

# Highlights from the 54th Meeting of the International Continence Society

Madrid 23–25 October 2024

Summary of a selection of key scientific communications on the management of lower urinary tract symptoms from the 54<sup>th</sup> ICS Meeting 2024

This material is intended for an international audience of healthcare professionals outside the UK and ROI.



## Highlights from the 54<sup>th</sup> Meeting of the International Continence Society

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#### **Round Table Discussion 1:**



Treatment of male lower urinary tract symptoms: are we in a new era?

## Shared patient-physician approach needed for BPE/BPH/BPO treatment decisions

While transurethral resection of prostate (TURP) has been the 'gold standard' treatment for lower urinary tract symptoms (LUTS) and benign prostatic enlargement (BPE)/benign prostatic hyperplasia (BPH) over the last 50 years, new alternative minimally invasive surgical treatments (MIST) have become available. The use of these MISTs is increasing given that this patient population is getting older, with increased chance of established comorbidities and/or frailty, for whom low-risk procedures may be more appropriate. The use of MISTs may also spare a patient's sexual function and, in addition, can be undertaken in an outpatient setting.

"Not all minimally invasive treatments are equivalent and most studies still need longer follow-up", highlighted Salvador Arlandis Guzmán (La Fe University and Polytechnic Hospital, Valencia, Spain).

MISTs include water vapour thermal therapy (Rezum), prostatic urethral lift (UroLift), temporary implanted nitinol device, prostate artery embolization, robotic water jet system (Aquabeam), transperineal prostate laser ablation, and the Optilume BPH catheter system. All MISTs have demonstrated efficacy and acceptable safety, with re-treatment rates of around 4–20% across a period of 1–5 years post-procedure – while these rates are comparable with those for the use of TURP in

BPH, further studies are required to directly compare these differing procedures.

When considering treatments for BPH, suitable surgical procedures need to be selected on an individual per patient basis. Patient factors for consideration need to include age, comorbidities, and anticoagulant use, along with prostate factors (for example, prostate size, severity of symptoms, and risk of progression), and other values and preferences (for example, sexual side effects, risk of incontinence, length of hospital stay, surgeon experience). Thus, there is no 'one size fits all' treatment for LUTS and management should be personalized, based upon the patient's medical history, prostate anatomy, and individual values and preferences. For example, use of MIST (or pharmacotherapy) may be more appropriate for an elderly comorbid patient for which anaesthesia is deemed unsuitable. Rezum or Urolift may be suitable options for a patient who requests minimally invasive treatment under local anaesthesia, while photovapourization, Aguabeam, or anatomic endoscopic enucleation may be more suitable for patients with a large prostate (>80 cc).

## Personalized approach to the use of surgery for LUTS remains important

Urologists play a key role in counselling and guiding patients to the most appropriate LUTS/BPH therapeutic strategy. Pharmacological classes such as  $\alpha\text{-adrenergic}$  blockers,  $5\alpha\text{-reductase}$  inhibitors,  $\beta_3\text{-adrenergic}$  agonists or antimuscarinics, and phosphodiesterase inhibitors are currently available for the management of LUTS, either as monotherapy or combined treatment.

"Prolonged medical treatment may lead to operating on older patients with poorer bladder function", highlighted Manuela Tutolo (San Raffaele Hospital, Milan, Italy).

Surgical treatment is usually required when patients experience recurrent or refractory symptoms, such as urinary retention, overflow incontinence, and recurrent urinary tract infections, or where patients have not achieved adequate relief from LUTS or post-void residual volume. Choice of surgical technique typically depends on prostate size, comorbidities, the ability to receive anaesthesia, and patient preferences.

