

Therapeutic strategies for the treatment of male lower urinary tract symptoms – Part Two

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- He completed his Higher urological surgical training in Ireland.
- He has previously been a Cancer Fellow in Leipzig, Germany and Vancouver Cancer Centre, British Columbia, Canada.
- Following this he was a Consultant Urological Cancer surgeon in the Essex Cancer Centre, UK for 9 years.
- He specialises in Urological cancer surgery (Kidney, bladder, prostate) and is a specialist in ROBOTIC, laparoscopic and open cancer surgery.



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TURP – transurethral resection of prostate (monopolar (M) and bipolar (B)) (Figure 5)

TURP employs a resectoscope and wire loop to remove prostate tissue from the centre of the prostate via the urethra (Figure 5). In a meta-analysis of 20 RCTs with up to five year follow up, M-TURP resulted in a substantial Qmax and PVR improvement, and symptom score including QoL with long term benefit. (Cornu)(Reich)

B-TURP is performed in normal saline thus preventing certain M-TURP complications such as dilutional hyponatraemia. Bipolar TURP is the most widely and thoroughly investigated alternative to M-TURP and a large meta-analysis concluded that no clinically relevant differences exist in efficacy over mid- to long-term follow-up (up to 60 months) (Kumar))

Kumar, N., et al. *Prospective Randomized Comparison of Monopolar TURP, Bipolar TURP and Photoselective Vaporization of the Prostate in Patients with Benign Prostatic Obstruction: 36 Months Outcome. LUTS: Lower Urinary Tract Symptoms, 2018. 10: 17.*

Investigational therapies

A number of other pharmacological potential therapeutic options are currently under investigation (Fig 4) and will not warrant further discussion at this time but may represent exciting potential bladder and prostate receptor targets for the future.

| |
|---|
| Phytotherapy |
| Anti-inflammatory agents |
| vitamin D3-receptor analogs |
| Cannabinoids |
| Luteinizing hormone-releasing antagonist |
| Transient receptor potential (TRP) channels |
| Purinergic receptor antagonists |
| Rho-kinase inhibitors |

Figure 4

Current Surgical Strategies

The surgical strategies deal with the BOO component of LUTS. Approximately 60-70% of patient with pre-existing OAB symptoms pre-operatively get improvement or resolution post-operatively.

Figure 5

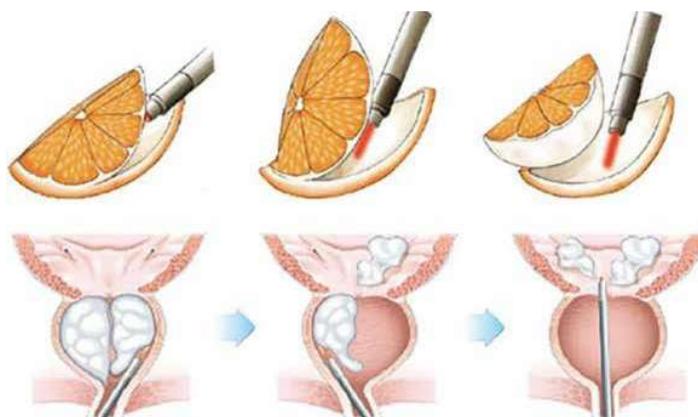
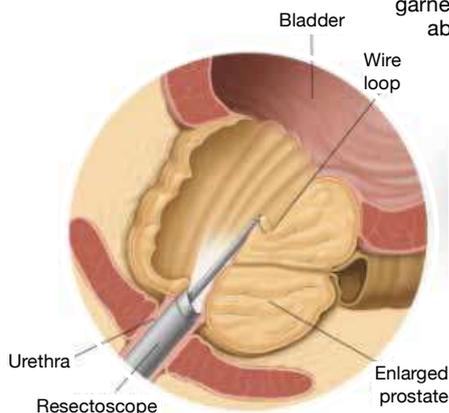


Figure 6

Cornu, J.N., et al. *A Systematic Review and Meta-analysis of Functional Outcomes and Complications Following Transurethral Procedures for Lower Urinary Tract Symptoms Resulting from Benign Prostatic Obstruction: An Update. Eur Urol, 2015. 67: 1066.*

