Recent advances in the surgical treatment of benign prostatic hyperplasia

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- Benign prostatic hyperplasia (BPH) is a histological diagnosis that refers to the proliferation of smooth muscle and epithelial cells within the prostatic transition zone .
- The enlarged gland is thought to lead to disease manifestations via two routes:
- (1) the static component: direct bladder outlet obstruction (BOO) from enlarged tissue; and
- (2) the dynamic component: from increased smooth muscle tone and resistance within the enlarged gland.
- Therapy for BPH typically targets one or both of the disease components (static or dynamic) to provide relief.

- Surgical intervention is an appropriate treatment alternative for patients with moderate-to-severe lower urinary tract symptoms (LUTS) and for patients who have developed acute urinary retention (AUR) or other BPH-related complications.
- In addition, medical therapy may not be viewed as a requirement because some patients may wish to pursue the most effective therapy as a primary treatment if their symptoms are particularly bothersome.

TURP

- Since the pioneering procedures performed in the 1960s and 1970s, TURP has undergone many changes:
- the development of optics, light sources, surgical and anaesthesia techniques, and the introduction of bipolar technology with the consequent use of physiological solution as intra-operatory bladder washing system, have greatly modified the procedure.

- The usual indications for TURP are acute urinary retention, bladder stones, obstructive kidney failure, and hematuria
- TURP can be performed either with general or spinal anaesthesia; the latter is characterized by less blood loss and earlier diagnosis of bladder boring and/or of water intoxication.
- Antibiotic therapy is recommended in every patient perioperatively and may consist of chotrimossazole, a second- or third-generation cephalosporin, ampicillins, lactamase inhibitors or fluoroquinolones

- Haemostasis can be enhanced during resection by lowering the energy density and increasing tissue contact time.
- Issa recommends lowering the cutting energy to 80–100 W instead of the usual 200 W, choosing a ‘blend’ instead of ‘pure’ cutting setting on the generator, and slowing down the speed with which the wire loop travels through the tissue so to increase the duration of tissue contact.

- Nonconductive irrigation fluid solutions such as glycine 1.5%, sorbitol 3% or mannitol 3% are preferred as bladder washing systems. These solutions are not isotonic and can cause TUR syndrome if excessively adsorbed:
- the patient reports nausea, hypertensive crisis, bradycardia, confusion, and sight trouble; if this syndrome is not diagnosed, it can progress to lung or cerebral oedema

- Traditional monopolar TURP is characterized by electric energy supplied from the resector loop and received by the electrode placed on patient’s skin, so the electric circuit created needs electric energy circulating into the patient to close itself .
- In bipolar TURP there is a closed circuit in the resector loop; the generated energy turns the physiologic solution, used as bladder irrigation, into an ionized particle plasma able to destroy tissue molecular ligaments and make resection possible

- Ahyai and coworkers performed a meta-analysis of functional outcomes and complications following many transurethral procedures.
- No differences were found between monopolar and bipolar TURP in IPSS, QoL, Q_{max}, or PVR. Moreover, they analysed intraoperative, perioperative and late complications.
- No significant differences were found between bipolar *versus* monopolar TURP intraoperative complications ($p = 0.407$), perioperative ($p = 0.029$), late ($p = 0.392$), or overall complications ($p = 0.058$). The risk of blood transfusion in both techniques is comparable and none of the analysed trials mentioned TUR syndrome as an adverse event of bipolar TURP.

Simple prostatectomy

- Open simple prostatectomy can be still considered a recommended treatment in the case of an enlarged prostate
- The upper volume of prostate over which simple prostatectomy is the gold standard is still discussed, usually 100 g is considered the limit of volume even if urologists trained in endoscopy can perform TURP also in these cases.

- Simple prostatectomy is an appealing technique in the case of concomitant pathologies needing a surgical approach as vesical stones, diverticula, voluminous adenomas, and inguinal hernia. Simple prostatectomy can be performed with retropubic or, more frequently, suprapubic (transvesical) approach.

- The Calabro-Sicilian Society of Urology has published one of the major present day series of simple prostatectomies performed between 1997 and 1998.
- Of 31,558 patients treated for symptomatic BPH, 5636 underwent surgery. Open prostatectomy accounted for 32% (*n* = 1804) of all surgical treatment. The postoperative median hospitalization time was 7 days. Concomitant lower urinary tract disease was present in 25% of the patients. Severe bleeding occurred in 11.6% of open prostatectomies.

