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Platinum Opinion Editorial

Management of Non-neurogenic Male Lower Urinary Tract Symptoms: Better Holistic than Sequential

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Introduction

The surgical armamentarium for management of non-neurogenic male lower urinary tract symptoms (M-LUTS) in the context of benign prostatic obstruction (BPO) has dramatically expanded in the past decades [1]. While urologists and their patients historically had to choose between three medical options (α-blockers, 5α-reductase inhibitors, and tadalafil, alone or in combination) and two main surgical options (transurethral resection of the prostate or open simple prostatectomy), a number of alternatives and new categories have been developed such as minimally invasive surgical therapies (MiSTs). Depending on the level of evidence available [2], recommendations of varying strength and practical considerations are included in the European Association of Urology (EAU) M-LUTS guidelines for each intervention available (Fig. 1) [3].

Progress for medical treatments and noninvasive therapies [4,5] in parallel with the emergence of MiSTs has led to consideration of a stepwise approach in male LUTS/BPO management [6]. According to their invasiveness (ie, potential adverse events and complications) and efficacy (capacity to relieve symptoms and bladder outlet obstruction), therapeutic options can be categorised as conservative, medical, minimally invasive, or ablative treatments. Consideration of the trade-off between invasiveness and adverse events and BPO relief and durability has led to the concept of sequential treatment option for LUTS/BPO as detailed in Fig. 2 [3,6,7].

However, while this concept is based on a clear summary of the current treatment armamentarium, it does not necessarily provide an adequate rationale for stepwise, categorical, and purely sequential LUTS/BPO management.

The devil is in the details

Standard management of BPO-related male LUTS, as illustrated in Fig. 2, involves several conceptual and practical limitations that deserve careful consideration.

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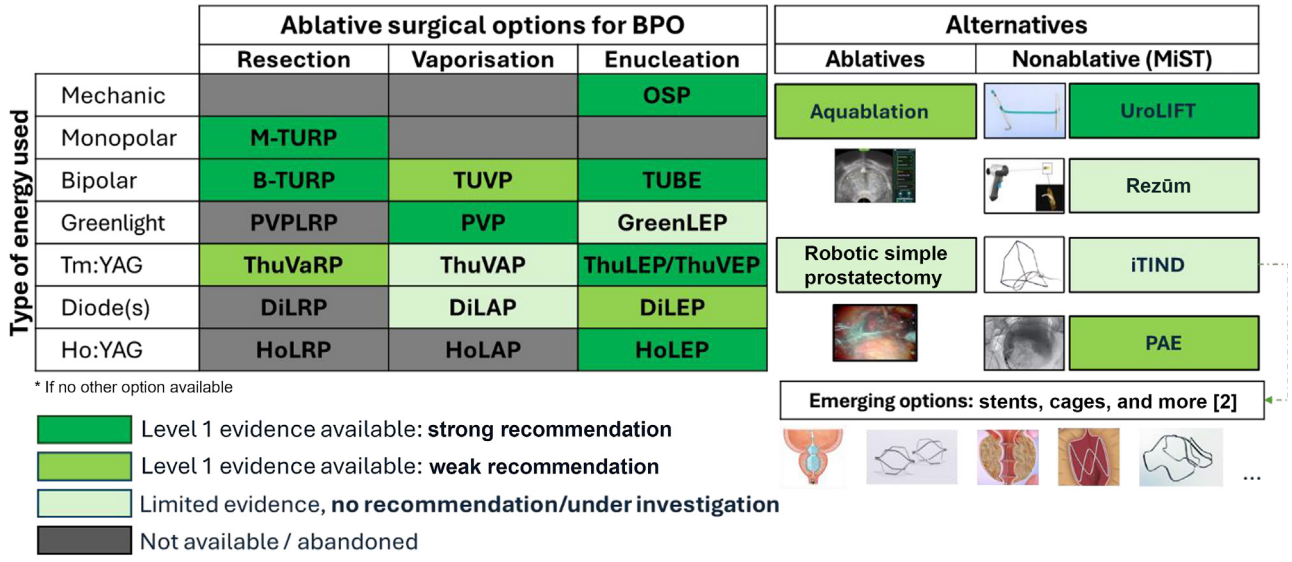

