

The practical assessment and management of bladder outflow obstruction

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Abstract

The initial management of bladder outflow obstruction typically related to benign prostatic hyperplasia (BPH) falls to a large extent within the remit of general practice. Referral onwards to secondary care typically arises following the failure to respond to conservative measures or when complications have supervened; the most significant of which is urinary retention. In the hospital setting, anaesthesia, constipation and immobility are the common precipitants. What follows is a practical guide to the management of these situations and provides an overview of the conservative, medical, minimally invasive and surgical treatments available.

Keywords Bladder outflow obstruction; BPH; post-void residual; prostate

Bladder outflow obstruction

At the most basic level, flow is proportional to ‘pipe’ size (dictated by the prostate) and pump pressure, which is determined by the bladder. The bladder is best seen as a reservoir which enables an individual to discharge urine at a ‘socially convenient’ time. A ‘normal’ bladder will hold up to 500 ml comfortably but will typically have a ‘working’ volume of 300–400 ml and should empty completely (leaving a post-void residual (PVR) of nothing) (Figures 1 and 2). Normal voiding frequency is 5–7 times a day and up to once at night. In terms of flow rates, urologists are interested in the maximum flow rate or Q_{\max} (Figure 3). Broadly speaking, a young man will void at a speed in excess of 25 ml/s. An individual will have noticed that their flow will have slowed when below 20 ml/s; more obviously slowed when less than 15 ml/s; significantly slowed below 10 ml/s; and a trickle when below 5 ml/s. As the flow reduces, so the PVR tends to increase leading to urinary frequency, which is a consequence of the loss of functional volume and commonly most bothersome at night (nocturia). Patients are often unaware of incomplete bladder emptying. Post-void residuals can be surprisingly large, with excessively large residuals indicative of detrusor failure (chronic retention). Huge residuals can lead to hydronephrosis and obstructive uropathy.

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In the acute setting, practical management is about eliciting whether an episode of urinary retention or acutely deteriorating symptoms is directly precipitated by an event (such as anaesthesia, surgery or constipation) in which case they are likely to return to their previous baseline level, or whether it is the precipitated deterioration in pre-existent symptoms, in which case treatment will often be required. A proper history is important, ideally supplemented by the International Prostate Symptom Score (IPSS). Weak stream, intermittent flow and straining to void all imply bladder outflow obstruction, although detrusor failure is an alternative cause. These symptoms typically arise as a consequence of bladder outflow obstruction (BOO) usually as a consequence of prostatic obstruction or occasionally urethral stricture disease. Palpation for a palpable bladder and digital rectal examination are mandatory. In terms of prostate size they are small (15–30 g) (not much to feel), medium (30–40 g) (obvious to feel and can manipulate finger to sides), large (50–80 g) (difficult to feel sides), huge (100–300 g) (finger bent backwards). Weight can be directly extrapolated as volume 1 ml = 1 g and estimations are notoriously inaccurate. In terms of texture they are either smooth (probably benign) or irregular and hard (probably malignant). Direct measurement from imaging is based on the sphere volume formula: width × height × length × 0.52.

The most useful investigation to do is a measurement of post-void residual (PVR) using a bladder scanner. There is no accepted definition of a significant PVR but anything above 100 ml is probably significant in practical terms. Viewing the residual as a percentage of voided volume adds significance, i.e. 100 ml residual following a 200 ml void equates to a residual of one-third bladder volume as opposed to 100 ml residual following 400 ml void in which case residual is one-fifth. Stratification of patients at risk of retention is largely based on age (older more likely >70), prostate volume (>40 ml), PVR >140 ml, Q_{\max} <12 and pre-existent symptoms.

Conservative treatment

The majority of men suffering from lower urinary tract symptoms (LUTS) are unlikely to progress to acute urinary retention or other complications (e.g. renal insufficiency, stones, urinary tract infections, etc.). In the placebo arm of the Medical Therapy of Prostatic Symptoms (MTOPS) study, clinically significant progression was 17% at 4.5 years or 4.5% per year. Urinary retention was 2% and surgical intervention 5% after 4.5 years.¹ As such, men with mild to moderate uncomplicated LUTS who are not too troubled by their symptoms are suitable for watchful waiting. This more conservative approach negates the risk of side effects and complications imposed by medical and surgical therapy. Watchful waiting should include a range of behavioural and dietary modifications including:

- Education (about the patient’s condition).
- Reassurance (that cancer is not a cause of the urinary symptoms, once malignancy has been excluded). Patients are equally likely to have cancer with or without LUTS.
- Lifestyle advice such as:
 - Reduction in fluid intake at specific times aimed at reducing urinary frequency when most convenient (e.g. at night or when going out in public).