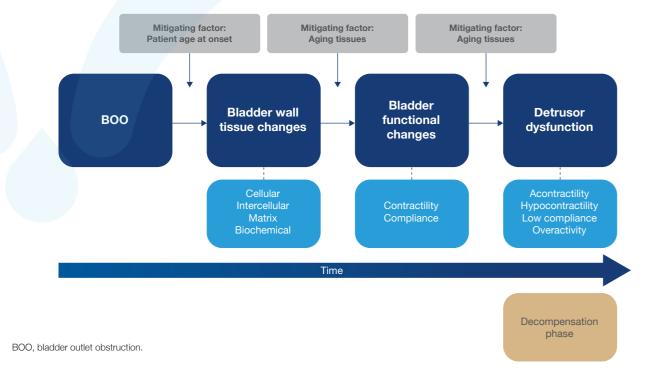
Widespread and prolonged medical treatment can delay surgical intervention so that patients who eventually require surgery for BPH end up with more advanced disease. So, can delayed BPH surgery provide similar functional outcomes as early surgical management? At least 50% of patients with LUTS and a urodynamic diagnosis of benign prostatic obstruction (BPO)/bladder outflow obstruction (BOO) also have detrusor overactivity. When de-obstructive surgery in patients with BPO is planned, detrusor overactivity is not a contraindication – normal detrusor activity can be observed post-operatively in around two thirds of patients with pre-operative detrusor overactivity. However, around one third of patients can present with de novo detrusor overactivity at mid-term follow-up following BPE surgery, suggesting that the main driver of detrusor overactivity pathogenesis may possibly be aging and not BPO. Thus, patients with BPO and detrusor overactivity should be counselled regarding a possible worse IPSS outcome following surgery.

The impact of BOO-induced bladder remodelling

– hypertrophy, compensation (increased detrusor contractility during the voiding phase, often in combination with filling phase detrusor overactivity), followed by decompensation (detrusor underactivity)

– over time and its impact on therapeutic (pharmacotherapy or surgery) outcome depending on remodelling stage also need to be acknowledged (Figure 1).

Figure 1. Proposed phases involved in the development of detrusor dysfunction as a result of BOO



Many therapeutic options are currently available for BPH and LUTS and one therapeutic approach is not suitable for all patients. Recent technological improvements of BPH surgery have decreased surgery side effects and complications, while the use of Rezum, Urolift, and Aquabeam can reduce the risk of sexual side effects. A personalized approach to treatment, along with improved patient assessment

or follow-up are needed. Early surgery should be considered for patients experiencing limited efficacy of medical treatment(s) and/or poor drug tolerance, or patients with complicated BPH or at high risk of progression. Of note, use of urodynamics may help to identify suitable candidates with LUTS who would benefit most from surgery.

#### **Early surgery for BPH/LUTS**

Pros	Cons
Preservation of detrusor function	Medical therapy has mild side effects
Better urinary outcomes	No influence on quality of life (QoL)
Cost-effectiveness	Risk of permanent dysfunction
<ul> <li>Medical therapy is not free of side effects</li> </ul>	<ul> <li>Risks associated with surgery</li> </ul>
<ul><li>Long-lasting results</li></ul>	
<ul> <li>Long-lasting results</li> </ul>	

## Preservation of ejaculation is possible with selective treatment for prostatic disease

Patients should be evaluated using the Male Sexual Health Questionnaire for assessing ejaculatory dysfunction and realistic advice should be provided based on the severity of the patient's benign prostatic disease and prostate size/volume and treatment outcome (Figure 2).

"When discussing ejaculatory preservation with a patient, it remains important to consider what is important for him and his spouse/partner", highlighted Karl-Dietrich Sievert (Klinikum Lippe, Bielefeld University, Germany).

Medical therapy with  $\alpha$ -receptor antagonists and  $5\alpha$ -reductase inhibitors has a number of possible side effects, including ejaculation disorders, reduced libido, and erectile dysfunction. In addition, ablative treatment can cause ejaculatory dysfunction in 40–80% of patients. While limited data are available, ejaculatory disorders related to treatment for prostatic disease, along with erectile dysfunction, appear to have a substantial deleterious effect on the QoL of men and previously regular sexual activity, inducing significantly increased levels of depression and anxiety.

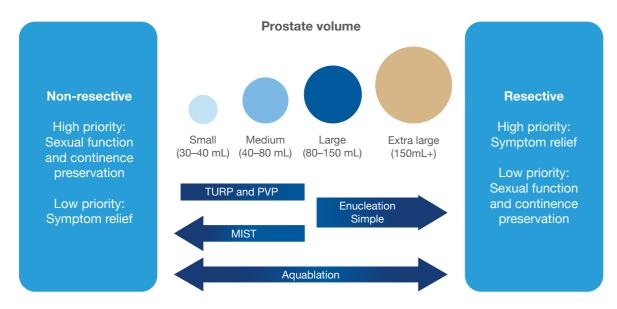
When considering the concept of ejaculatory preservation, it is commonly thought that absence of closure of the bladder will result in retrograde emission

of sperm. However, as long as the tissues around the verumontanum are not injured, ejaculation should still occur even with a well-opened bladder neck.

