



SIU-ICUD CONSULTATION

INDIVIDUALIZED MANAGEMENT OF MALE LUTS

Editors: Dean Elterman, Stavros Gravas, and Andrea Tubaro

Managing Editor: Stavros Gravas



www.siu-urology.org



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Edinburgh, Scotland



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MARCH 2026

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Table of Contents

Preface	IV
Evidence-Based Medicine Overview of the Main Steps for Developing and Grading Guideline Recommendations	VII
Past ICUD Consultations	XIII
2026 SIU-ICUD Consultation	
Editors	XVII
Committee Overview	XVIII
Committee Table of Contents	XIX
Abbreviations	XXXIII
Committees (Chapters)	1

Preface



Prof. Stavros Gravas, MD, PhD, FEBU

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General Secretary, Société Internationale d'Urologie

Managing Editor, SIU-ICUD Consultation
on Individualized Management of Male LUTS

It is more important to know what sort of person has a disease, than to know what sort of disease a person has.

—Hippocrates (460–375 BC)

Established in the early 1980s, the International Consultation on Urological Diseases (ICUD) has provided comprehensive book-length review of major topics in urology for 45 years, promoting the improvement of the management urological diseases worldwide.

The initiative began as a voluntary collaboration of international and national urological associations. The World Health Organization (WHO) and the Union for International Cancer Control (UICC) also provided support. The ICUD was formally established as a scientific, international, non-profit NGO under Belgian law on June 28, 1994, to facilitate collaboration on an “organization-to-organization” basis with the WHO and UICC. The ICUD was led for many years by Prof Saad Khoury (Paris, France) and then by Prof Paul Abrams (Bristol, UK). From its early stages, the SIU was engaged as a collaborating partner and subsequently took over the full management and ownership of the initiative in 2021.

The explicit goal of these Consultations is to assemble experts from around the globe to develop chapters based on a rigorous, evidence-based analysis of the available literature, while recognizing that differences in economics, culture, politics, demographics, and healthcare delivery influence practice patterns and approaches to clinical problems.

SIU-ICUD Consultations bring together numerous international experts grouped into working committees that focus on specific aspects of the Consultation topic. Their conclusions are presented during the SIU Congress and subsequently published in a comprehensive volume that serves as a valuable international reference. These publications are freely available online through the SIU's eLearning platform and website.

Personalized or Individualized medicine is an approach to medical care that tailors therapy to the individual characteristics of each patient. The concept has been successfully used in oncology for many years. The **SIU-ICUD Consultation on the Individualized Management of Male LUTS** represents an extremely important and timely contribution to the ever-evolving practice of urology. This monograph is the very first publication focused on the individualized management of male LUTS and signals the first attempt to adopt the concept of personalized medicine in chronic benign diseases or conditions in urology.

To meet these expectations, Andrea Tubaro, Dean Elterman, and I invited leading experts in LUTS to steer seven committees, with each committee dedicated to one important aspect of clinical care and research. The committee chairs, in turn, invited both established experts and rising stars in the field from all over the world to produce a comprehensive review on the respective topics, including the most recent advances and the most controversial issues in the field, such as predictive models for patient outcomes and success criteria as well as management of complications and persistent symptoms after surgical therapy. The resulting recommendations have been developed using both levels of evidence and grades of recommendation according to the ICUD Modified Oxford Centre for Evidence-Based Medicine Grading System (**Tables 1 and 2**). The recommendations were reviewed by the three Co-Editors together with the Chair(s) from each unique committee. Based on the recommendations, two algorithms on the medical and invasive management of male LUTS were also developed, leveraging clinical expertise and evidence-based medicine. Moreover, the SIU-ICUD Consultation on the Individualized Management of Male LUTS is the first publication of its kind to incorporate online procedural videos, offering an additional resource that significantly complements and augments the Consultation's educational value.

This Consultation represents a substantial collegial and collaborative effort. I would like to thank my Co-Editors, Andrea Tubaro and Dean Elterman, for their leadership and dedication. As Co-Editors of this Consultation and on behalf of the SIU, we would like to express our deep appreciation and thanks to the Committee Chairs and Members for their amazing work in preparing this Consultation.

TABLE 1 Summary of the International Consultation on Urological Disease Modified Oxford Centre for Evidence-Based Medicine Levels of Evidence

Level of Evidence	Criteria
I	Meta-analysis of RCTs or high-quality randomized controlled trial (RCT)
II	Low-quality RCT or good-quality prospective cohort study
III	Good-quality retrospective case-control study or cohort study
IV	Expert opinion

TABLE 2 Summary of the International Consultation on Urological Disease Modified Oxford Centre for Evidence-Based Medicine Grading System for Guideline Recommendations

Grade of Recommendation	Criteria
A	Usually consistent with level I evidence
B	Consistent level II or III evidence or "majority evidence" from randomized controlled trials (RCTs)
C	Level IV evidence or "majority evidence" from level II or III studies
D	No recommendation possible because of inadequate or conflicting evidence

It is our pleasure to convey our gratitude to our industry partners for their unrestricted support, which was critical to the success of this initiative.

We would also like to acknowledge the skill and tireless efforts of the SIU Central Office, whose work was instrumental in bringing all the pieces together, with the support of the production team from Medit Global.

We believe that this Consultation will improve the understanding of key issues in male LUTS and the need for a personalized approach by clinicians worldwide, resulting in better outcomes and improved quality of life for our patients.



Prof. Stavros Gravas, MD, PhD, FEBU

Evidence-Based Medicine Overview of the Main Steps for Developing and Grading Guideline Recommendations

P. Abrams, S. Khoury, A. Grant

Introduction

The International Consultation on Urological Diseases (ICUD) is a non-governmental organization registered with the World Health Organisation (WHO). For more than 10 years, consultations have been organized on BPH, prostate cancer, urinary stone disease, nosocomial infections, erectile dysfunction, and urinary incontinence. These consultations have looked at published evidence and produced recommendations at four levels: highly recommended, recommended, optional, and not recommended. This method has been useful but the ICUD believes that there should be more explicit statements of the levels of evidence that generate the subsequent grades of recommendations.

The Agency for Health Care Policy and Research (AHCPR) have used specified evidence levels to justify recommendations for the investigation and treatment of a variety of conditions. The Oxford Centre for Evidence-Based Medicine have produced a widely accepted adaptation of the work of AHCPR. (June 5th 2001, www.cebm.net).

The ICUD has examined the Oxford guidelines and discussed with the Oxford group their applicability to the consultations organized by ICUD. It is highly desirable that the recommendations made by the consultations follow an accepted grading system supported by explicit levels of evidence.

The ICUD proposes that future consultations should use a modified version of the Oxford system which can be directly "mapped" onto the Oxford system.

1. First Step

Define the specific questions or statements that the recommendations are supposed to address.

2. Second Step

Analyze and rate (level of evidence) the relevant papers published in the literature.

The analysis of the literature is an important step in preparing recommendations and their guarantee of quality.