Reich, O., et al. *Techniques and long-term results of surgical procedures for BPH. Eur Urol, 2006. 49: 970.*

Holep – Holmium laser enucleation of the prostate (Figure 6)

Holep is carried out in a similar fashion to a TURP but a laser is used to enucleate the prostate tissue at a prostate capsule level rather than resect it (Figure 6). The holmium:yttrium-aluminium garnet (Ho:YAG) laser is absorbed by water-containing tissues resulting in tissue coagulation and haemostasis. Meta-analyses of HOLEP trials with TURP or Open prostatectomy (OP) as comparators, found that symptom improvement was at least comparable with HoLEP (Tan). Further benefits include Qmax(Cornu), low reoperation rates and durable functional results (Elmansy)(Li).

HoLEP has shorter catheterisation, hospitalisation times and blood loss but a longer operation time compared with TURP (Tan). No difference exists in complications such as (incontinence or stricture rate). Further benefits include the ability to perform HOLEP with prostate volumes over 100gms and on anticoagulant/antiplatelet medications. The impact on erectile function and retrograde ejaculation is comparable between HoLEP and TURP/OP (Briganti).

Tan, A., et al. *Meta-analysis of holmium laser enucleation versus transurethral resection of the prostate for symptomatic prostatic obstruction. Br J Surg, 2007. 94: 1201.*

Cornu, J.N., et al. *A Systematic Review and Meta-analysis of Functional Outcomes and Complications Following Transurethral Procedures for Lower Urinary Tract Symptoms Resulting from Benign Prostatic Obstruction: An Update. Eur Urol, 2015. 67: 1066.*

Elmansy, H.M., et al. *Holmium laser enucleation of the prostate: long-term durability of clinical outcomes and complication rates during 10 years of follow-up. J Urol, 2011. 186: 1972.*

Briganti, A., et al. *Impact on sexual function of holmium laser*

enucleation versus transurethral resection of the prostate: results of a prospective, 2-center, randomized trial. *J Urol*, 2006. 175: 1817.

Li, M., et al. Endoscopic enucleation versus open prostatectomy for treating large benign prostatic hyperplasia: a meta-analysis of randomized controlled trials. *PLoS One*, 2015. 10: e0121265.

Open prostatectomy (Millen/Freyer) (Figure 7)

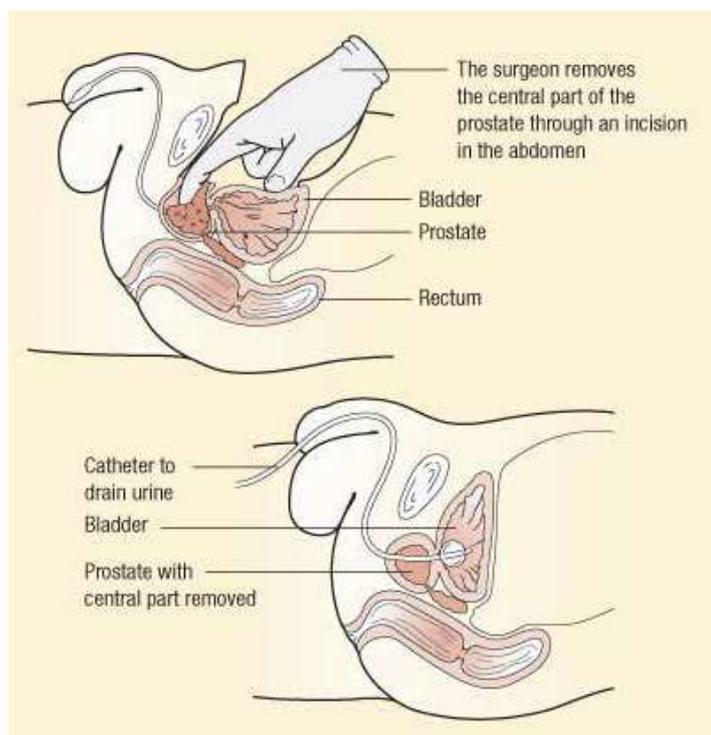
Obstructive prostate tissue is enucleated along the prostate capsule using the index finger, approaching from within the bladder (Freyer) or through the anterior prostatic capsule (Millin). It is used for substantially enlarged glands (> 80-100 mL).