While ejaculation preservation (EP) rates of EP-TURP reportedly ranges from 66-91%, these data are based on studies with either a short follow-up or lacking a control group – although EP-TURP generally appears better at EP than standard TURP. Similar findings and study limitations have been reported for EP-anatomic photo-selective vaporization of the prostate. Use of Holmium laser enucleation of the prostate (HoLEP) has also been associated with reduced ejaculatory volume and decreased orgasmic intensity - EP-HoLEP has a preservation rate of 46% vs 27% for standard HoLEP. but again these findings are based on short study follow-up. Ejaculation-sparing thulium laser enucleation of the prostate has recently shown promise with EP reported in >90% of patients, representing a potential ejaculation-sparing alternative in the treatment of BPH.

EP rates of up to 100% have been reported with MISTs – consistently better than those reported with TURP – and their use appears most suited to younger patients with a small prostate and moderate symptoms, along with a strong desire to preserve their sexuality.

Figure 2. Treatment of prostatic disease based on prostate volume



MIST, minimally invasive treatments; PVP, photoselective vaporization of the prostate; TURP, transurethral resection of prostate.

## Urodynamics is key to effective assessment of patients with bothersome LUTS following any intervention

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A large number of patients maintain medical treatment after surgical intervention for BPE. The aetiology of post-operative LUTS may be due to an incorrect preoperative diagnosis (such as detrusor underactivity/overactivity, nocturia) or the incomplete removal of prostatic tissue leading to insufficient relief from BOO. Male LUTS are not solely due to the prostate (Figure 3); multifactorial pathophysiology of progression from histological BPH to male LUTS and BPO can include aging, prostatic enlargement, comorbidities, and bad bladder habits.

"Symptoms alone are unreliable in predicting urodynamic findings with respect to obstruction and detrusor instability after TURP", highlighted Tufan Tarcan (Koç University School of Medicine, Istanbul, Turkey).

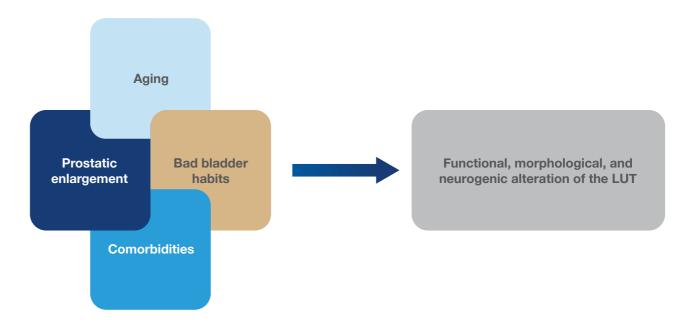
There may be a urodynamic explanation for persistent LUTS after TURP – some patients may not have had BOO in the first place. Available evidence suggests that half of patients with persistent LUTS had a small prostate volume and small resected adenoma weight, indicating that some of these patients may

not have had BOO. Factors associated with poor surgical outcomes include absent or equivocal BOO on urodynamics, low maximum cystometric capacity, early and high-amplitude detrusor overactivity, terminal detrusor overactivity, and older age.

The use of urodynamics remains important when assessing patients with bothersome LUTS following any intervention to decrease bladder outflow resistance in order to prevent unnecessary redosurgery and to plan a suitable disease-specific treatment strategy.

Clinical evidence also suggest that MISTs may result in similar or worse effects concerning urinary symptoms and QoL compared with TURP at short-term follow-up. There may be a decreased need for medical treatment if MISTs are utilized at an earlier stage before irreversible changes occur in the bladder. However, there may be an increased need for medical treatment if MISTs are less effective in relieving BOO and related symptoms. Improved urodynamic characterization of LUTS is needed along with head-to-head randomized controlled studies of MISTs with longer follow-up.

Figure 3. Male LUTS have a multifactorial pathophysiology



LUT, lower urinary tract; LUTS, lower urinary tract symptoms.

#### **Scientific Podium Short Oral Session S7:**

Male lower urinary tract symptoms



New MISTs more effective than gold standard TURP in non-neurogenic LUTS secondary to mid-volume benign prostatic obstruction

Antonio Luigi Pastore (Sapienza University of Rome, Faculty of Pharmacy and Medicine, Department of Urology, ICOT, Latina, Italy)

For patients with non-neurogenic LUTS secondary to BPO for mid prostate volumes, post-operative urodynamics improved following TURP, Aquabeam (water-jet ablation), or Rezum (convective water vapour energy), although outcomes were more effective following Aquabeam or Rezum groups in terms of sexual function and overall satisfaction.

