The reoperation rate was comparable at 1-yr follow-up (3.4% in both groups) [33]. Long-term data are necessary to confirm the efficacy of PVP and to determine if the reoperation rate is higher in the PVP group.

### 4.3.1. Real-life practice with PVP, an illustrative case study

The case of a 60-yr-old man with moderate to severe symptoms (IPSS score of 18) and worsening obstructive voiding problems, despite medical combination therapy, was presented. He had a $Q_{\text{max}}$ of 7 ml/s with a rather obstructed-looking pattern. On examination, the patient appeared fit and well, with a soft abdomen and no palpable bladder. The patient had a benign-feeling prostate, around 40 ml. The urinalysis was normal. PSA and PVR (150 ml) were normal for his age. The patient was evaluated to be at good risk with an ASA score of 1. The patient was potent and wished to preserve erectile function.

Voting on this case study indicated a large preference for TURP/transurethral incision of the prostate (TUIP; 62%) and PVP (22%; Fig. 4). During the subsequent discussion, it was indicated that the choice of intervention is primarily based on the availability and expertise with the technique at hand, as well as the wishes of the patient. Though there is a large consensus towards TURP, one fifth of the delegates would recommend PVP, which seems to be the best alternative in this case. Major advantages of the technique include the short procedure time and low morbidity. In this respect, the chairman asked a specific question about retrograde ejaculation, which is a potential complication after partly taking away the bladder neck with PVP. The expert could confirm that the short-term rate of retrograde ejaculation following PVP is similar to TURP, but PVP is associated with a lower risk of impotence. Unfortunately, the outcomes of long-term studies are not known yet. It is generally accepted by the panel experts that in most cases TURP is preferred over PVP in case of a large prostate in a young patient. Treating a prostate $>$30 ml can involve a long operation time ($>$1 h) and likely requires two expensive laser fibres.

The patient actually has been satisfactorily treated with a GreenLight PVP with normal saline as the irrigant. After a short procedure time (1 h), the patient could leave the hospital the same day, catheter-free, without bleeding. At 6 mo the patient had an IPSS score of 6, a $Q_{\text{max}}$ of 19.5 ml/s, and a

**Fig. 4** – Outcomes of interactive voting on a representative case (for details, see text) show that >80% of the attendees indicated transurethral resection of the prostate/transurethral incision of the prostate (TURP/TUIP) or photoselective laser vaporisation (PVP) as appropriate treatment options.
residual volume that dropped down to 30 ml. Potency was preserved.

In conclusion, energy-based ablative techniques may have a role between oral pharmacotherapy and TURP. The efficacy of TUMT is similar to TURP over 5 yr, but TUMT seems to have a better tolerability and shorter hospitalisation time. There is emerging evidence for durable efficacy after TUMT from long-term (>5 yr) follow-up studies. Follow-up data with TUNA up to 5 yr looks promising, but retreatment rates appear higher than TURP. PVP presents as a safe treatment with shorter catheterisation time and hospitalisation. It is a treatment possibility for patients receiving anticoagulant therapy but can be expensive. No long-term follow-up data (>5 yr) are yet available.

5. Pharmacologic and mechanical alternatives to TURP

5.1. Botulinum toxin type A (BoNTA)

One of the emerging minimally invasive and office-based treatments for LUTS/BPH is BoNTA injected transperineally into the prostate. Injection of BoNTA results essentially in a chemodenervation of the injected organ [34]. BoNTA injection has been popular in cosmetic surgery as well as in several areas of medicine [35,36]. Chuang et al [37,38] recently presented a 1-yr follow-up study in which 41 patients with LUTS/BPH were treated with either 100 or 200 U BoNTA transperineally injected, depending on their prostate size (< or >30 ml). Some men (12 of 40) with no change in prostate volume did show symptomatic improvement. IPSS and QoL scores improved by >30% in 31 of the 41 men (76%). The efficacy was sustained up to 12 mo (Fig. 5). BoNTA injected into the prostate appears safe and effective for BPH. The authors conclude that mechanisms of relief of symptoms might not depend totally on the volume shrinkage; the inhibitory effect on the smooth muscle tone and aberrant sensory function might also be important. Long-term multicentre follow-up studies are needed to confirm the efficacy and long-term safety of BoNTA.

5.2. Stents

In a recent systematic review of a self-expanding thermoexpandable metallic stent (MemoKath®) in patients who are unfit for surgery, 14 case series including 839 men were evaluated by two independent reviewers [39]. The MemoKath stent of the nonepithelialising type can provide a safe, effective treatment of LUTS/BPH in men with high operative risk. The reduction in IPSS of a MemoKath is comparable to that seen after TURP [40]. However, inadequate follow-up does not yet allow us to draw firm conclusions on stent durability.

In conclusion, urethral stents may have a place in patients at significant risk for anaesthesia or who refuse interventional therapy. Most stents only provide a temporary solution. BoNTA treatment is still in its infancy, but looks promising. More research is needed to check efficacy and tolerability.

6. Conclusions

Various promising alternatives to conventional TURP are currently available, which seem to have a comparable efficacy and better safety profile than TURP. Energy-based ablative techniques may have a role between oral pharmacotherapy and TURP. Mechanical stenting is recommended for patients at high risk from other forms of intervention. BoNTA injections provide an interesting new modality. However, though several studies illustrate the short-term efficacy of all these techniques, more long-term data (>5 yr of follow-up) are needed to confirm if the efficacy is sustained over time. Faced with the plethora of new, minimally invasive alternatives to TURP, the question of which modality...
to use in any given clinical setting is pertinent. It is apparent that different groups of clinicians have different skill sets and access to equipment; this translates in real-life practice to centres that have expertise in certain areas. In reality, improved efficacy and safety profiles are only two of many factors that lead to the adoption of a new surgical technology [41]. Until both procedural and contextual factors are in favour of a shift to a new “gold standard,” TURP will remain the primary choice for most practicing urologists.

Conflicts of interest

The author has nothing to disclose.

References


[38] Chuang YC, Giannantoni A, Chancellor MB. The potential and promise of using botulinum toxin in the prostate gland. BJU Int 2006;98:28–32.