- . Blood transfusions were given in 8.2% of cases.
- Sepsis was reported in 8.6% of the patients.
- Reinterventions, within 2 years, mainly due to bladder neck stenosis, were reported in 3.6% of cases.
- The authors concluded that this procedure, even if performed today in Western countries, shows the same significant rate of early and late complications reported in the past or in less-developed countries

Laparoscopic simple prostatectomy

- In 2002, Mariano and colleagues described the first laparoscopic simple prostatectomy .
- The patient was placed in a steep Trendelenburg position and five intraperitoneal trocars were placed. After vascular control was achieved, the prostatic capsule and bladder neck were opened in the midline, and adenoma was enucleated.

- McCullough and colleagues compared 96 extraperitoneal laparoscopic simple prostatectomies with 189 open procedures; surgical time was longer in laparoscopy (95.1 ± 32.9 minutes) than in the open approach (54.7 ± 19.7 minutes) .
- Whereas patients who had undergone laparoscopic surgery needed a shorter hospital stay and time of catheterization, there were no differences in terms of blood loss and postsurgical bladder washing.

- In 2008, a Cleveland Clinic group described the first laparoscopic single-port, simple prostatectomy ;
- the trocar is placed into the bladder that is then straightened with CO_2. They described three procedures whose surgical time decreased from 6 to 1.5 hours; they did not report any data about blood loss or functional outcomes.
- A theoretical advantage of the laparoscopic approach is the reduction of bleeding during adenoma excision thanks to the pressure created by the insufflation into the bladder.

Robotic simple prostatectomy

- Sotelo and colleagues described the first robotic simple prostatectomy, with a surgical technique similar to laparoscopy . Seven procedures were performed: average blood loss was 382 ml, average surgical time was 195 minutes and average hospital stay was 1.33 days.
- No functional outcome was described.

- Coelho and colleagues described a new technique of robotic-assisted simple prostatectomy (RASP) that includes the standard operative with the addition of some technical modifications during the reconstructive part of the procedure .
- Following the resection of the adenoma, instead of performing the classical ‘trigonization’ of the bladder neck and closure of the prostatic capsule, they performed three modified surgical steps: plication of the posterior prostatic capsule, a modified van Velthoven continuous vesicourethral anastomosis and, finally, suture of the anterior prostatic capsule to the anterior bladder wall.

- They obtained significant improvement from baseline reported in the average IPSS (average preoperative *versus* postoperative, 19.8 ± 9.6 *versus* 5.5 ± 3.1, $p = 0.01$) and in mean maximum urine flow (average preoperative *versus* postoperative 7.75 ± 3.3 *versus* 18.2 ± 6.5 ml/s, $p = 0.019$) at 2 months after RASP.
- As far as functional outcome is concerned, all patients were continent 2 months after RASP.

Laser vaporization

- Prostate laser vaporization has been developed in the last 15 years as an alternative to TURP. Laser resections can be performed using different kinds of energy:
- coagulative laser: neodymium: yttrium–aluminium–garnet (Nd:YAG), diode laser;
- cutting laser: holmium:YAG (Ho:YAG) and thulium:YAG (Tm:YAG);
- vaporizing laser: Nd:YAG, Ho:YAG, diode, KTP (potassium–titanyl–phosphate) and lithium triborate (LBO).

- These energy sources have been tested and compared with TURP and their outcomes proved not to be lasting and effective enough compared with the gold standard.

- The latest innovation today is represented by the green light laser HPS 120W that can be used also for prostates larger than 80 g.
- Indications for prostate laser vaporization, according to the American Urological Association and European Urological Association guidelines are patients using anticoagulant therapy who cannot be interrupted before the procedure, patients who cannot undergo TURP or patients wishing for a regular ejaculation after the surgery.

HoLEP

- Since the first description by Gilling and colleagues, HoLEP has been increasingly used for the surgical management of BOO as an alternative to traditional TURP [Gilling *et al*. 1995]. Multiple studies report that it is a safe and effective procedure for treating symptomatic BPH, independent of prostate size, and with low morbidity and a short hospital stay.

- Nevertheless, Shah and colleagues showed that a limitation of this technique is the experience and training required [Shah *et al*. 2007]: the learning curve is the most important impediment for adopting this attractive technique. They reported data from their initial experience on 280 patients: eight required conversion to TURP, due to failure to progress during enucleation of the lateral lobes. Their most common complication was capsular perforation which occurred in 9.6% of cases. No patient had any evidence of TUR syndrome.

- Ahyai and colleagues randomized 200 patients with urodynamic proven obstruction and a prostate volume less than 100 ml to HoLEP or TURP [Ahyai *et al*. 2007]; after 2 and 3 years of follow up, HoLEP micturition outcomes were better than TURP, and late complications were similar.

- Briganti and colleagues compared the impact of HoLEP and TURP on sexual function obtaining no differences between the techniques [Briganti *et al*. 2006]: both significantly lowered the international index of erectile function (IIEF) orgasmic function domain because of retrograde ejaculation.