"Aquabeam and Rezum were more effective at antegrade ejaculation sparing compared with TURP in this patient population with middle-volume prostates", highlighted Antonio Luigi Pastore.

This prospective randomized study was the first to compare the new minimally invasive approaches Aquabeam and Rezum (convective water vapour energy) with TURP in the treatment of non-neurogenic LUTS secondary to BPO for mid prostate volumes

(30-80 mL). TURP is still considered to be the 'gold standard' treatment for this patient population. Patients were non-responders to medical therapy for at least 6 months prior to surgery. Urodynamics and preoperative evaluation were undertaken in all patients. The study included 349 patients (mean age: 63.6 years) who were randomized to receive Rezum (n=112), Aguabeam (n=118), or bipolar TURP (n=119).

For post-operative urodynamics, flowmetry parameters were significantly increased for all patients, particularly those who underwent TURP (p<0.005 vs Rezum and Aquabeam). Both QoL and sexual satisfaction evaluated using a post-operative male sexual health questionnaire, had a greater improvement after

Rezum and Aquabeam than after TURP. In addition, antegrade ejaculation was spared in all Rezum and Aguabeam patients, whereas all TURP patients reported retrograde ejaculation. Operating time and length of hospital stay were longer after TURP (56.9 min and 3 days, respectively) when compared with the Rezum (2.4 min and 0.6 days, respectively) and Aquabeam (5.2 min and 1 day, respectively). Mean

estimated blood loss (evaluated as postoperative drop in haemoglobin) was also significantly greater with TURP compared with either Rezum or Aguabeam (p<0.005).

Abstract #59: https://www.ics.org/2024/abstract/59

#### Consider detrusor overactivity and prostatic inflammation in clinical decisionmaking for benign prostatic hyperplasia-related bladder outlet obstruction

Michael Samarinas (Urology Department, General Hospital of Larissa, Larissa, Greece).

There is a significant correlation between detrusor overactivity and prostatic inflammation in patients with BPH and BOO.

"We found a higher prevalence of prostatic inflammation in individuals exhibiting detrusor overactivity, suggesting a potential link between bladder wall neuromuscular disturbances and prostatic inflammation", highlighted Michael Samarinas.

This prospective observational study included men presenting with LUTS attributable to BPH who had undergone either a-blocker monotherapy or a combination of 5a-reductase inhibitors. Eligible individuals exhibited an International Prostate Symptom Score of ≥7, prostate volume of ≥30 mL, documented BOO confirmed through pressure-flow studies and were deemed suitable candidates for TURP. A total of 127 individuals met the eligibility criteria, of whom 125 successfully completed the study.

Postoperatively, detrusor overactivity resolution was observed in 75.3% (55/73) of participants; however, all 18 individuals with persistent detrusor overactivity post-surgery showed evidence of moderate (33.3%) and severe (66.7%) inflammation. The severity of prostatic inflammation therefore appears to impact the persistence of detrusor overactivity postTURP, emphasizing the importance of addressing inflammation in the management of BPH-related BOO. In addition, this finding suggests a potential link between neuromuscular disturbances in the bladder wall, characteristic of detrusor overactivity, and the inflammatory processes occurring within the prostate gland.

The findings from this study underscore the significance of considering both or overactivity and prostatic inflammation in clinical decision-making for benign prostatic hyperplasia-related BOO and further research is needed to explore targeted inflammatory therapies.

#### Abstract #60:

https://www.ics.org/2024/abstract/60

#### State of the Art Lecture 1: How do male lower urinary tract symptoms guide our management of benign prostatic obstruction?

Paul Abrams (Bristol Urological Institute, Bristol, UK)

#### Men continue to receive surgical treatment for LUTS even when possible cause(s) are insufficiently investigated

Thirty years ago, an article in the British Medical Journal introduced the term 'LUTS' and stressed the need for the correct use of the terms BPH, BPE, and BPO. These proposals were adopted in the 2002 ICS Terminology Report which has since been cited more that 13,000 times (Figure 4).

"Despite the disappearance of the term 'prostatism', men are still being disadvantaged by the repetition of mantras stating or implying that the prostate is the cause of most male LUTS",

highlighted Paul Abrams.