2.1 What papers should be included in the analysis?

- Papers published, or accepted for publication in the peer-reviewed issues of journals.
- The committee should do its best to search for papers accepted for publication by the peer-reviewed journals in the relevant field but not yet published.
- Abstracts published in peer-reviewed journals should be identified. If of sufficient interest, the author(s) should be asked for full details of methodology and results. The relevant committee members can then "peer review" the data, and if the data confirms the details in the abstract, then that abstract may be included, with an explanatory footnote. This is a complex issue—it may actually increase publication bias as "uninteresting" abstracts commonly do not progress to full publication.
- Papers published in non-peer-reviewed supplements will not be included. An exhaustive list should be obtained through:
 - I. The major databases covering the past 10 years (e.g., Medline, Embase, Cochrane Library, Biosis, Science Citation Index).
 - II. The table of contents of the major journals of urology and other relevant journals, for the past 3 months, to take into account the possible delay in the indexation of the published papers in the databases.

It is expected that the highly experienced and expert committee members provide additional assurance that no important study would be missed using this review process.

2.2 How are papers analyzed?

Papers published in peer-reviewed journals have differing quality and level of evidence. Each committee will rate the included papers according to levels of evidence (see below).

The level (strength) of evidence provided by an individual study depends on the ability of the study design to minimize the possibility of bias and to maximize attribution.

It is influenced by:

The type of study, whose hierarchy is outlined below:

- Systematic reviews and meta-analysis of randomized controlled trials
- Randomized controlled trials
- Non-randomized cohort studies
- Case-control studies
- Case series
- Expert opinion

How well the study was designed and carried out

Failure to give due attention to key aspects of study methodology increases the risk of bias or confounding factors, and thus reduces the study's reliability.

The use of **standard checklists** is recommended to ensure that all relevant aspects are considered and that a consistent approach is used in the methodological assessment of the evidence.

The objective of the checklist is to give a quality rating for individual studies.

How well the study was reported

The ICUD has adopted the CONSORT statement and its widely accepted checklist. The CONSORT statement and the checklist are available at www.consort-statement.org.

2.3 How are papers rated?

Papers are rated following a level of evidence scale.

ICUD has modified the Oxford Centre for Evidence-Based Medicine levels of evidence.

The levels of evidence scales vary between types of studies (i.e., therapy, diagnosis, differential diagnosis/symptom prevalence study) the Oxford Centre for Evidence-Based Medicine website: www.cebm.net.

3. Third Step: Synthesis of the Evidence

After the selection of the papers and the rating of the level of evidence of each study, the next step is to compile a summary of the individual studies and the overall direction of the evidence in an **Evidence Table**.

4. Fourth Step: Considered Judgment (Integration of Individual Clinical Expertise)

Having completed a rigorous and objective synthesis of the evidence base, the committee must then make a judgment as to the grade of the recommendation on the basis of this evidence. This requires the exercise of judgment based on clinical experience as well as knowledge of the evidence and the methods used to generate it. Evidence-based medicine requires the integration of individual clinical expertise with the best available external clinical evidence from systematic research. Without the former, practice quickly becomes tyrannized by evidence, for even excellent external evidence may be inapplicable to, or inappropriate for, an individual patient. On the other hand, without current best evidence, practice quickly becomes out of date. Although it is not practical to lay our "rules" for exercising judgment, guideline development groups are asked to consider the evidence in terms of quantity, quality, and consistency, as well as applicability, generalizability, and clinical impact.

5. Fifth Step: Final Grading

The grading of the recommendation is intended to strike an appropriate balance between incorporating the complexity of type and quality of the evidence, and maintaining clarity for guideline users.

The recommendations for grading follow the Oxford Centre for Evidence-Based Medicine. The levels of evidence shown below have again been modified in the light of previous consultations. There are now four levels of evidence instead of five.

The grades of recommendation have not been reduced and a “no recommendation possible” grade has been added.

6. Levels of Evidence and Grades of Recommendation for Therapeutic Interventions

All interventions should be judged by the body of evidence for their efficacy, tolerability, safety, clinical effectiveness, and cost-effectiveness. It is accepted that, at present, little data exists on cost-effectiveness for most interventions.

6.1 Levels of evidence

Firstly, it should be stated that any level of evidence may be positive (the therapy works) or negative (the therapy doesn't work). A level of evidence is given to each individual study.

Level of Evidence	Criteria
I	- Incorporates Oxford 1a, 1b - Usually involves: - meta-analysis of trials (randomized controlled trials [RCTs]) or, - a good-quality RCT or, “all or none” studies in which treatment is not an option (e.g., in vesico-vaginal fistula).
II	- Incorporates Oxford 2a, 2b, and 2c - Includes: low-quality RCT (e.g., > 80% follow-up), meta-analysis (with homogeneity) of good-quality prospective cohort studies - May include a single group when individuals who develop the condition are compared with others from within the original cohort group. - There can be parallel cohorts, where those with the condition in the first group are compared with those in the second group.
III	- Incorporates Oxford 3a, 3b, and 4 - Includes: good-quality retrospective case-control studies, where a group of patients who have a condition are matched appropriately (e.g., for age, sex, etc.) with control individuals who do not have the condition. good-quality case series, where a complete group of patients, all with the same condition, disease or therapeutic intervention, are described without a comparison control group.
IV	- Incorporates Oxford 4 - Includes expert opinion, where the opinion is based not on evidence but on “first principles” (e.g., physiological or anatomical) or bench research. - The Delphi process can be used to give expert opinion greater authority: - involves a series of questions posed to a panel, - answers are collected into a series of “options”, - these “options” are serially ranked; if a 75% agreement is reached, then a Delphi consensus statement can be made.

6.2 Grades of recommendation

The ICUD will use the four grades from the Oxford system. As with levels of evidence, the grades of evidence may apply either positively (procedure is recommended) or negatively (procedure is not recommended). Where there is disparity of evidence, for example, if there were three well-conducted RCTs indicating that Drug A was superior to placebo, but one RCT whose results show no difference, then there has to be an individual judgment as to the grade of recommendation given and the rationale explained.

Grade A recommendation usually depends on consistent level I evidence and often means that the recommendation is effectively mandatory and placed within a clinical-care pathway. However, there will be occasions where excellent evidence (level I) does not lead to a Grade A recommendation, for example, if the therapy is prohibitively expensive, dangerous, or unethical. Grade A recommendation can follow from Level II evidence. However, a Grade A recommendation needs a greater body of evidence if based on anything except Level I evidence.

Grade B recommendation usually depends on consistent level 2/3 studies, or "majority evidence" from RCTs.

Grade C recommendation usually depends on level 4 studies or "majority evidence" from level 2/3 studies or Delphi processed expert opinion.

Grade D "No recommendation possible" would be used where the evidence is inadequate or conflicting and when expert opinion is delivered without a formal analytical process, such as by Delphi.

7. Levels of Evidence and Grades of Recommendation for Methods of Assessment and Investigation

From initial discussions with the Oxford group, it is clear that application of levels of evidence/grades of recommendation for diagnostic techniques is much more complex than for interventions. The ICUD recommends that, as a minimum, any test should be subjected to three questions:

1. Does the test have good technical performance? For example, do three aliquots of the same urine sample give the same result when subjected to dipstick testing?
2. Does the test have good diagnostic performance, ideally against a "gold standard" measure?
3. Does the test have good therapeutic performance, that is, does the use of the test alter clinical management? Does the use of the test improve outcome? For the third component (therapeutic performance) the same approach can be used as for section 6.