- As far as a comparison between HoLEP and open transvesical prostatectomy is concerned, Kuntz and colleagues performed a randomized study on 120 patients, urodynamically obstructed, with prostates >100 g [Kuntz *et al*. 2004]. HoLEP entailed significantly less blood loss and a much shorter catheter time and hospital stay. The rate of late complications was equally low with each procedure. The postoperative micturition improvement was significant and equivalent between the two groups, confirming HoLEP to be an endourologic alternative to open surgical enucleation of the prostate for large glands

Minimally invasive treatments

- For patients at high operative risk, a minimally invasive technique, which could be performed without anaesthesia, is required as an alternative treatment modality.
- Thermotherapy, where heat energy is delivered to the prostatic tissue, causes haemorrhagic necrosis around the urethra which is about 10–25 mm in diameter and is surrounded by cells with apoptotic features [Brehmer, 1997; Nissenkorn *et al*. 1993]. Histological changes induced by heating are directly dependent on the temperature achieved in the tissue. Thermocoagulation is obtained above 45°C and thermoablation above 60°C

- The first study for the treatment of BPH under an FDA-approved protocol was in 1991. The development of transurethral microwave heat treatment was partially prompted by the failure of the transrectal or transurethral hyperthermia devices. Five years later, after rigorous testing, the Prostatron device, manufactured by Urologix, received final FDA approval. Nowadays there are many different types of thermotherapy for BPH.

- **Prostatron**
- **Targis**
- **Coretherm (ProstaLund)**

Transurethral needle ablation

- Transurethral needle ablation (TUNA) is characterized by a specific catheter connected to a radiofrequency generator; the catheter tip contains two needles that deploy an acute angle to each other and to the catheter. Each needle’s retractable shield controls the urethral temperature and lesion geometry. During the treatment, the temperature is checked in the urethra, in the prostate gland and in the rectum, where a specific probe with a thermocouple is placed.

- Zlotta and colleagues presented the clinical outcome of patients treated by TUNA and followed for 5 years [Zlotta *et al*. 2003]. A total of 188 patients with symptomatic BPH were treated with TUNA. At a mean follow up of 63 months, mean urinary peak flow rate increased from 8.6 to 12.1 ml/s , IPSS and PVR decreased from 20.9 and 179 ml to 8.7 and 122 ml, respectively .
- The percentage of patients who improved by at least 50% their peak uroflow and IPSS was 24% and 78%, respectively.

- Mean prostate volume and prostate-specific antigen (PSA) levels did not change significantly (53.9 *versus* 53.8 ml and 3.3 *versus* 3.6 ng/ml, respectively, at 5 years, both p values > 0.05, Student's t-test). Two patients died of unrelated comorbidities and 10 were lost to 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 23.3% required additional treatment at 5 years follow up following the original TUNA procedure.

- According to an FDA suggestion, microwave thermotherapy for BPH should be excluded in patients with a prior radiation therapy to the pelvic area, as they have a bigger risk of rectal fistula formation. Moreover, the FDA recommend care not to oversedate the patient, as patient perception of pain is an important safety mechanism to ensure that the heating of the tissue is not excessive.
- General or spinal anaesthesia should not be used.

TUMT

- In 2008, Hoffman and colleagues published a review collecting all randomized controlled trials evaluating TUMT for men with symptomatic BPH [Hoffman *et al*. 2008]. Comparison groups included TURP, minimally invasive prostatectomy techniques, sham thermotherapy procedures and medications.

- Outcome measures included urinary symptoms, urinary function, prostate volume, mortality, morbidity and retreatment. Fourteen studies involving 1493 patients met inclusion criteria, including six comparisons of microwave thermotherapy with TURP, seven comparisons with sham thermotherapy procedures and one comparison with an alpha blocker.
- Study durations ranged from 3 to 60 months.

- The authors concluded that microwave thermotherapy techniques are effective alternatives to TURP and alpha blockers for treating symptomatic BPH for men with no history of urinary retention or previous prostate procedures and prostate volumes between 30 and 100 ml.
- However, TURP provided greater symptom score and urinary flow improvements and reduced the need for subsequent BPH treatments compared with TUMT.

Conclusions

- Open prostatectomy and monopolar TURP remain as gold standards by which newer transurethral approaches must be compared. Nowadays TURP and its alternative techniques seem to have comparable efficacy and overall morbidity. Bipolar TURP and HoLEP have more consistent data and passed the phase of feasibility, while TUVP, KTP and minimally invasive treatments need more evidence and longer follow up. Laparoscopic and robotic approaches are under investigation.