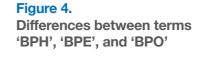
Terms such as 'LUTS due to BPH', 'LUTS due to BPE'. and 'Surgery for BPH' continue to persist, which remain harmful to men given that symptoms are still ascribed to the prostate even though there are no proven associations between LUTS and the prostate which make them pathognomonic of BPO. Thus, many men still undergo surgery for LUTS even when its cause has been poorly investigated – the possibility of overactive bladder (OAB) or detrusor underactivity may not have been considered in these patients.

No LUTS are diagnostic of obstruction and a validated symptom score questionnaire including bother and QoL assessment should be used during the

initial assessment of male LUTS and subsequent re-evaluation. Previous response to non-surgical treatments for OAB and/or presumed BPO should be considered by the clinician, and men should be empowered by being given advice on how best to -care, such as quantity/timing of liquid intake and bladder training, and when to seek treatment.

Importantly, men need to be fully informed as to what their doctors, including urologists, "know" as opposed to "believe" about LUTS management. Professor Abrams suggested that physicians should consider following the current European Association of Urology (EAU) LUTS Guidelines (2024) rather than the American Urological Association Guidelines on BPH/LUTS (2024) given that the latter contains a number of ambiguities regarding terminology and when urodynamics should be used or not, which may cause confusion.

In summary, assessment and treatment of LUTS based on robust clinical evidence provides an optimal therapeutic approach with a higher likelihood of improved patient QoL – the risk of inappropriate treatment selection may also be reduced.



**BPH BPE Prostate** Used when there is Reserved for the histological pattern it describes

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gland enlargement and is usually a presumptive diagnosis based on the size of the prostate

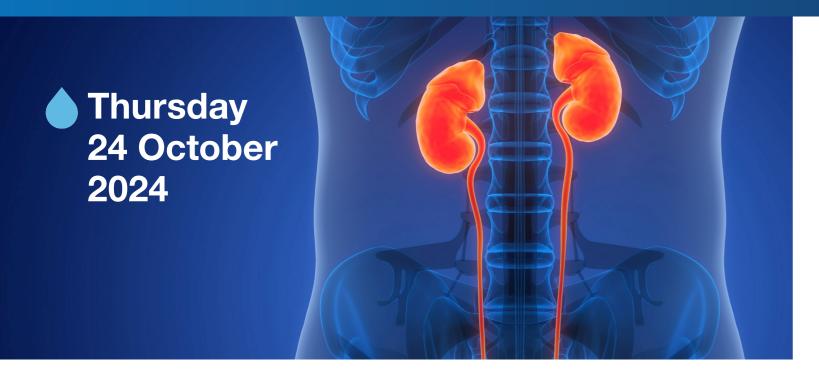
#### **BPO**

Used when obstruction has been proven by pressure flow studies, or is highly suspected from

flow rates and if the prostate is enlarged

BPE, benign prostate enlargement; BPH, benign prostate hyperplasia; BPO, benign prostate obstruction.

**Urinary flow** 



#### **State of the Art Lecture 2:**

European Union Continence Strategy



#### Optimal continence health remains a worldwide challenge

Philip Edward Van Kerrebroeck (University Maastricht, Maastricht, The Netherlands).

In Europe, around 55–60 million women and men suffer from continence (bladder and bowel) health problems, and without policy change, the costs of continence care and the ecological impact are expected to significantly increase over the coming years.

"Although optimal continence health should be a reality for everyone, this is not the case yet, even in the European Union", highlighted Philip Edward Van Kerrebroeck.

Urinary incontinence caused an economic burden of €69.1 billion in 2023 and these costs could increase by 25% reaching €100.2 billion (including caregiver costs) by 2030. Urinary incontinence reduces productivity due to presenteeism and absenteeism. Addressing continence health will enhance workplace productivity, benefitting both the economy and individual livelihoods. Of note, the economic burden of urinary incontinence is four times higher for women than men. It is also important to remember that continence health problems can be present in people across different stages of life and a wide variety of health conditions, including pregnant and post-partum

women, the aging population, individuals with mental health issues or neurodegenerative diseases, and cancer patients.

Urinary incontinence also has a substantial negative impact on the environment – disposing of incontinence pad waste is associated with significant carbon emissions. However, shifting to 100% recycling could reduce the overall carbon footprint by 1.1 billion kg CO<sub>2</sub> from 2024–2030.

The EAU, the EAU Policy Office in cooperation with the EAU Patient Office, the International Continence Society (ICS), the World Federation of Incontinence and Pelvic Problems, the Sociedad IberoAmericana de NeuroUrologia y UroGinecologia (SINUG), and 19 other stakeholders, including the national urological societies within Europe, have now launched a campaign – "An Urge to Act" – which aims to transform European Union (EU) continence health. As a first step in this campaign, a Manifesto for Policy Reform has been prepared to organize and guarantee optimal continence health in the EU via policy action – this manifesto, including ten action points, is currently in the process of being implemented.