OP reduces LUTS significantly, improves QoL score, increases mean Qmax by 375%, and reduces PVR with long term efficacy proven. However, while operation time is shorter, the catheterisation time, need for blood transfusion and hospitalisation is longer.

OP is the surgical treatment of choice for men with prostates > 80 mls. especially if the urological unit does not have access to a holmium laser or B-TURP system available (Lin).

Lin, Y., et al. Transurethral enucleation of the prostate versus transvesical open prostatectomy for large benign prostatic hyperplasia: a systematic review

Figure 7



and meta-analysis of randomized controlled trials. *World J Urol*, 2016. 34: 1207.

Prostatic urethral lift (Figure 8)

The prostatic urethral lift (PUL) is a new minimally invasive approach. Encroaching lateral lobes are compressed by small permanent suture-based implants delivered under cystoscopic guidance, under local or general anaesthesia, causing the prostatic urethra to widen thus leaving a continuous channel through the prostatic fossa.

PUL improves IPSS, Qmax and QoL however, these improvements are inferior to TURP at 24 months. Prostatic urethral lift seems to have no significant impact on ejaculatory function and indeed is chosen by younger patients for this reason. (Gratzke)

Gratzke, C., et al. Prostatic urethral lift vs transurethral resection of the prostate: 2-year results of the BPH6 prospective, multicentre, randomized study. *BJU International*, 2017. 119: 767.

iTIND (Figure 9)

The iTIND is a device that is composed of three elongated nitinol struts and an anchoring leaflet and is inserted and deployed to expand and thus compress and cause necrosis in prostate tissue over 5 days at which point it is removed. Ongoing research is required but early results demonstrate reduction in symptoms and improve Qmax, QoL and symptoms. Notably there are no reported cases of erectile or ejaculatory dysfunction afterwards. (porpiglia)

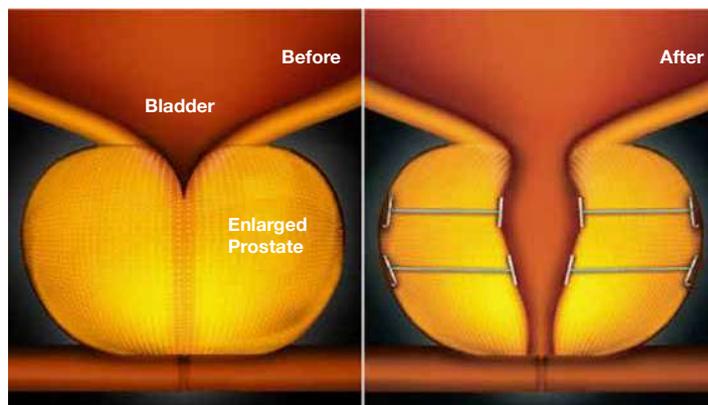


Figure 8

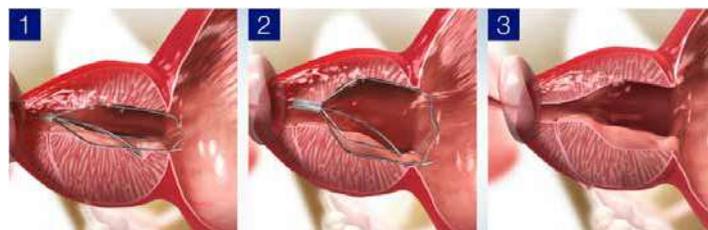


Figure 9

Porpiglia, F., et al. 3-Year follow-up of temporary implantable nitinol device implantation for the treatment of benign prostatic obstruction. *BJU Int*, 2018. 122: 106.

Convective wave vapour energy ablation (Figure 10)

Radiofrequency power is employed via a delivery device to create water vapour, which in turn deposits the stored thermal energy when the steam phase shifts to liquid upon cell contact. The steam disperses through the tissue interstices and releases stored thermal energy onto prostatic tissue causing cell necrosis.