8. Levels of Evidence and Grades of Recommendation for Basic Science and Epidemiology Studies

The proposed ICUD system does not easily fit into these areas of science. Further research needs to be carried out in order to develop explicit levels of evidence that can lead to recommendations as to the soundness of data in these important aspects of medicine.

Conclusion

The ICUD believes that its consultations should follow the ICUD system of levels of evidence and grades of recommendation, where possible. This system can be mapped to the Oxford system.

There are aspects to the ICUD system that require further research and development, particularly diagnostic performance and cost-effectiveness, and also factors such as patient preference.

Summary of the International Consultation on Urological Disease Modified Oxford Centre for Evidence-Based Medicine Grading System for Guideline Recommendations

Level of Evidence	Criteria
I	Meta-analysis of RCTs or high-quality randomized controlled trial (RCT)
II	Low-quality RCT or good-quality prospective cohort study
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Summary of the International Consultation on Urological Disease Modified Oxford Centre for Evidence-Based Medicine Grading System for Guideline Recommendations

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C	Level IV evidence or "majority evidence" from level II or III studies
D	No recommendation possible because of inadequate or conflicting evidence

Past ICUD Consultations

Below is a list of all past ICUD Consultations. To download a PDF of an ICUD, please visit the [SIU-ICUD Joint Consultations page](#).

2024 – 3RD WUOF/SIU ICUD Consultation on Localized Prostate Cancer

New Delhi, India

Editors: Scott Eggener, Mack Roach 3rd, and Laurence Klotz

2022 – 2nd WUOF/SIU ICUD on Kidney Cancer

Montreal, Canada

Editors: Grant D. Stewart, Robert G. Uzzo, and Toni K. Choueiri

2020 – 1st ICUD-WUOF International Consultation on Molecular Biomarkers in Urologic Oncology

Montreal, Canada

Editors: Yair Lotan, Nathan Lawrentschuk, and Jack Schalken

2018 ICUD-SIU. Congenital Lifelong Urology: Caring for the Adolescent and Adult Patient with Congenital and Childhood GU Conditions

Seoul, South Korea

Editors: Dan Wood and Hadley M. Wood

2017 ICUD-SIU. Bladder Cancer

Lisbon, Portugal

Editors: Peter Black and Paulo Gontero

2016 ICUD-ISC. 6th International Consultation on Incontinence

Tokyo, Japan

Chairs: Paul Abrams, Linda Cardozo, Adrian Wagg, and Alan Wein

2016 ICUD-SIU. Urological Management of the Spinal Cord Injured Patient

Buenos Aires, Argentina

Editors: Sean Elliott and Reynaldo Gómez

2015 ICUD-SIU. Image Guided Therapy in Urology

Melbourne, Australia

Editors: Rafael Sánchez-Salas and Mihir Desai

2014 ICUD-EAU. Minimally Invasive Surgery in Urology

Stockholm, Sweden

Chairs: Walter Artibani and Jens Rassweiler

2014 ICUD. Men's Health (facilitated by AUA)

Orlando, United States

Chairs: Ajay Nehra, Ridwan Shabsigh, and Graeme Jackson

2014 ICUD-SIU. Stone Disease

Glasgow, Scotland

Editors: Jean de la Rosette and John Denstedt

2014 ICUD-EAU. Medical Management of Urological Malignancy (MMUM)

Lisbon, Portugal

Chairs: Christian Stief and Christopher Evans

2013 ICUD-AUA. Topic Consultation on Anticoagulation in Urological Surgery

Chair: Stuart Wolf

2013 ICUD-SIU. Children's Congenital Anomalies

Vancouver, Canada

Editors: Catherine deVries and Rien Nijman

2013 ICUD-SIU. Upper Tract Urothelial Carcinoma

Vancouver, Canada

Editors: Shahrokh F. Shariat, Surena Matin, and Arnulf Stenzl

2012 ICUD-EAU. 5th International Consultation on Incontinence

Paris, France

Chairs: Paul Abrams, Linda Cardozo, and Alan Wein

2012 ICUD-SIU. Male LUTS

Fukuoka, Japan

Chairs: Chris Chapple, Kevin McVary, and Claus Roehrborn

2011 – 2nd International Consultation on Bladder Cancer

Vienna, Austria

Chairs: Mark Soloway and Henk van der Poel

2011 – 4th International Consultation on Prostate Cancer

Berlin, Germany

Chairs: Manfred Wirth and Gerald Andriole

2010 – 1st ICUD-EAU International Consultation on Renal Cell Cancer

Barcelona, Spain

Chairs: Peter Mulders and Zya Kirkali

2010 – 1st ICUD-SIU International Consultation on Urethral Stricture

Marrakesh, Morocco

Chair: Gerry Jordan

2010 – 1st ICUD-SIU International Consultation on Obstetric Vesico-Vaginal Fistula

Marrakesh, Morocco

Chairs: Dirk de Ridder and Sherif Mourad

2009 – 3rd International Consultation on Sexual Medicine

Paris, France

2009 – 1st International Consultation on Genito-Urinary Infections

Stockholm, Sweden

2009 – 1st ICUD-SIU International Consultation on Testicular Cancer

Shanghai, China

Editors: Susanne Osanto and Jerome P. Richie

2008 – 4th International Consultation on Incontinence

Paris, France

2008 – 1st International Consultation on Penile Cancer

Santiago, Chile

Editors: Antonio Carlos L. Pompeo, Chris F. Heyns, and Paul Abrams

2007 – 2nd International Consultation on Stone Disease

Paris, France

Chairs: John Denstedt and Saad Khoury

2006 – 1st Consultation on Congenital Anomalies

Cape Town, South Africa

2005 – 6th International Consultation on New Developments in Prostate Cancer & Prostate Diseases

Paris, France

2004 – 1st International Consultation on Incontinence

Monte Carlo, Monaco

2004 – 1st International Consultation on Bladder Tumors

Honolulu, Hawaii

Editors: Mark Soloway, Adrienne Carmack, and Saad Khoury

2003 – 2nd International Consultation on Erectile and Sexual Dysfunctions

Paris, France

2002 – Consultation on Genitourinary Trauma

Stockholm, Sweden

Chair: Jack McAninch

2002 – 3rd International Consultation on Prostate Cancer New Treatment Modalities

Paris, France

2001 – 2nd International Consultation on Incontinence

Paris, France

2001 – 1st International Consultation on Stone Diseases

Paris, France

2000 – 5th International Consultation on Benign Prostatic Hyperplasia

Paris, France

2000 – 1st International Consultation on Nosocomial Infections in Urology

Paris, France

1999 – 2nd International Consultation on Prostate Cancer

Paris, France

1999 – 1st International Consultation on Erectile Dysfunction

Paris, France

1998 – 1st International Consultation on Incontinence

Monte Carlo, Monaco

1997 – 4th International Consultation on Benign Prostatic Hyperplasia

Paris, France

1996 – 1st Consultation on Prostate Cancer

Monte Carlo, Monaco

1995 – 3rd International Consultation on Benign Prostatic Hyperplasia

Monte Carlo, Monaco

1994 – 4th International Symposium on Recent Advances in Urological Cancer Diagnosis & Treatment