#### **Open Discussion ePosters**

## One third of women with overactive bladder and urgency urinary incontinence discontinue anticholinergic treatment

Judith Lleberia Juanós (Fundació Hospital Esperit Sant, Spain).

Treatment with anticholinergics was stopped earlier than planned in one third of women affected by overactive bladder and urgency urinary incontinence.

## "Our data suggest that lack of treatment effectiveness was a significant cause of treatment discontinuation in our sample",

highlighted Judith Lleberia Juanós

This mixed quantitative-qualitative cross-sectional study included 122 women (mean age: 67 years) with urinary urgency with pure urgency urinary incontinence for whom treatment with anticholinergic drugs were prescribed. Only patients who had not previously improved with non-pharmacological measures such as bladder re-education, attention to the intake of bladder stimulants, and evaluation of diuretic use were included. Drugs prescribed were fesoterodine (n=73; 59.8%), solifenacine (n=43; 35.3%), desfesoterodine (n=3; 2.5%), oxybutynin (n=2; 1.6%), and tolterodine (n=1; 0.8%).

Treatment was considered subjectively effective in 80 cases, according to the patient's opinion (66.7%) and partially effective in 8 cases (6.7%). Of the 122 women treated with anticholinergics, treatment was

discontinued in 32.8% of them – 22 patients (55%) stopped treatment due to the appearance of adverse effects associated with the use of anticholinergics (dryness of the mucous membranes, cognitive impairment, epigastric pain, oedema in the lower extremities), 14 (35%) due to the lack of any treatment effect, and 4 patients (10%) for economic reasons (inability to afford it despite being financed by the National Health System).

A comparative analysis showed that there was no relationship between treatment discontinuation and the type of anticholinergic drug used, patient age, having diabetes mellitus, pelvic organ prolapse or nocturia, the number of urgency urinary incontinence episodes, or the International Consultation on Incontinence Questionnaire-Short Form score. However, significant differences were observed between the effectiveness of treatment and discontinuation. Thus, discontinuation of anticholinergic treatment in this patient sample was not related to demographic variables or the clinical symptoms present at the time of the consultation.

Abstract #550: https://www.ics.org/2024/abstract/550



Comments by Elisabetta
Costantini Associate
Professor in Urology
University of Perugia | UNIPG
Chief of Andrological and
Urogynaecological Urology
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Terni, Italy

"One third of women with OAB and urgency urinary incontinence discontinue anticholinergic treatment. The reasons for the abandonment can be different and due to different reasons. This study analyzed some of this reasons and reported on 122 women treated with anticholinercs drug, independently of the type of anticholinergic used that 35% discontinued for the appearance of adverse effects associated with the use of anticholinergics (dryness of the mucous membranes, cognitive impairment, epigastric pain, edema in the lower extremities),

35% due to lack of treatment effect and 10% for economic reasons (inability to afford it despite being financed by the National Health System). The 2023 review by Dudley Robinson and Linda Cardozo demonstrated that adherence to therapy in OAB patients remains a clinical challenge and that this may be due to poor awareness of the condition and the need for long-term treatment. Consequently, educating patients and clinicians as well as improving clinical guidelines may facilitate referral and ensure appropriate treatment. The authors concluded that empowering the patients with information regarding the causes and consequences of OAB, in addition to the available management options, should facilitate patient driven decision-making and allow for tailored treatment regimen based on patient expectations and personal goals. This should lead to improved acceptability and ultimately improved compliance."



Giannina Cinthia Melgarejo-García (Hospital Nacional Alberto Sabogal Sologuren, Lima, Peru).

Coexisting overactive-underactive bladder was significantly correlated with the absence of detrusor overactivity, suggesting the latter may have potential use as a future predictor.

"Coexisting overactive-underactive bladder is a complex syndrome with undefined clinical and urodynamic characteristics and no 'gold standard' diagnostic criteria", highlighted Giannina Cinthia Melgarejo-García.