Figure 1 Probe position for post-void bladder scan.

- Avoidance or moderation of intake of caffeine or alcohol, which may have a diuretic and irritant effect, thereby increasing fluid output and enhancing frequency, urgency and nocturia.
- Use of relaxed and double-voiding techniques.
- Urethral milking to prevent post micturition dribble.
- Distraction techniques such as penile squeeze, breathing exercises, perineal pressure, and mental tricks to take the mind off the bladder and toilet, to help control storage symptoms.
- Bladder retraining that encourages men to hold on when they have sensory urgency to increase their bladder capacity and the time between voids.
- Reviewing the medication and optimizing the time of administration or substituting drugs for others that have fewer urinary effects (in particular diuretics).
- Treatment of constipation.
- Weight reduction (causal relationship established between metabolic syndrome and LUTS).

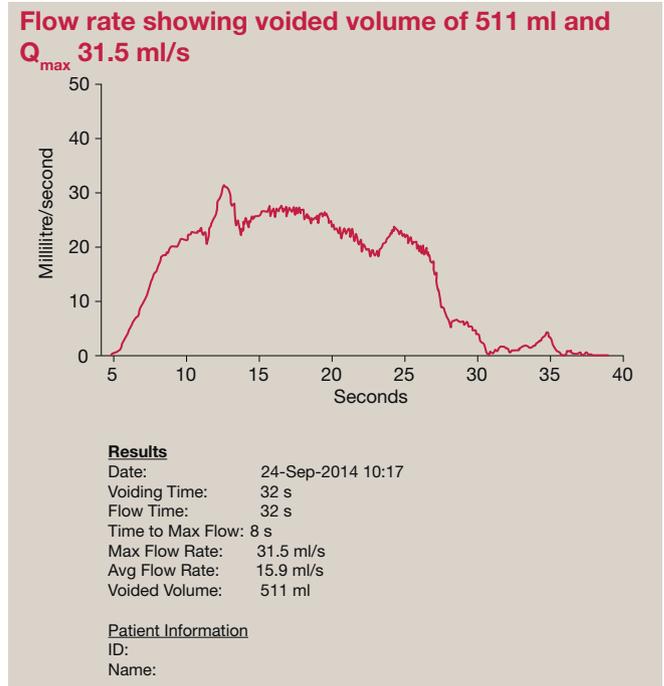


Figure 3

- Review presence of sleep apnoea and snoring given the strong relationship between this and nocturnal polyuria, (apnoea causes right heart strain which leads to release of atrial natriuretic peptide (ANP) and subsequent diuresis).

Patients at high risk of BPH progression, i.e. age >70 years, increasing symptom bother, PSA >1.4 ng/ml, prostate >30 g, low peak flow rate (Q_{max} <12 ml/s) and high post void residuals

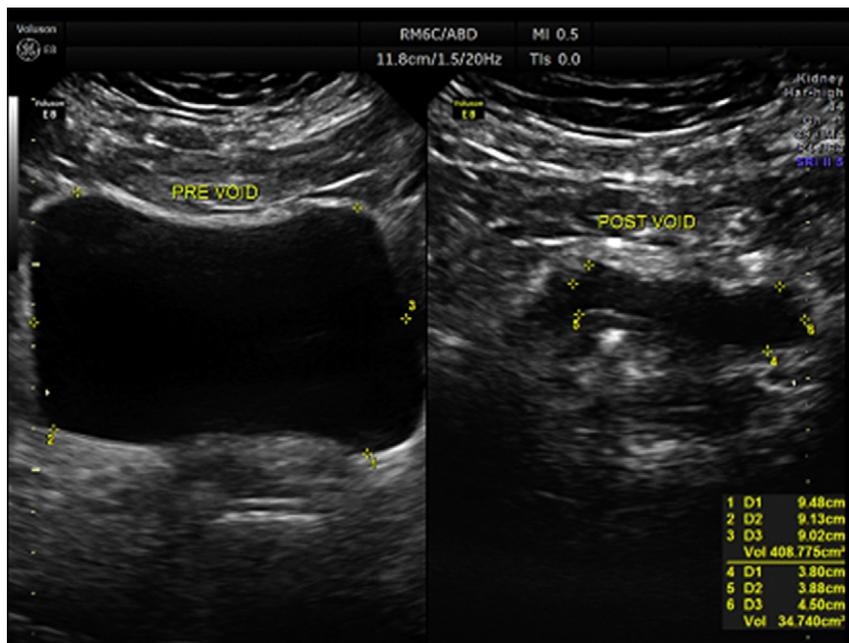


Figure 2 Pre-and post-void bladder scan ultrasound images (pre-void 408 ml, post-void volume 35 ml).

are the strongest predictors of clinical failure and in these patients, medical therapy should be considered.