Paris, France

1993 – 2nd International Consultation on Benign Prostatic Hyperplasia

Paris, France

1991 – 1st International Consultation on Benign Prostatic Hyperplasia

Paris, France

1990 – 3rd International Symposium on Progress Urinary Tumors

Paris, France

1989 – 2nd International Symposium on Progress Urinary Tumors

Paris, France

1987 – 1st International Symposium on Progress Urinary Tumors

Paris, France

1986 – Prostate Cancer

Paris, France

1985 – Bladder Tumors

Paris, France

**1984 – 1st International Symposium
on Testicular Cancer**

Paris, France

1983 – Kidney Tumors

Paris, France

1981 – Prostate Cancer

Paris, France

2026 SIU-ICUD Consultation Editors



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2026 SIU-ICUD Consultation Committee Overview

COMMITTEE 1:

Lower Urinary Tract Symptoms in Men

Co-Chairs: Karel C.M.M. Everaert and Philip E.V. van Kerrebroeck

1

COMMITTEE 2:

Patient Assessment

Chair: Marcus J. Drake

48

COMMITTEE 3:

Lifestyle Intervention and Pharmacological Treatments

Chair: Andrea Tubaro

95

COMMITTEE 4:

Invasive Surgical Treatments

Co-Chairs: Peter Gilling and Henry Woo

151

COMMITTEE 5:

BPH Minimally Invasive Treatments

Co-Chairs: Bradley C. Gill and Kevin C. Zorn

213

COMMITTEE 6:

Predictive Models—Nomograms for Patient Outcome and Success Criteria

Chair: Stavros Gravas

299

COMMITTEE 7:

Managing Patients with Complications and Persistent Symptoms

Chair: Enrico Finazzi Agrò

331

COMMITTEE 8:

Algorithms for the Management of Male LUTS

Co-Chairs: Dean Elterman, Stavros Gravas, and Andrea Tubaro

371

Committee Table of Contents

Committee 01

Lower Urinary Tract Symptoms in Men	1
Introduction	5
Epidemiology of Male LUTS	6
Male LUTS, including underactive and overactive bladder	6
Urinary incontinence	7
Overactive bladder (OAB)	7
Underactive Bladder (UAB)	10
LUTS and the prostate	12
Definition of BPH	12
Clinical	12
Anatomic	13
Biochemical	13
Physiological	13
Epidemiology of BPH	13
Based on histology	13
Based on symptoms	14
Risk Factors Associated with Male LUTS Mainly Related to Prostate	14
Demographics	14
Age/frailty	14
Other demographic factors	15
Behavioral	16
Dietary	16
Systemic disease	16
Nocturia and obstructive sleep apnea	17
Metabolic syndrome and LUTS mainly related to prostate	18
Natural History of Male LUTS and BPH	19
Progression of male LUTS	19

Progression of BPH	20
Progression of LUTS associated with prostate	22
Risk factors for clinical progression in male LUTS	22
Age	23
Clinical presentation	23
Lifestyle, education, and psychosocial factors	24
Genes	24
Metabolic syndrome	25
Prostatic inflammation	25
Systemic inflammation	25
Implications for Prognosis and Management	26
Conclusion	28
References	29

Committee 02

Patient Assessment	48
History and Examination <i>by Marcus J. Drake, DM, FRCS (Urol)</i>	52
Conclusion	52
Symptom Scores <i>by Hiroki Ito, MD, PhD</i>	52
Conclusion	54
Bladder Diaries <i>by Paulina Bueno-Garcia-Reyes, MD</i>	54
Conclusion	56
Flow Rate Testing <i>by Tufan Tarcan, MD, PhD</i>	57
Conclusion	59
Urinalysis <i>by Alex Ciudin, MD, PhD, FEBU</i>	59
Conclusion	60
Prostate-Specific Antigen <i>by Filipe Abadesso Lopes, MD</i>	60
Conclusion	61
Prostate Size and Shape Assessment <i>by Qi-Xiang Song, MD, PhD</i>	62
Conclusion	63
Cystoscopy <i>by Alex Ciudin, MD, PhD, FEBU</i>	63
Conclusion	64

Urodynamics by Ricardo Pereira e Silva, MD, FEBU	64
Videourodynamics by Ricardo Pereira e Silva, MD, FEBU	67
Ambulatory Urodynamics by Ricardo Pereira e Silva, MD, FEBU	67
Conclusion	68
Frail Older Men by William Gibson, MBChB(MD), PhD, FRCP	68
Conclusion	69
Suspected Neurological Mechanism by Marcio A. Averbeck, MD, MSc, PhD	70
Conclusion	72
Experimental Methods by John E. Speich, PhD	73
Electronic bladder diaries	73
Urodynamic pressure measurement	73
Near-infrared spectroscopy	74
Imaging methods	74
Artificial intelligence	74
Experimental uroflowmetry	75
Conclusion	75
Summary of Recommendations by Marcus J. Drake, DM, FRCS (Urol)	76
References	78

Committee 03

Lifestyle Intervention and Pharmacological Treatments	95
Introduction	99
Watchful Waiting and Lifestyle Interventions by Souhil Lebdai, MD, PhD	99
Alpha1-Adrenoceptor Antagonists (α1-Blockers) by Yoshihisa Matsukawa, MD, PhD	100
Mechanisms of action of α 1-adrenoceptor antagonists (α 1-blockers)	100
The α 1-blockers	101
Clinical efficacy of α 1-blockers	101
Factors contributing to treatment resistance to α 1-blockers	102
Prostatic volume and intravesical prostatic protrusion (IPP)	102
Presence of detrusor underactivity (DU)	102
Baseline severity of symptoms and duration of LUTS	102
Tolerability and safety	102

Orthostatic hypotension and dizziness	102
Ejaculatory dysfunction	103
Nasal congestion and fatigue	103
Real-world tolerability and discontinuation rates	103
Practical considerations and future perspectives	104
Conclusions	104
5-Alpha-Reductase Inhibitors (5-ARIs) by Petros Sountoulides, MD, PhD, MSc, FEBU	104
Mechanism of action	104
5-ARI monotherapy	105
The ideal patient for combination therapy	105
Combination therapy from the start versus add-on therapy	108
Withdrawal of α -blocker	109
Impact of 5-ARIs on progression	109
Safety and adverse events	110
5-ARIs in prostate cancer prevention	111
Additional risks associated with 5-ARIs	112
Conclusion	112
Phosphodiesterase Type 5 Inhibitors (Monotherapy and in Combination)	
<i>by Souhil Lebdai, MD, PhD</i>	113
Mechanism of action	113
Efficacy and safety	113
PDE5Is as part of combination therapy	114
Phytotherapy for Male LUTS by Prof. Stavros Gravas, MD, PhD, FEBU	115
Mechanism of action	115
Efficacy and safety	116
Phytotherapy and guidelines	117
Conclusions—Future directions	118
Muscarinic Receptor Antagonists (Monotherapy and in Combination) and β-3 Agonists (Monotherapy and in Combination) by Mélanie Aubé-Peterkin, MD; Sender Herschorn, MD	119
Muscarinic receptor antagonists (antimuscarinics)	119
Monotherapy	119
Combination with α -blockers	120
Side effects and long-term risks	121
Patient and drug selection, dose escalation	121