Fig. 1 – Current treatment armamentarium for instrumental management of male lower urinary tract symptoms due to benign prostatic obstruction (BPO) and associated recommendations according to the most recent version of the European Association of Urology guidelines. Levels of evidence and strength of recommendations for emerging options are as described by Speakman et al [2]. MiST = minimally invasive surgical technique; M-TURP/B-TURP = monopolar/bipolar transurethral resection of the prostate; OSP = open simple prostatectomy. TUVP = transurethral vaporisation of the prostate; TUBE: transurethral bipolar enucleation; PVP = photovaporisation of the prostate; LRP = laser resection of the prostate; LEP = laser enucleation of the prostate; Thu = thulium; VaRP = vaporesection of the prostate; VAP = vaporisation of the prostate; LEP = laser enucleation of the prostate; VEP = vapoenucleation of the prostate; Di = diode; LAP = laser ablation of the prostate; Ho = holmium; iTIND = temporary implantable nitinol device; PAE = prostate artery embolisation.

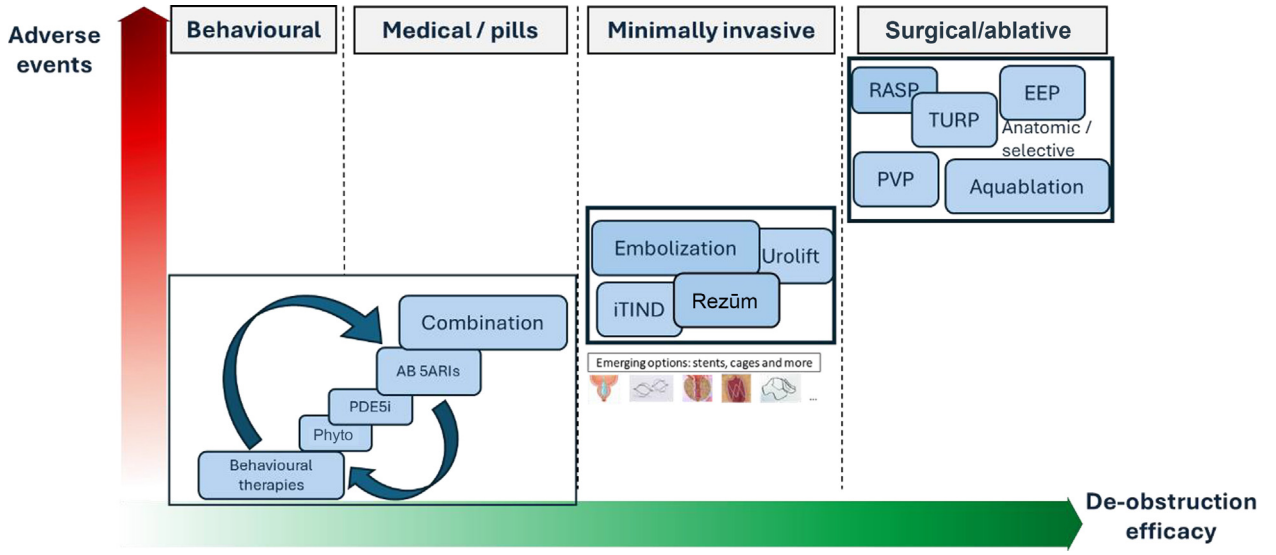

Fig. 2 – Trade-off between the efficacy and aggressiveness of treatment options for male lower urinary tract symptoms due to benign prostatic obstruction. Phyto = phytotherapy and plants extracts. PDE5i = phosphodiesterase type 5 inhibitor; AB = α blocker; 5ARIs = 5α-reductase inhibitors; iTIND = temporary implantable nitinol device; RASP = robot-assisted simple prostatectomy; TURP = transurethral resection of the prostate; EEP = endoscopic enucleation of the prostate; PVP = photovaporisation of the prostate.

- Within each category (behavioural, medical, minimally invasive, and surgical options), not all treatment strategies been compared head-to-head, and thus their relative position remains uncertain. For example, few trials have investigated outcomes of robotic simple prostatectomy [3,8]. For MiSTs, the number of randomised controlled trials remains limited [1] and there are no relevant comparative trials between currently marketed options. A network meta-analysis used sham treatment as an intermediate comparator [9]. Among noninterventional therapies, some recent noninvasive behavioural therapies have shown short-term efficacy comparable to that of drugs, but patients were not randomised [4,5]. Some combination regimens (including triple and quadruple combinations) are used in clinical practice, but very limited evidence exists [10,11].
- Although treatments are often categorised by their level of invasiveness, clinical decisions may justify choosing one option earlier or later in the sequence, depending on the patient's profile. However, high-quality evidence

to support such flexibility remains limited. For example, most MiSTs have demonstrated modest efficacy in terms of relieving obstruction, but are associated with a favourable safety profile, particularly regarding sexual function [9,12]. In selected patients, MiSTs may represent a valuable alternative to combination drug therapy. Nevertheless, direct comparisons between MiSTs and pharmacological combinations are still lacking, and results from ongoing randomised controlled trials are eagerly awaited to inform evidence-based decisions [13].