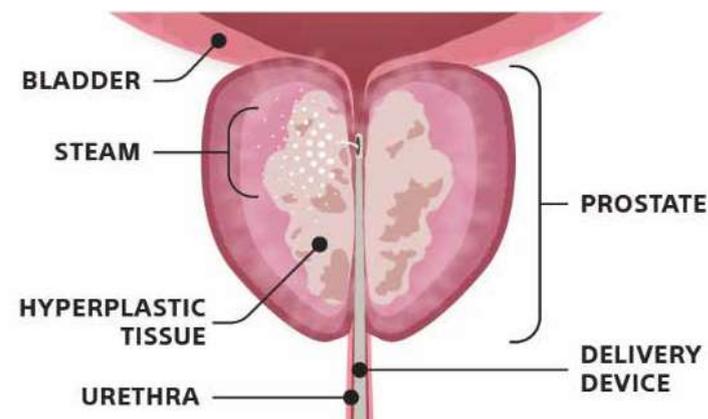
There are no randomised controlled trials completed to date to determine efficacy but early reports against placebo demonstrate improved symptoms and Qmax at 24 months. No

relevant impact was observed on PVR. QoL was significantly improved also. Surgical retreatment rate was only 4.4% over the four years of follow up. Preservation of erectile and ejaculatory function was demonstrated. The procedure can be performed as an out-patient procedure and is applicable to the prostatic median lobe, unlike PUL. (Roehrborn)(McVary).

Roehrborn, C.G., et al. Convective Thermal Therapy: Durable 2-Year Results of Randomized Controlled and Prospective Crossover Studies for Treatment of Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia. *J Urol*, 2017. 197: 1507.

McVary, K.T., et al. Rezum Water Vapor Thermal Therapy for

Figure 10



Lower Urinary Tract Symptoms Associated With Benign Prostatic Hyperplasia: 4-Year Results From Randomized Controlled Study. Urology, 2019. 126: 171.

Aquablation (Figure 11)

Aquablation uses hydro-dissection to ablate prostatic parenchyma while sparing collagenous structures like blood vessels and the surgical capsule using. The generation of thermal energy is minimal and is performed under real-time transrectal ultrasound guidance. Haemostasis is performed with a Foley balloon catheter on traction or diathermy.

Aquablation has been proven to be non-inferior to TURP at one year in relation to symptoms score, QoL, Qmax, reduction in PVR and reoperation rate. (Gilling)

Larger prostates (50-80 mL) demonstrated a more pronounced benefit.

Aquablation shows a reduction in ejaculation dysfunction but the risk of bleeding especially in prostates larger than 80 mL is higher (WATER II trial). Further comparative studies are needed. (Desai)

Gilling, P.J., et al. Randomized Controlled Trial of Aquablation versus Transurethral Resection of the Prostate in Benign Prostatic Hyperplasia: One-year Outcomes. Urology, 2019. 125: 169.

Desai, M., et al. Aquablation for benign prostatic hyperplasia in large prostates (80-150 mL): 6-month results from the WATER II trial. BJU Int, 2019.

Prostate artery embolization (PAE) (Figure 12)

Prostatic artery embolisation is performed as a day procedure under local anaesthesia with access through the femoral or radial arteries. The appropriate prostatic arterial supply is selectively embolised thus cutting off the blood supply to the prostate.

While PAE shows benefit in clinical parameters, compared to TURP it is less effective and in the reduction in prostate volume at only 26% at 3 years (Malling). It is however better than TURP in terms of anaesthetic requirement, blood loss, catheter time and hospital stay.