Beta-3 adrenoceptor agonists	122
Monotherapy	122
Combination with α -blockers	123
Side effects	123
Patient and drug selection, dose escalation	124
Combination therapy: Antimuscarinics and β -3 agonists	124
Special considerations: Subpopulations and real-world challenges	125
Challenges in Medical Treatment of LUTS	
<i>by Marcus J. Drake, DM, FRCS (Urol); Ferdinando Fusco, MD, PhD</i>	126
The challenge of intravesical prostatic protrusion (IPP)	126
The challenge of treatment adherence	127
The challenge of nocturia and nocturnal polyuria	128
Strategy in treatment selection	130
Follow-up	131
References	133

Committee 04

Invasive Surgical treatments	151
Introduction <i>by Prof. Peter Gilling, CNZM, MD, FRACS</i>	155
Principles of Electrosurgery <i>by Lori Lerner, MD</i>	155
Physics	156
Mechanisms of delivery: electrosurgery and tissue effect	158
Types of electrodes	161
Applications in BPH	162
Complications	163
Conclusion	165
Transurethral Incision of the Prostate (TUIP) <i>by Lori Lerner, MD</i>	165
Transurethral Resection of the Prostate (TURP) <i>by Akhil Das, MD, FACS</i>	168
Equipment	169
Technique	169
Open Simple Prostatectomy <i>by Tevita Aho, FRACS(Urol), FRCS(Eng)</i>	170
Reducing the morbidity of OSP	171
Level 1 evidence comparing endoscopic BPO therapies to OSP	172

Studies comparing OSP to less invasive nonendoscopic forms of AEP (LSP and RASP)	172
Conclusion	173
Anatomical Endoscopic Enucleation of the Prostate by Naeem Bhojani, MD	178
Introduction	178
Energy sources used for AEEP	179
Holmium laser enucleation of the prostate (HoLEP)	179
Thulium:YAG laser enucleation of the prostate	179
LBO:YAG enucleation of the prostate (PVP-EP)	179
Thulium fiber laser enucleation of the prostate	180
Bipolar enucleation of the prostate (Bipolar)	180
Surgical techniques: <i>en bloc</i> vs. lobe-based approaches	180
Early apical release	180
Safe morcellation: key principles	181
Advantages of AEEP	181
Disadvantages of AEEP	181
Patient selection and preoperative considerations	181
Preoperative evaluation	181
Future perspectives in AEEP	182
Conclusion	182
Vaporization of the Prostate by Luca Cindolo, MD, PhD, FEBU	182
Robotic Simple Prostatectomy by Juliet Han, MD	185
Benefits and comparison with other techniques	185
Surgical technique	187
Transperitoneal: transvesical approach	187
Transperitoneal: transcapsular approach (Millin technique)	188
Intrafascial simple prostatectomy	189
Comparing enucleation techniques	190
Mucosal reconstruction: trigonization or circular anastomosis	190
Single-port robotic simple prostatectomy	190
Conclusion	190
Aquablation by Christopher Kelly, MD	191
Conclusion by Prof. Henry Woo, MBBS, DMedSc, FRACS(Urol), FACS	196
Procedural Video	197
References	198

Committee 05

BPH Minimally Invasive Treatments 213

Introduction and Overview 220

Water Vapor Thermal Therapy—Rezūm 220

Prostate volume: optimal range and efficacy	220
Anatomical features: median lobe and complex variants	221
Symptom severity: IPSS and patient selection	221
Prior treatment history: medical and surgical	221
Comorbidities and contraindications	221
Durability of symptom relief and retreatment rates	222
Sexual function: erectile and ejaculatory outcomes	222
Patient-reported outcomes and satisfaction	223
Patient preferences, goals, and quality-of-life considerations	223
Effectiveness and safety in special populations	223
Limitations and gaps in the evidence	224
Conclusion	224

Prostatic Urethral Lift—UroLift 225

Prostate size and UroLift eligibility	225
Anatomical features: median lobe, prostate shape, and variants	225
Median lobe and intravesical prostatic protrusion	225
Prostate shape and imaging	225
Rare anatomical variants	226
Symptom severity and types	226
Prior treatment history	226
Comorbidities and contraindications	226
Comorbidity burden	226
Bleeding risk and anticoagulation	227
Infection risk	227
Absolute and relative contraindications	227
Long-term durability and retreatment	228
Sexual function outcomes	228
Patient preferences and quality-of-life considerations	228
Special populations and complex histories	228

Management of retreatment after UroLift failure	229
Safety and efficacy in large prostates and complex anatomy	229
Emerging contraindications and patient factors	229
Conclusion	230
Temporary Intraprostatic Devices—iTIND	231
Prostate volume and iTIND outcomes	231
Anatomical features: median lobe and intravesical prostatic protrusion	231
Symptom severity and quality of life	232
Prior BPH treatments and iTIND candidacy	232
Comorbidities and contraindications to other therapies	232
Long-term efficacy, safety, and retreatment	233
Patient subgroups: age, symptom severity, ethnicity	234
Clinical decision tools and patient selection algorithms	234
Rare or emerging contraindications	234
Real-world retreatment rate and patient satisfaction beyond 3 years	234
Conclusion	235
Intraprostatic Balloon Treatment—Optilume BPH	236
Efficacy and safety outcomes of Optilume across patient subgroups	236
Prostate size, anatomy, and symptom severity	236
Anatomical variants: median lobe and complex anatomy	236
Patients with prior failed BPH interventions	236
Patients with significant comorbidities	237
Long-term efficacy and retreatment rates	237
Guideline and expert consensus on patient selection	238
Contraindications and less effective scenarios	238
Comparative effectiveness and ongoing research	239
Real-world and registry data	239
Off-label or investigational use	239
Summary: the optimal BPH patient for Optilume	240
Conclusion	240
Prostate Artery Embolization	241
Patient selection criteria for PAE	241
Efficacy and safety across patient subgroups	241

Prostate volume	241
Symptom severity	242
Comorbidities and age	242
Urinary retention and high-risk populations	242
Sexual function and quality of life	242
Prior failed therapies	242
Small prostate volumes and atypical anatomy	243
Comparative effectiveness: PAE vs. TURP and other therapies	243
Long-term efficacy and durability	243
Technical and anatomical predictors of success	243
Cost-effectiveness	244
Emerging and investigational indications	244
Contraindications and populations with reduced efficacy	245
Conclusion	245
Emerging Therapies—Transperineal Laser Ablation	246
Patient selection: prostate size and anatomy	246
Impact of prior BPH treatments	246
Comorbidities and contraindications	246
Functional outcomes: symptom relief, sexual function, and durability	247
Procedural safety and complication rates	248
Long-term outcomes and retreatment	248
Special populations: large prostates, anatomical variants, and prior radiation	248
Technical and operator-dependent factors	249
Patient-reported outcomes, preferences, and satisfaction	249
Cost-effectiveness	249
Predictors of outcomes and complications	250
Conclusion	250
Ultrasound Ablation	251
Guideline-based indications and patient selection criteria	251
Prostate size ranges: optimal and limiting factors	251
Symptom severity and prior treatment history	252
Comorbidities and contraindications	252
Efficacy, safety, and patient-reported outcomes	253
Long-term efficacy, safety, and retreatment	253