- The concepts of efficacy and safety are broad and cannot be fully captured in a simplified diagram. The perceived effectiveness of a treatment can vary significantly depending on the metric used, whether it is a reduction in the International Prostate Symptom Score (IPSS), an improvement in maximum flow rate, or changes in urodynamic parameters. A recent systematic review [14] highlighted that medical and surgical therapies may result in different outcomes, depending on whether the IPSS or Bladder Outlet Obstruction Index is used for assessment. Similarly, safety is a complex, multidimensional concept that encompasses short-term complications (eg, bleeding), long-term issues, incontinence, and sexual side effects such as ejaculatory dysfunction. Therefore, any representation of these dimensions in a figure is necessarily an approximation.
- Prostate size can also dramatically impact the results of surgery, and Fig. 2 should be split into at least two versions: small versus large prostates. In terms of efficacy, first, because for some techniques (e.g., resection or vaporisation), size can be a limitation, having been linked to undertreatment and lower durability, while some other approaches (eg, endoscopic enucleation of the prostate [EEP]) provide similar BPO relief regardless of size. In terms of safety, prostate size has been identified as a risk factor for complications following ablative treatments [15]. Furthermore, prostate shape can jeopardise some MiST options or lower the efficacy of medical treatment (eg, median lobe involvement).
- Patient characteristics play a crucial role in determining the most appropriate treatment, even within a given category. Factors such as age, comorbidities, anticoagulation, and anaesthetic risk (eg, American Society of Anesthesiologists score) can exclude certain options because of safety concerns, while others are not affected. However, this level of nuance is not adequately reflected in current stepwise algorithms. A rigid categorisation fails to account for how individual profiles influence the therapeutic trade-off between efficacy and safety.
- The strength of recommendations in Fig. 2 depends on the quantity and quality of supporting data, which vary widely across treatments. While some options are backed by multiple studies (eg, EEP), there is very limited evidence for others (eg, the temporary implantable nitinol device [iTIND] and Rezūm), so generalisations about their place in the algorithm are premature.

These reflections highlight the limits of assigning fixed positions to treatment options within a therapeutic strategy. Categorisation of interventions mainly reflects their conceptual level of invasiveness and does not capture any clinical nuance. For instance, MiSTs currently appear closer in profile to pharmacological therapies than to ablative surgeries, but more robust data are needed, especially for newer techniques such as water vapour therapy and iTIND. Caution is warranted before widely adopting such approaches given past experiences with rapidly abandoned innovations. Ultimately, comparisons between treatments are only meaningful when options are equally suited to a given patient. While algorithms and diagrams may assist in care planning or cost analyses, they must not replace individualised, patient-centred decision-making.

A plea for holistic management of M-LUTS

Any aim to categorise patients into predefined boxes (eg, medical, MiST, surgery) upfront and thereby set the scene for "lines" of treatment is likely to be counterproductive and may reduce the quality of care. M-LUTS specialists should take inspiration from the recent history of the management of overactive bladder (OAB) in females. For many years, patient profiles were often overlooked, with cases boldly categorised as either "idiopathic" or "neurogenic" and offered a treatment pathway consisting of dietary modifications ± physiotherapy, followed by a first antimuscarinic, a second antimuscarinic, mirabegron, and sometimes posterior tibial nerve stimulation (PTNS) [16]. For cases in which first-line noninterventional treatment failed, patients would then be moved to second-line surgical treatment (eg, choosing between botulinum toxin injection and sacral neuromodulation), usually after a more extensive preoperative workup [17]. Invasive surgery such as bladder augmentation was categorised as the third-line option [17]. Over time, two main issues arose with this strategy: (1) dismantling of the concept of "idiopathic" OAB, which highlighted that what should be called "non-neurogenic OAB" can have several underlying aetiologies [18] and is probably almost never idiopathic; and (2) emerging evidence that some patients—depending on symptom types and intensity, medical history, comorbidities, and/or specific expectations—would benefit from direct prescription of PTNS or mirabegron, for example, instead of strictly following the algorithm [16,17].