This retrospective study included 76 patients with LUTS who presented with urgency and increased voiding frequency or nocturia with or without urgency urinary incontinence and who underwent invasive urodynamic testing. Patients were divided into two groups: those with coexisting overactive-underactive bladder (Group A) and those with only OAB with or without detrusor overactivity (Group B). The mean age between these groups was similar: 44.0 years and 46.7 years in Group A and Group B, respectively. Sex, age, body mass index, comorbidities, previous surgeries, bladder pain syndrome, urinary frequency,

first desire to urinating, maximum bladder capacity, and post-void residual volume were compared between the two groups.

Both groups showed a similar prevalence of hypersensitivity bladder (72.73% in Group A vs 77.44% in Group B). Abnormal uroflowmetry was identified in 60.6% and 67.4% of patients in Group A and B, respectively (p=0.1). The presence of coexisting overactive-underactive bladder was significantly correlated with the absence of detrusor overactivity (24.24% in Group A and 46.5% in Group B; p=0.46). Of note, while bladder contractility typically becomes impaired with age, coexisting overactive-underactive bladder was identified in some young patients in the study sample.

Further studies are warranted to confirm the absence of detrusor overactivity as a potential predictor of the development of underactive bladder, given the small sample size in this study.

Abstract #553:

https://www.ics.org/2024/abstract/553



#### **Scientific Podium Short Oral Session S21:**

Overactive bladder: pharmacotherapy and patient phenotyping



Urologists need to acknowledge anticholinergic burden when treating overactive bladder

João Oliveira (Centro Hospitalar e Universitário São João, Portugal).

Patients with OAB and a high anticholinergic burden typically demonstrate worse treatment outcomes.

"Physicians should integrate anticholinergic burden determination into their clinical practice and may need to consider drugs targeting other pathways", highlighted João Oliveira.

This retrospective study reviewed patients referred to an outpatient clinic for OAB from January 2021 to December 2022. Over the 2-year study period, 102 treatment-naïve patients with OAB were referred to the outpatient clinic. Mean patient age was 62.4 years and most (82.4%) were women. Wet OAB was the most frequent phenotype – 74.5% of patients reported urge incontinence and typically used around three pads per day. Anticholinergic drugs were selected as the initial treatment in 98% of patients and were the most frequently prescribed therapy across all Drug Burden Index (DBI) groups.

At follow-up, 61.5% of patients reported symptom improvement with their prescribed therapy. However, only 25.9% of patients with a DBI >1 reported symptom improvement after anticholinergic treatment compared

with 77.1% and 52.0% for patients with a DBI of 0 or between 0 and 1, respectively (p<0.001). In addition, DBI was significantly higher in those patients reporting no improvement after anticholinergic treatment compared with those who reported improvement (p<0.001).

While OAB is a bothersome condition for which anticholinergic drugs are one of the cornerstones of treatment, many patients have established comorbidities which may requiring drugs with anticholinergic properties. However, urologists appear to still not be fully aware of anticholinergic burden when treating OAB given that anticholinergic drugs were the most prescribed medication irrespective of DBI in this study. Patients with a higher anticholinergic burden also demonstrated worse treatment outcomes, confirming it to be an important determinant of anticholinergic therapy success, suggesting that these patients may benefit from alternative treatment pathways, such as  $\beta_3$ -adrenergic receptor agonists.

Abstract #215: https://www.ics.org/2024/abstract/215



Stefania Musco - MD Urology, Neuro-Urology Dep, Spinal Unit, Careggi University Hospital, Florence

"Treatments with anticholinergic effects are associated with an increased risk of cognitive impairment, falls and all-cause mortality in older and frail people. For these potential harmful outcomes many international guidelines recommend special cautions about the uncertainty of long-term effects of anticholinergic medicines on cognitive function when prescribing antimuscarinics to treat OAB and minimize their use where possible.¹ Anticholinergic burden (ABu) refers to the cumulative effect of using multiple medications with anticholinergic properties concomitantly and it may be

calculated by several validated scales<sup>2,3</sup>.

The study presented by Oliveira retrospectively describe the index of ABu in 102 naïve dry or wet (74.5%) OAB patients (82.4 % women), mainly treated by anticholinergics and correlate the clinical efficacy on OAB symptoms according to ABu. Authors concluded that the prevalence of anticholinergic prescription in OAB is still very high (95%) despite ABu and the OAB treatment response is significantly correlated with a low DBI.