Cost-effectiveness and resource utilization	254
Real-world adoption and accessibility	254
Ongoing clinical trials and recent evidence	255
Patient perspectives and preferences	255
Guideline updates	255
Conclusion	256
Temporary Intraprostatic Devices/Stents	257
Temporary prostatic stents: devices and clinical context	257
Published indications and ideal patient selection criteria	257
Contraindications and patient factors limiting suitability	257
Device-specific differences in patient selection	258
Clinical outcomes and complication rates compared to other BPH management options	258
Long-term clinical outcomes and durability	259
Patient-reported outcomes and quality of life	259
Cost-effectiveness and healthcare resource implications	259
Real-world adherence and satisfaction	260
Patient subgroups: who derives the greatest benefit or risk?	260
Device-specific features influencing selection and outcomes	261
Conclusion	261
Permanent Intraprostatic Devices/Stents	262
Patient selection criteria for permanent prostatic stents or implants	262
Guideline-based indications and quantitative selection parameters	262
Contraindications and special considerations	262
Influence of comorbidities	263
Comparative outcomes, risks, and long-term data	263
Functional outcomes and complication rates	263
Comparative efficacy with other BPH therapies	264
Long-term durability and patient-reported outcomes	264
Device-specific technical considerations and selection	265
Technical attributes and customization	265
Device-specific selection criteria and advantages	266
Real-world effectiveness, cost-effectiveness, and health economic outcomes	267
Real-world registry and post-marketing data	267

Cost-effectiveness and health economic outcomes	267
Implementation, monitoring, and future directions	268
Stepwise implementation and monitoring	268
Future research and ongoing trials	268
Conclusion and actionable recommendations	268
Procedural Videos	270
References	271

Committee 06

Predictive Models—Nomograms for Patient Outcome and Success Criteria	299
Definition of Predictive Models and Nomograms	303
Introduction	303
Predictive Models: Definition, Purpose, Construction, Validation	303
Definition	303
Purpose	303
Construction	304
Validation	304
Nomograms: Definition, Purpose, Construction, Validation	304
Definition	304
Purpose	304
Construction	304
Validation	305
Application in male LUTS	305
Models and Nomograms for Medical Therapy	305
Monoparametric and multiparametric models	305
Monoparametric models	305
Based on objective parameter	305
Based on subjective parameter	306
Multiparametric models	307
Predictive models—nomograms for patient outcome and success criteria	309
Models and Nomograms for Invasive Therapy	311
Transurethral resection of the prostate (TURP)	311

Predictive models for functional outcomes	311
Predictive models for complications and mortality	312
Photoselective vaporization of the prostate (PVP)	313
Aquablation	313
Enucleation techniques	314
Models and Nomograms for Minimally Invasive Treatment	317
Prostatic artery embolization (PAE)	317
Water vapor thermal therapy (WVTT)—Rezūm	318
Prostatic urethral lift (PUL)	318
Temporary implantable nitinol device (iTIND)	319
Clinical Utility	319
Future Directions: AI, Biomarkers, and Beyond	321
Artificial intelligence and machine learning	322
Integration of biomarkers and multi-omic data	322
Patient-centered data and digital health integration	322
Data infrastructure and model validation	323
Ethical and Regulatory Considerations	323
Conclusion	323
Statements and recommendations	324
References	325

Committee 07

Managing Patients with Complications and Persistent Symptoms	331
Introduction by <i>Enrico Finazzi Agrò, MD</i>	335
Epidemiology of Complications After BPO Surgery (Including MISTs)	335
Incontinence after BPO surgery by <i>Tufan Tarcan, MD</i>	335
Epidemiology and risk factors for SUI after BPO surgery	336
Treatment of SUI after BPO surgery	337
Other Complications After BPO Surgery by <i>Anastasios D. Asimakopoulos, MD</i>	341
Introduction	341
What mechanisms can BPH surgery cause sexual dysfunction (SD)?	341

Impact of the main BPH surgical treatments on sexual dysfunction	342
Transurethral incision of the prostate (TUIP)	342
Transurethral resection of the prostate (TURP)	342
Prostate enucleation/vaporization	343
Minimally invasive surgical therapies (MISTs)	344
What about orgasmic function after BPH-related surgery?	346
Conclusion	346
Persisting/de novo LUTS after BPO surgery (including MISTs)	348
Etiology of persisting/de novo LUTS by <i>Mikołaj Przydacz, MD</i>	348
Assessment of persisting/de novo LUTS by <i>Mikołaj Przydacz, MD</i>	349
Voiding symptoms	349
Storage symptoms	349
Management of persisting/de novo LUTS by <i>Mikołaj Przydacz, MD</i>	349
Short-term voiding symptoms	349
Short-term storage symptoms	350
Long-term voiding symptoms	350
Long-term storage symptoms	350
Conclusion	351
Medical therapy after BPO surgery by <i>Stephan Madersbacher, MD</i>	352
Prevalence of medical therapy after BPO surgery	352
Risk factors associated with LUTS-related pharmacotherapy after BPO surgery	352
Reasons for the use of LUTS-related pharmacotherapy after BPO surgery	353
Conclusion	353
Surgical reintervention after BPO surgery by <i>Eleonora Rosato, MD</i>	354
Introduction	354
Surgical treatment of urethral stricture after BPO surgery	355
Surgical treatment of incomplete prostate resection or regrowing prostate adenoma	355
Prostatic artery embolization after MISTs surgery	356
Rezūm system after previous BPO surgery	356
HoLEP after BPO surgery	356
Conclusion by <i>Enrico Finazzi Agrò, MD</i>	358
References	360

Committee 08

Algorithms for the Management of Male LUTS	371
FIGURE 1 Medical Algorithm for the individualized management of male LUTS	374
FIGURE 2 Surgical Algorithm for the individualized management of male LUTS	375
References	377

Abbreviations Used in the Text

Abbreviation	Full Term	Chapter #
5-ARI	5α-reductase inhibitor	2,3,6,8
AEEP	anatomic endoscopic enucleation of the prostate	4
AEs	adverse events	5,8
AI	artificial intelligence	2,4,6
ANP	atrial natriuretic peptide	1
AS	active surveillance	3
ASA	American Society of Anesthesiologists	5
ATOMS®	adjustable trans-obturator male system	7
ATP	adenosine triphosphate	3
AUA	American Urological Association	1,3,4,5,6,8
AUASI	American Urological Association Symptom Index	1
AUC	area under the curve	6
AUPRC	area under the precision–recall curve	6
AUR	acute urinary retention	2,3,6
AUROC	area under the receiver operating characteristic curve	6
AUSs	artificial urinary sphincters	7
AVP	arginine vasopressin	3
BCI	Bladder Contractility Index	1,2
BDs	bladder diaries	2
BE	bladder voiding efficacy	6
BMI	body mass index	1,6,7
BOO	bladder outlet obstruction	1,2,3,4,6,7
BOOI	BOO Index	2,6
BPE	benign prostatic enlargement	1,2,3,6
BPH	benign prostatic hyperplasia	1,2,3,4,5,6,7
BPO	benign prostatic obstruction	1,4,6,7
B-SAQ	Bladder Control Self-Assessment Questionnaire	2
B-TUEP	bipolar transurethral enucleation of the prostate	6
CaP	prostate cancer	5
CBI	continuous bladder irrigation	4
CCI	Charlson comorbidity index	6