Pharmacological treatments

Flow improvement medication

Alpha antagonists: α -1 Blockers are considered the first-line drug treatment for male LUTS because of their rapid onset of action (1–2 days), good efficacy and low rate and severity of adverse events. Alpha-1 blockers aim to inhibit the effect of endogenously released noradrenaline on smooth muscle cells in the prostate thereby reducing prostate/bladder neck tone and bladder outflow obstruction (BOO).¹ Typically, this class of drugs increases maximal flow rates (Q_{max}) by 2–4 ml/s with a reduction in post void residuals by 30 ml. In practical terms this is just enough difference to be noticeable but reduces IPSS by a surprisingly large amount (30–50%). They do not reduce prostate size nor prevent acute urinary retention. Tamsulosin, a selective α -1 receptor antagonist is a popular choice given its tolerability and modest adverse effects (anejaculation, asthenia, postural hypotension). Other options (which include alfuzosin and doxazosin) are less selective to the prostate leading to a broader side effect profile. Doxazosin, however, has the advantage of titratable dosing to minimize side effects. An adverse ocular event termed intraoperative floppy iris syndrome has been reported due to effects on ocular α -receptors and is particularly relevant in patients undergoing cataract surgery.

In a post retention trial without catheter (TWOC) scenario a patient will have approximately 50% chance of success, which is further improved by 50% with prior treatment for at least 2 days with an alpha antagonist.²

5-Alpha reductase inhibitors: Treatment with 5- α reductase inhibitors (5ARIs), dutasteride and finasteride, can be considered in men with moderate to severe LUTS and an enlarged prostate (>40 ml) and/or elevated PSA (>1.4–1.6 ng/ml). They inhibit the enzymatic conversion of testosterone to dihydrotestosterone (DHT) thus reducing the epithelial components of the prostate and ultimately prostate size. Clinical effects are seen after minimum treatment duration of at least 6–12 months. The 5ARIs improve IPSS by approximately 15–30%, decrease prostate volume by 18–28% and increase Q_{max} by approximately 1.5–2.0 ml/s. This class of drug reduces the risk of acute urinary retention by 57–68% and need for surgery by 34–55%. The number needed to treat (NNT) to prevent one event of urinary retention is 50, whereas the NNT to prevent surgery is in the order of 33–50.¹ Although dutasteride leads to a greater reduction in serum DHT than finasteride (90% versus 70%), clinical improvements are comparable. The main side effects include reduced libido, erectile dysfunction (ED), retrograde ejaculation and decreased semen volume. There is no short-term value in prescribing 5- α reductase inhibitors to increase the success of a trial without catheter; however, if a TWOC is successful then there is long-term value in trying to avoid repeat retention or surgery.

Combination therapy: Having commenced with an alpha blocker and in the context of ongoing moderate to severe LUTS in patients with prostate volumes more than 40 ml and PSA >1.4 μ g/l, adding in a 5ARI should be considered. Combination

therapy reduces the relative risk of AUR by 68%; BPH-related surgery by 71% and symptom deterioration by 41% compared with tamsulosin alone.³ Further studies have shown that the risk of clinical progression (that is to say, AUR, UTI, incontinence, increase in creatinine >50%) was reduced by 66% with combination therapy (compared to placebo) and to a greater extent than with either finasteride or doxazosin monotherapy (34% and 39%, respectively).¹ The benefits of combination therapy should be weighed against the significantly higher frequency of adverse events compared to monotherapy.