The latter scenario closely aligns with the approach supported by the EAU M-LUTS guidelines panel. Every case should start with a rigorous clinical evaluation to determine the relative contribution of storage and voiding symptoms, to rule out differential diagnoses, and to detect nocturnal polyuria if present. A thorough assessment of the clinical picture (context, comorbidities, and medical history) will allow urologists to postulate on possible causes underlying the LUTS and set the scene for any therapeutic interventions.

Before considering any interventional treatment, a proper analysis of BPO is essential for the following reasons.

1. The presence of BPO largely determines any improvement in voiding symptoms. In the absence of signs suggestive of BPO on uroflowmetry (flow rate >10 ml/s and no postvoid residual volume [PVR]), further investigations are needed to confirm BPO or rule out a differential diagnosis (eg, detrusor underactivity).

2. The presence of BPO combined with an impaired or damaged bladder influences treatment success (eg, detrusor underactivity or overactivity).
3. Chronic BPO can have long-term consequences and may impact the timing and nature of any intervention (eg, choosing a method that maximises BPO relief).

Beyond the standard evaluation comprising uroflowmetry and PVR measurement, the role of urodynamics (UDS) was assessed in the UPSTREAM trial [19]. While standard care was found to be noninferior to standard care + UDS, a secondary analysis identified several characteristics associated with a high risk of surgical failure, whereas a typical clinical picture was associated with a high likelihood of obstruction, making UDS optional [20]. It is noteworthy that despite being a computed measurement, BPO is often considered a binary variable (present or absent), particularly if UDS is not available. When BPO is present or suspected, its duration should be estimated and its impact on detrusor function should be evaluated.

The prostate anatomy (on urethrocystoscopy) and size (on imaging) are investigated to establish possible treatment options and the anticipated level of BPO relief needed. At this stage, associated conditions and comorbidities must be integrated into the clinical picture to assess the risk of complications and determine the preferred type of anaesthesia and surgical approach.

Finally, an essential component of holistic management is early establishment of therapeutic priorities via shared decision-making. This requires clarification of whether the primary goal is to improve symptoms, relieve BPO, prevent disease progression, preserve sexual function, or avoid future reinterventions. These goals are often inter-related but not identical, and their relative importance may vary greatly among patients. Thus, tailoring of the treatment process begins not with choosing an option from the armamentarium, but with jointly defining the desired outcomes with the patient.

This complete synthesis, once established, must then be aligned with patient expectations, which should be part of a broader, individualised health plan [21]. This holistic approach—from patient assessment to treatment—is likely to be a more effective way to achieve treatment goals than a sequential approach, whereby treatments are sorted before being assigned to patients solely according to a diagram.

Conflicts of interest: Jean-Nicolas Cornu reports consultant roles for B. Braun Medical, Boston Scientific, Coloplast, Medtronic, Stimuli Technology, AbbVie, and Recordati. Cosimo de Nunzio reports speaker roles for Bayer, Ferring, Janssen, Pierre Fabre, Sanofi, and Ipsen; investigator roles for Janssen, Ipsen, Bayer, Teleflex, PierreFabre, and Stimuli Technology; and travel grants from Ipsen, AB Medica, PierreFabre, Janssen, and Idipharma. Mauro Gacci reports grant support from Elesta SpA and a speaker role for Teleflex Medical. Hashim Hashim reports speaker roles for Medtronic, Boston Scientific, Astellas, and AbbVie; investigator roles for Medtronic and Coloplast, and consultant roles for Stimuli Technology and Coloplast. Thomas Herrmann reports a consultant role for Karl Storz. Sachin Malde reports consultant roles for Medtronic and Procept Biorobotics. Christopher Netsch reports a speaker role for Richard Wolf GmbH, and consultant roles for Richard Wolf GmbH, Lisa Laser, Olympus, KLS-Martin, and Biolitec. Malte Rieken reports consultant roles for Boston Scientific and Schwabe Pharma AG. Vasileios Sakalis reports travel grants from Anastasios Mavrogenis S.A., Ariti S.A., and Demo Pharmaceutical Industry, and a consultant role for Ipsen Epe. Michael Baboudjian reports consultant roles for Ambu A/S and Coloplast. Massimiliano Creta reports a speaker role for Medac Pharma S.r.l. The remaining authors have nothing to disclose.

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