CFS	Clinical Frailty Scale	2
cGMP	cyclic guanosine monophosphate	3
CI	confidence interval	1
CNS	central nervous system	3
CPAP	continuous positive airway pressure	1
CPU	conformal planning unit	4
CT	computed tomography	1
CTS	clinical trial simulations	6
CUA	Canadian Urological Association	4
CV	cardiovascular	3
CVD	cardiovascular disease	3
CYR61	cysteine-rich protein 61	1
DAN-PSS	Danish Prostate Symptom Score	2
DHT	dihydrotestosterone	3
DL	deep learning	6
DNN	deep neural networks	6
DO	detrusor overactivity	2,6,7
DRE	digital rectal examination	1,2,7
DU	detrusor underactivity	1,2,3,7
DVIU	direct visual internal urethrotomy	7
DWT	detrusor wall thickness	2
EAU	European Association of Urology	1,2,3,4,6,7,8
EBL	estimated blood loss	4
ED	erectile dysfunction	3,5,7,8
EEP	endoscopic enucleation of the prostate	4,6,7
EF	erectile function	7
EFS	Edmonton Frail Scale	2
EjD	ejaculatory dysfunction	7
EjF	ejaculatory function	7
EMA	European Medicines Agency	3
EMG	electromyography	2
Epi-LUTS	Epidemiology of LUTS	1
ESU	electrosurgical units	4
FBNC	focal bladder neck cauterization	4
FDA	U.S. Food and Drug Administration	3
FVC	frequency-volume chart	2
GoR	Grade of Recommendation	3,4

GS	Gleason score	3
GSTP1	glutathione S-transferase P1	1
HDL	high-density lipoprotein	1
HESr	Hexanic <i>Serenoa repens</i>	3
HIFU	high-intensity focused ultrasound	5
HMPC	Committee on Herbal Medicinal Products	3
HoLAP	holmium laser ablation of the prostate	7
HoLEP	holmium laser enucleation of prostate	4,6,7
Ho:YAG	holmium:yttrium aluminum garnet	4
HR	hazard ratio	1,3
ICIQ	International Consultation on Incontinence Questionnaires	2
ICIQ-MLUTS	ICIQ Male LUTS module	2
ICIQ-OAB	ICIQ overactive bladder	2
ICS	International Continence Society	1,2,7
IFIS	intraoperative floppy iris syndrome	3
IIEF	International Index of Erectile Function	2,4,5
IIEF-5	International Index of Erectile Function 5-item version	2,3,5,7
IIEF-15	International Index of Erectile Function 15-item version	2
IL-2	interleukin 2	1
IPP	intravesical prostatic protrusion	2,3,5,6,8
IPSS	International Prostate Symptom Score	1,2,3,4,5,6
IPSS-T	total IPSS	6
IPSS-V/S	IPSS voiding/storage	6
iTIND	temporary implantable nitinol device	5,7,8
KTP	Potassium/kalium titanyl phosphate	4
LBO	lithium triborate	4
LBO:YAG	lithium triborate:yttrium aluminum garnet	4
LEP	laser enucleation of the prostate	7
LoE	Level of Evidence	2,3,4,7,8
LSP	laparoscopic simple prostatectomy	4
LUTD	lower urinary tract dysfunction	3
LUTS	lower urinary tract symptoms	1,2,3,4,5,6,7,8
MCID	minimal clinically important difference	6
MD	mean difference	4

MetS	metabolic syndrome	1
MISTs	minimally invasive treatments	5,6,7
ML	machine learning	6
mo	months	5
mpMRI	multiparametric magnetic resonance imaging	2
MRI	magnetic resonance imaging	1,4,5,6
MSHQ	Male Sexual Health Questionnaire	2
MSHQ-EjD	Male Sexual Health Questionnaire–Ejaculatory Dysfunction	4,5,7
MTOPS	Medical Therapy of Prostatic Symptoms study	2
NAF	naftopidil	6
NASH	non-alcoholic steatohepatitis	1
NHANES	National Health and Nutrition Examination Survey	1
NIRS	near-infrared spectroscopy	2
NLUTD	neurogenic lower urinary tract dysfunction	2
NNT	number needed to treat	3
NP	nocturnal polyuria	3
NPI	nocturnal polyuria index	2
NYHA	New York Heart Association	3
OAB	overactive bladder	1,2,3,6
OABq	overactive bladder questionnaire	6
OABSS	Overactive Bladder Symptom Score	2,6
OML	obstructive median lobe	5
OP	open prostatectomy	6,7
OPC	objective performance criterion	4
OR	odds ratio	3,4,6
OSA	obstructive sleep apnea	1
OSP	open simple prostatectomy	4
PAE	prostatic artery embolization	4,5,7,8
PCa	prostate cancer	3
PCAR	presumed circle area ratio	2
PCPT	Prostate Cancer Prevention Trial	3
PDE5Is	phosphodiesterase type 5 inhibitors	3
PFMT	pelvic floor muscle training	7
PFS	pressure-flow studies	1,2
PFS	post-finasteride syndrome	3

PINS	Prostatic Inflammation Nomogram Study	3,6
PLANET	PLanning Appropriate Nocturia Evaluation and Treatment study	3
PLESS	Proscar™ Long-Term Efficacy and Safety Study	3
PPUS	permanent prostatic urethral stent	7
PPV	positive predictive value	2
ProACT™	adjustable continence therapy	7
PROMs	patient-reported outcome measures	2,5,6,7
PRP	post-radical prostatectomy	7
PSA	prostate-specific antigen	1,2,3,4,6
PTNS	percutaneous tibial nerve stimulation	7
PUA	prostatic urethral angle	2
PUL	prostatic urethral lift	5,7,8
PVP	photoselective vaporization of the prostate	7
PVP-EP	photoselective vaporization and enucleation of the prostate	4
PVR	post-void residual	2,3,4,5,6
PVR-R	post-void residual urine ratio	6
PZ	peripheral zone	2
QALYs	quality-adjusted life years	5
Q_{ave}	average flow rate	2
Q_{max}	maximum flow rate	2,3,5
QoL	quality of life	2,3,4,5,6,7
RASP	robotic-assisted simple prostatectomy	4,6
RBCs	red blood cells	2
RCTs	randomized controlled trials	3,4,5,6,7
RE	retrograde ejaculation	4
REDUCE	Reduction by Dutasteride of Prostate Cancer Events study	3
Rezūm	water vapor thermal therapy	7
RP	radical prostatectomy	7
RSP	robotic simple prostatectomy	4
RT	randomized trial	4
RWRr	real-world retrospective	6
SD	sexual dysfunction	7
SDM	shared decision-making	6
SHIM	Sexual Health Inventory for Men	2,4,5,7