This study confirms the importance to consider  $\beta_3$  adrenergic as first-line pharmacological treatment especially in those individual with multimorbidity pharmacological treatment and polypharmacy to avoid ABu complications and objectively measures in all patients the risk of ABu in the shared-decision making models"

1.Dengler KL, Urogynecology (Phila). 2023 Jan 1;29(1S Suppl 1):S1-S19 2.Lozano-Ortega G, Arch Gerontol Geriatr. 2020 Mar-Apr;87:103885) 3.Hilmer SN, A drug burden index to define the functional burden of medications in older people. Arch Intern Med. 2007 Apr 23;167(8):781-7.

## **SIUD Lecture:** The natural history of bladder outlet obstruction – a focus on detrusor function





Bladder tissue remodelling caused by bladder outlet obstruction can be reversed prior to 'point of no return'

"Compensatory adaptations to bladder outlet obstruction may be limited in a time-dependent manner", highlighted Ferdinando Fusco.

BOO leads to progressive bladder tissue remodelling and these changes progress through three hypothetical sequential stages – hypertrophy, compensation, and decompensation (Figure 5).

In early stages of bladder wall remodelling, the increased bladder wall thickness is mainly caused by hypertrophy and hyperplasia of smooth muscle cells. Hypertrophy causes increased oxygen demand and decreased oxygen delivery (detrusor hypoxia) due

to compression of the muscle vasculature –detrusor resistive index has been correlated with prostate volume and severity of obstruction. Detrusor hypoxia acts as a further stress factor in the development of hypertrophy. Compensatory responses to hypoxia have been demonstrated in the bladder, which include hypoxia-induced pathways, such as hypoxia inducible factor and vascular endothelial growth factor, although these may counteract hypoxia only for a limited period of time.

Figure 5. Bladder tissue remodelling: a hypothetical three-stage process

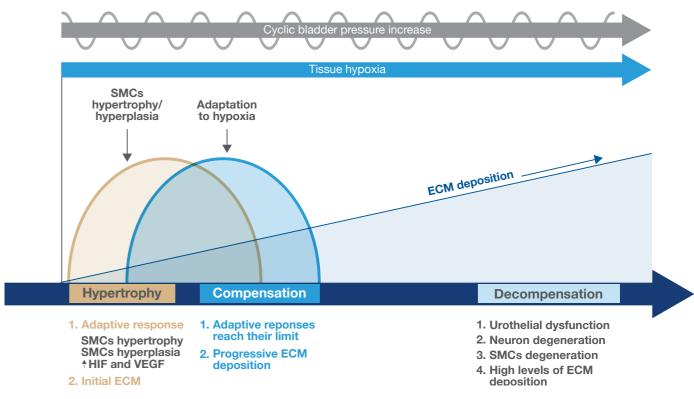


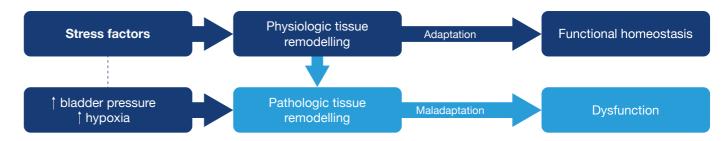
Figure reproduced and adapted from Fusco, Ferdinando et al. "Progressive bladder remodeling due to bladder outlet obstruction: a systematic review of morphological and molecular evidences in humans." BMC Urology 2018;18(1):15. doi: 10.1186/s12894-018-0329-4, under the Creative Commons CC BY 4.0 license.

ECM, extracellular matrix; HIF, hypoxia inducible factor; SMCs, smooth muscle cells; VEGF, vascular endothelial growth factor

Persistent hypoxia inhibits proliferation of human bladder smooth muscle cells, thus providing transition from the hypertrophy to compensation phase as adaptive responses reach their limit. Increased signalling involved in extracellular matrix remodelling and collagen accumulation characterize the transition from the compensation to decompensation phase.

The decompensation phase is characterized by progressively increasing levels of fibrosis in the bladder and a high collagen to muscle ratio (compared with the low collagen to muscle ratio typically seen in the hypertrophy phase; (Figure 6).

Figure 6. Increased bladder pressure and hypoxia can stimulate maladaptive pathways



Bladder remodelling can be reversed and signalling pathways restored, along with improvements of symptoms and bladder function via a number of 'de-obstruction' approaches, surgery and use of  $\alpha$ -adrenergic antagonists. However, no consensus has yet been reached as to the 'point of no return' beyond which bladder function will not recover after the removal of the outlet obstruction.

In summary, when selecting optimal targets for the treatment of lower urinary tract symptoms related to BPO, clinicians may need to consider both symptomatic (palliative) and pathogenetic (deobstruction) treatments.