Phosphodiesterase inhibitors: Phosphodiesterase type-5 inhibitors (PDE5I) increase intracellular cyclic guanosine monophosphate thus reducing smooth muscle tone of the detrusor, prostate and urethra. Traditionally solely used in the context of erectile dysfunction, emerging evidence in men with ED and LUTS shows that tadalafil (the only licensed PDE5I for male LUTS), can reduce IPSS by 22–37%. Combination therapy with α -blockers improves the IPSS score (a reduction by 1.8), International Index of Erectile Function score (+3.6) and Q_{max} (+1.5 ml/s) compared with alpha blockers alone. There is sparse data regarding its effects on disease progression and prostate size. PDE5I are contraindicated in patients using nitrates, nicorandil, or the α -blockers doxazosin or terazosin. They are also contraindicated in patients who have unstable angina, have had a recent myocardial infarction (<3 months) or stroke (<6 months), hypotension, poorly controlled hypertension and significant hepatic or renal insufficiency.

Bladder frequency and urgency medication

Antimuscarinics: The detrusor muscle is innervated by parasympathetic nerves whose main neurotransmitter is acetylcholine, which stimulates muscarinic receptors on smooth muscle cells. Antimuscarinic medication aims to inhibit unstable bladder contractions that are the potential cause of urgency, frequency and urge incontinence. Muscarinic receptors are also present on other cell types, such as salivary glands, bowel and the central nervous system explaining the frequently reported side effects of dry mouth, constipation and blurred vision.

Approximately 20% of men with BOO secondary to BPH have associated detrusor instability which manifests itself as urgency frequency and nocturia (storage symptoms). They present with predominantly storage symptoms and can therefore be managed with antimuscarinics in combination with an alpha blocker. All the antimuscarinic drugs (oxybutynin, tolterodine, solifenacin and trospium) have similar efficacy and side effect profiles. These drugs have a slow wash in of two weeks and only modest efficacy in reducing frequency. They can have a role in reducing catheter related bladder spasms and by-passing. There is evidence that long term use may be associated with an increased risk of dementia and should be used with caution in the elderly.⁴

Mirabegron (B3 agonists): This class of medication has provided an alternative for patients with storage symptoms, and aims to ‘relax’ the bladder as opposed to inhibit contractility. It has a similar efficacy to anticholinergic medications but appears to have fewer side effects in terms of dry mouth and visual disturbance. Despite its theoretical potential for cardiac and

hypertensive side effects these seem very mild and it is only contra-indicated in uncontrolled hypertension.

Surgical therapy for BPH

All bladder outflow surgery shares the common goal of increasing the intra-prostatic radius to improve flow. The techniques vary and the differences in technique largely dependent on the energy source used to cut or ablate tissue. The application and suitability of each procedure is dependent on the size of the prostate and the amount of tissue that needs to be removed. All prostatic procedures carry a risk of ejaculatory, sexual dysfunction and incontinence and are loosely proportional to the extent of the tissue removed. Similarly, the durability and voiding success of the procedure is largely proportional to the extent of tissue removed. The number of treatment options reflects the range in patient priorities and expectations. Treatments for bladder outflow obstruction are becoming increasingly personalized.

Transurethral resection of the prostate

Monopolar transurethral resection of the prostate (TURP) is the 'gold standard' for the surgical management of BOO. Indications include moderate to severe LUTS (not controlled with medical therapy or because of patient choice), acute urinary retention, recurrent UTI, recurrent haematuria and obstructive uropathy. TURP involves the removal of tissue from the transition zone of the prostate using a 26-Fr resectoscope inserted via the urethra. Vision is maintained using irrigating fluid, most commonly glycine (although bipolar resection using normal saline is increasingly being used). A stepwise approach is adopted to resect the two lateral lobes and the middle lobe, followed by haemostasis using a rollerball diathermy. Resection time is usually limited to 1 hour to prevent trans urethral resection (TUR) syndrome which occurs as a consequence of excessive glycine absorption via open venous channels. The prostate chips are subsequently removed and a three-way catheter is inserted to irrigate the bladder until the urine is clear. TURP leads to a greater and more sustained improvement in LUTS than medical therapy and one can expect to see a mean increase in the Q_{max} by 10–15 ml/s, a decrease in the IPSS by 16 points and a reduction in the PVR by 100 ml. Commonly encountered short-term complications include bleeding requiring a transfusion (2%), TUR syndrome (0.8%), AUR (4.5%), clot retention (4.9%) and UTI (4.1%). Long-term complications relate to urinary incontinence (2.2%), urinary retention and UTIs, bladder neck contracture (4.7%), urethral stricture (3.8%), retrograde ejaculation (65.4%) and erectile dysfunction (6.5%).⁵

Bipolar TURP using normal saline as the irrigating fluid results in no clinically relevant differences in the short term, although it may be preferable due to a more favourable perioperative safety profile such as a reduction in the TUR syndrome, lower rates of clot retention and blood transfusion rates, shorter irrigation, catheterization and possibly hospitalization times.⁶ Younger men with BOO and those with prostate volumes <30 ml, may benefit from a bladder neck incision (BNI) rather than undergoing a complete TURP thus reducing the incidence of complications in particular those affecting fertility.