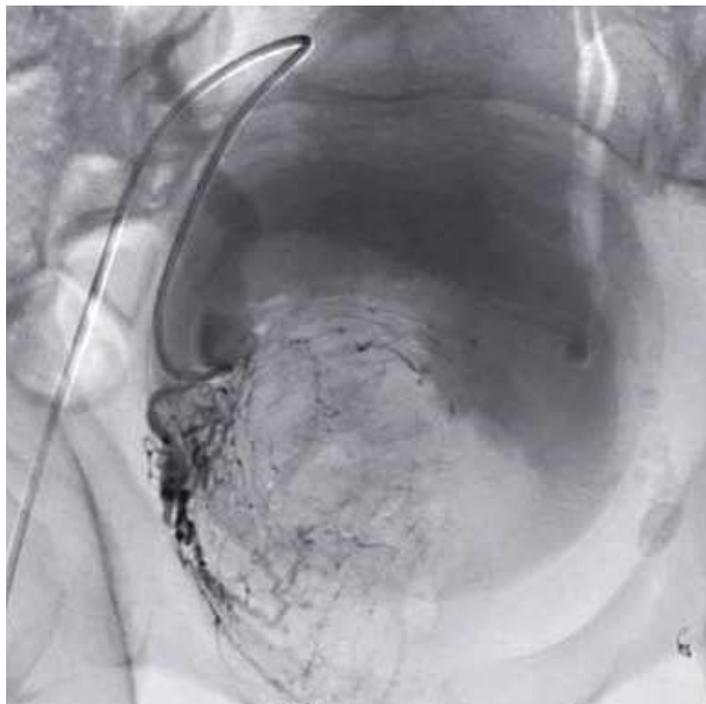
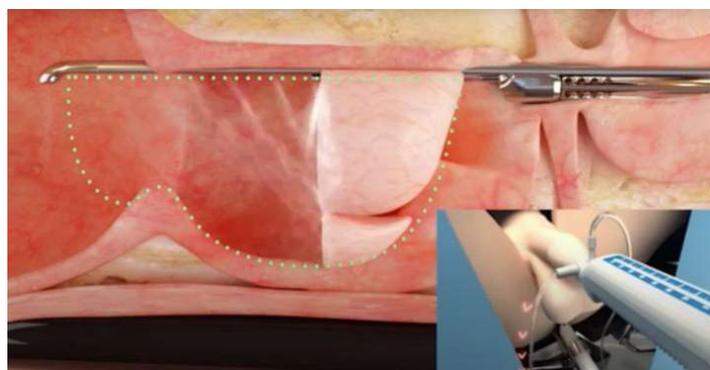


Figure 12

Figure 11



PAE seems to be an alternate for patients who have significant co-morbidities precluding standard surgical treatment, especially those with very large prostates (>80 ml) (Bhatia).

Malling, B., et al. Prostate artery embolisation for benign prostatic hyperplasia: a systematic review and meta-analysis. Eur Radiol, 2019. 29: 287.

Bhatia, S., et al. Prostate Artery Embolization in Patients with Prostate Volumes of 80 mL or More: A Single-Institution Retrospective Experience of 93

Patients. J Vasc Interv Radiol, 2018. 29: 1392.

Conclusion

There are a large variety of treatment options, both pharmacological and surgical, for male LUTS. All choices of treatment are based on failure of conservative measures, patient choice, co-morbidities, and the potential treatment benefits and side effects.

Surgical options tend to be reserved in the modern era for patients who have failed the other non-invasive options.

News

Major service improvements needed for people with high cancer risk

The Irish Cancer Society has told an Oireachtas Committee that cancer genetic services in Ireland need to be better resourced in line with what is laid out in the National Cancer Strategy.

Director of Advocacy, Rachel Morrogh, told the Oireachtas Health Committee that the demand for genetic testing in Ireland has increased but services further downstream haven't been resourced to keep pace, leading to long waiting times that must be addressed.

The Society has highlighted

instances of women at a high genetic risk of cancer who have had or are waiting for preventative surgeries such as mastectomies to help reduce their risk, but who are still in the dark as to when they can get a follow-up breast reconstruction.

Irish Cancer Society Director of Advocacy Rachel Morrogh said: "Approximately 1,800 new patients avail of the cancer genetics service every year and this is rising with increased awareness amongst patients and healthcare professionals.

"It is critical given rising cancer cases generally that the number of preventable cancers are reduced. One way to do this is to ensure people who are taking positive actions about their health and trying to reduce their risk of cancer by accessing genetic services are tested, diagnosed and treated within a timeframe that gives them the best chance of living a life free of cancer.

"In particular we need to see sweeping service improvements for those who carry the high-risk BRCA gene so they have access to a dedicated group

of physicians as part of their pathway, along with an audited, quality-assured BRCA screening service bringing standardised care across the country.

"We must always be mindful that cancer kills over 9,000 people in Ireland every year, and we cannot let it become the forgotten C during this pandemic."

Anyone with a cancer-related query or concern can talk to a specialist cancer nurse on the Irish Cancer Society Support Line on Freephone 1800 200 700 and supportline@irishcancer.ie.