There are a number of alternative minimally invasive endoscopic techniques that have gained popularity in recent years, which appeal to both patients and clinicians alike. There is great potential benefit to patients unfit for general anaesthetic, or to those who wish to reduce or eliminate risk to sexual function. These treatments are fit to be delivered as a day case, allowing for greater throughput, lower waiting times and possible cost savings.

Rezum

Rezum utilizes radiofrequency to create steam, which is then injected directly into obstructive prostate tissue via a side firing needle under direct vision. The injured tissue then undergoes apoptosis rather than coagulative necrosis and is slowly reabsorbed over the next 2–3 months resulting in a small TURP-like cavity in the prostate. The procedure lasts up to 20 minutes and can be performed as a day-case under local anaesthetic. It is indicated in cases with a median lobe and prostate volumes greater than 30 cm³. In case series⁷ and when compared to sham,⁸ there were significant improvements in quality and functional parameter compared to baseline up to 36 months. There were no significant differences in measures of erectile and ejaculatory function. At present there is no comparison between Rezum and other LUTS procedures and further studies will address its use in larger prostates and men with urinary retention. Urinary tract infection and retention are the most common adverse effects.⁷

Urolift

The urolift procedure involves opening the prostatic urethra by pinning the lateral lobes laterally. The lobes are physically compressed laterally and then anchored laterally by a side-fired staple (Figure 5). The appeal of urolift is that symptomatic relief can be achieved without cutting or removing tissue and can be performed with local anaesthetic or sedation. It is the only reversible procedure as the staples can be partially removed. Current recommendations are for its use in men aged 50 years and older, with a prostate less than 100 ml without an obstructing middle lobe.

Medium-term (12–24 months) durability and superiority to sham intervention has been established.⁹ Adverse events are mild to moderate and transient in nature. The use of Urolift in men with an obstructing middle lobe and also in the context of acute urinary retention is under investigation.

Temporary implantable nitinol device (TIND)

The TIND is a 50 × 30 mm nitinol expandable wire cage (Figure 6), introduced to the bladder transurethrally. It is expanded under direct vision and hooked to the bladder, to cover the prostatic urethra and induce mechanical pressure. The aim is to induce tissue necrosis results in a number of prostatic/bladder neck incisions, and the device is removed after 5 days via an open-ended catheter. The first published case series has shown TIND implant to be feasible and safe, with encouraging functional and quality of life results at 36 months.¹⁰ In this small series, no intra-operative complications were reported, the mean operative time was 5.8 min and the median postoperative stay was 1 day.¹¹ Postoperative complications were limited to urinary tract infection and urinary retention.¹⁰ Larger case series and comparative studies with established medical and surgical

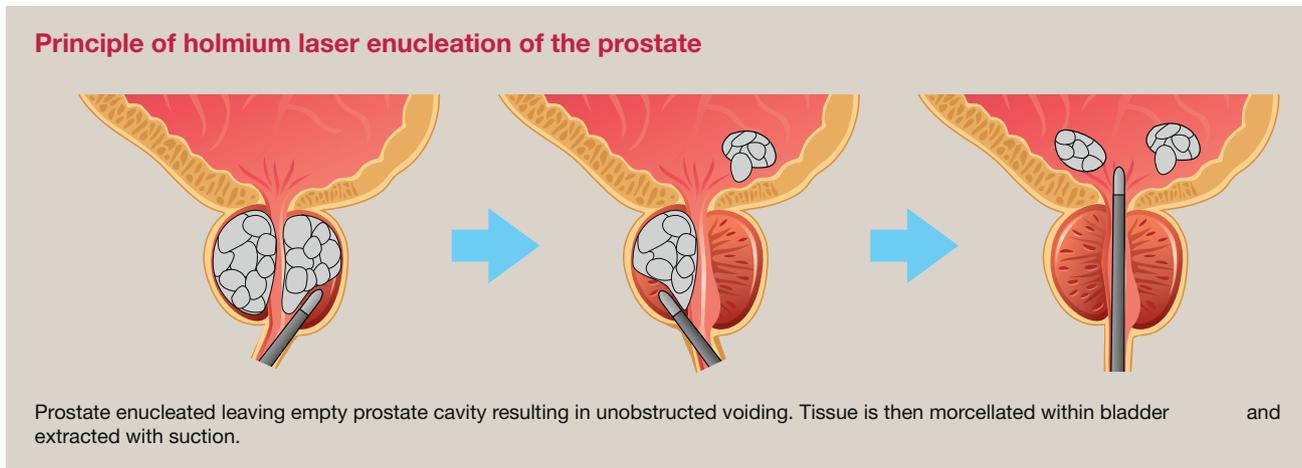


Figure 4

treatments are required to establish the role this new technology is likely to have in the management of bladder outflow obstruction.

Prostate artery embolization (PAE)

PAE has achieved mainstream appeal as it is a minimally invasive technique performed with local anaesthetic or sedation. Patient selection should be performed by both a urologist and interventional radiologist, and should be carried out by an interventional radiologist with specific training and expertise. Efficacy and safety has been demonstrated in case series and systematic reviews, which also suggest PAE is not as effective as established surgical therapies but risks fewer side effects.¹² Potential side effects range from mild (dysuria, suprapubic discomfort, haematuria) to those requiring medical or surgical intervention (non-target embolization of bladder or bowel, complications of angiography and pulmonary embolization).¹³ Exclusion criteria are yet to be fully established, but includes evidence of bladder dysfunction, structural abnormalities and prostate or bladder malignancy.¹³ It has been suggested that the role of PAE lies between medical therapy and surgical intervention.

Laser prostate surgery

Holmium laser enucleation of the prostate (HoLEP): works at a wavelength of 2140 nm and is a pulsed solid-state laser that is absorbed by water and water-containing tissues. The obstructing

transition zone tissue is enucleated along the anatomical plane between the transition and peripheral zones. The extreme heat provides excellent coagulation and the minimal tissue penetration allows precise enucleation of the prostatic lobes, which are then pushed into the bladder and subsequently morcellated (Figure 4). HoLEP has the significant advantage of enabling any size of prostate to be operated on as the procedure is not time limited by either the absorption of glycine irrigation or bleeding. As such they are particularly useful in larger prostates (those greater than 80 ml) and in anticoagulated patients. It also has the significant advantage of providing prostate tissue for analysis. The downside of the procedure is the steep learning curve and expensive equipment.

Green light laser photoselective vaporization: the laser alternative to HoLEP is potassium titanyl phosphate (KTP) photoselective vaporization of the prostate (PVP), otherwise known as green light laser prostatectomy. KTP lasers work at a wavelength of 532 nm and absorb haemoglobin, but not water. Vaporization leads to immediate removal of prostate tissue (therefore no tissue is available for histology), relief of BOO and LUTs. In effect a non-anatomical cavity is created in the prostate. The durability of the procedure is variable and there are reported issues with postoperative dysuria. It has been approved by NICE, in non-

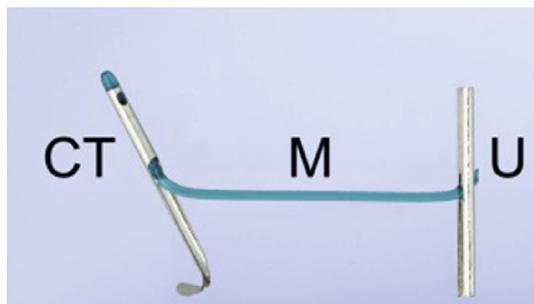


Figure 5 UroLift implant composed of capsular tab (CT), monofilament (M), and urethral end piece (U).¹⁵



Figure 6 Longitudinal view of the temporary implantable nitinol device.¹¹

high-risk patients, i.e. those with an increased risk of bleeding, prostates larger than 100 ml or in urinary retention.

Open retropubic prostatectomy (Millin's prostatectomy)

This was the historical procedure for bladder outflow surgery. A retroperitoneal approach is used, the prostate is incised anteriorly and the inner obstructing transitional zone is digitally enucleated. The advantage is that any size of prostate can be treated although nowadays this is largely reserved for large prostates over 100 g in volume. Bleeding can be profuse (23%) and the length of stay is usually several days.¹⁴ HoLEP is an identical procedure done endoscopically with a negligible risk of transfusion. ◆

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