SP	simple prostatectomy	7
SP	single-port	4
SSRIs	selective serotonin reuptake inhibitors	3
SUI	stress urinary incontinence	1,7
TAM	tamsulosin	6
TAUS	transabdominal ultrasound	2
TFL	thulium fiber laser	4
ThuLEP	thulium laser enucleation of the prostate	7
Thulium:YAG	thulium:yttrium aluminum garnet	4
TIPDs	temporary implanted prostatic devices	5
TPLA	transperineal laser ablation	5
TPS	Triangular Prostatic Stent	5
TRUS	transrectal ultrasound	2,4
TUIP	transurethral incision of the prostate	4,7,8
TULSA	transurethral ultrasound ablation	5
TUMT	transurethral microwave therapy	7
TUNA	transurethral needle ablation	7
TUR	transurethral resection procedures	4
TURP	transurethral resection of the prostate	3,4,5,6,7,8
TWOC	trial without catheter	6
TXA	perioperative tranexamic acid	4
TZ	transitional zone	2
TZI	Transitional Zone Index	6
UAB	underactive bladder	1
UDS	urodynamics	2
UEBW	ultrasound-estimated bladder weight	2
UI	urinary incontinence	1,6,7
UPSTREAM	Urodynamics for Prostate Surgery Trial: Randomised Evaluation of Assessment Methods study	2
USP	Urinary Symptom Profile	2
UTI	urinary tract infection	2,5,6,7
UUI	urgency urinary incontinence	2,7
UUT	upper urinary tract	2
VE	voiding efficiency	6
VEGF	vascular endothelial growth factor	1
VPZ	verumontanum protection zone	4

VUDS	videourodynamics	2
VUR	vesicoureteral reflux	2
VV	voided volume	2
WATER	Waterjet Ablation Therapy for Endoscopic Resection of Prostate Tissue trial	4
WBCs	white blood cells	2
WMD	weighted mean difference	4
WVT	water vapor thermal therapy	5,8
WW	watchful waiting	3
XGB	extreme gradient boosting	6
yr	years	5

COMMITTEE

01

**LOWER URINARY TRACT
SYMPTOMS IN MEN**

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Table of Contents

Introduction	5
Epidemiology of Male LUTS	6
Male LUTS, including underactive and overactive bladder	6
Urinary incontinence	7
Overactive bladder (OAB)	7
Underactive Bladder (UAB)	10
LUTS and the prostate	12
Definition of BPH	12
Clinical	12
Anatomic	13
Biochemical	13
Physiological	13
Epidemiology of BPH	13
Based on histology	13
Based on symptoms	14
Risk Factors Associated with Male LUTS Mainly Related to Prostate	14
Demographics	14
Age/frailty	14
Other demographic factors	15
Behavioral	16
Dietary	16
Systemic disease	16
Nocturia and obstructive sleep apnea	17
Metabolic syndrome and LUTS mainly related to prostate	18
Natural History of Male LUTS and BPH	19
Progression of male LUTS	19
Progression of BPH	20
Progression of LUTS associated with prostate	22
Risk factors for clinical progression in male LUTS	22

Table of Contents

Age	23
Clinical presentation	23
Lifestyle, education, and psychosocial factors	24
Genes	24
Metabolic syndrome	25
Prostatic inflammation	25
Systemic inflammation	25
Implications for Prognosis and Management	26
Conclusion	28
References	29

Introduction

When discussing male lower urinary tract symptoms (LUTS), there is often a tendency to link LUTS to prostate pathology. This perspective overlooks LUTS in children and young adults, and neglects symptoms originating from the bladder, nervous tissue, cardiovascular system, urethral valves, strictures, and other causes. However, an increasing number of studies have shown that LUTS are frequently unrelated to the prostate.¹

LUTS in men may arise from various causes or combinations of etiologies. These can be categorized as follows:

1. LUTS attributable to the prostate and associated with benign prostatic obstruction (BPO);
2. LUTS attributable to the prostate—such as benign prostatic hyperplasia (BPH) or benign prostatic enlargement (BPE)—but without evidence of BPO;
3. LUTS originating from other components of the lower urinary tract—such as the bladder, urethra, bladder neck, or sphincter—independent of the prostate;
4. LUTS unrelated to the lower urinary tract, including the prostate, such as nocturia due to nocturnal polyuria; and
5. combinations of the above.¹

For educational clarity and in line with current evidence, we propose classifying LUTS into three categories:

1. LUTS mainly related to the prostate (BPH, BPE, BPO);
2. LUTS mainly related to the lower urinary tract excluding the prostate; and
3. LUTS unrelated to both the lower urinary tract and the prostate.

Special attention will be given to use this classification throughout the Consultation, although in some cases the terms BPH, BPO, or bladder outlet obstruction (BOO) will be used as reported by the original studies.

LUTS are typically categorized into storage, voiding, or post-voiding/post-micturition phases. However, Peyronnet *et al.* proposed adding a fourth category: “systemic LUTS” or “LUTS with a non-LUT origin” to the classification.² This is somewhat analogous to the International Children’s Continence Society’s terminology of monosymptomatic or non-monosymptomatic nocturnal enuresis—where the former refers to a nighttime-only issue (likely renal or diuretic in origin) and the latter involves both nighttime and daytime symptoms (indicating a lower urinary tract or mixed cause).

Symptoms such as increased frequency, urgency, and nocturia are related to the storage phase, while hesitancy, weak stream, and straining are associated with the voiding phase. These symptoms often occur together, forming syndromes that do not always clearly reveal the underlying cause. For instance, nocturia—whether due to an overactive bladder or bladder outlet obstruction—often also has a non-LUT origin. Similarly, voiding-phase symptoms can be indicative of either underactive bladder or bladder outlet obstruction.

Male LUTS, whether prostate related or not, are highly prevalent and bothersome. Understanding the natural history of these conditions, along with factors influencing their progression, is clinically valuable.¹ Insight into risk factors for clinical progression can aid in prevention, treatment, and cost management. A key question is whether we can differentiate between age-related changes and changes due to specific diseases or pathologies that result in LUTS, as this distinction could guide more targeted approaches.

To fully understand LUTS, we must acknowledge their role throughout an individual's life.³ Unlike the term “chronic,” which implies a persistent but external issue, “lifelong” is a more appropriate descriptor, reflecting that these symptoms are not merely persistent conditions but are integral to the individual's existence. LUTS evolve as a person ages, and in tandem with their overall health and psychological state. Recognizing LUTS as “lifelong” allows us to appreciate them not just as conditions to manage, but as aspects of a person's health that evolve with time.

Epidemiology of Male LUTS

Male LUTS, including underactive and overactive bladder

Epidemiological studies on male LUTS are challenging to conduct, and their results can be complex to interpret and compare. Most epidemiological studies evaluating male LUTS are designed to report prevalence, rather than incidence, and often use the validated International Prostate Symptom Score (IPSS) questionnaire.⁴ Prevalence estimates vary depending on whether a single LUTS is considered or a range of IPSS scores (from mild to severe). However, the IPSS questionnaire does not assess urinary incontinence, pain, terminal dribble, or post-void dribble.

Methodological factors can significantly influence study results. These include the definition of LUTS, sampling methods, questionnaire selection, survey administration mode (e.g., face-to-face interviews, telephone surveys, or postal questionnaires), and response rates. These methodological variations may account for differences in reported LUTS prevalence across geographical regions, rather than being attributed to ethnic, social, cultural, or economic factors.

It's also important to note that reporting a symptom does not mean that it is bothersome. Only about 50% of individuals reporting symptoms describe them as being bothersome, and an even smaller proportion of them seek treatment.^{5,6} A high prevalence of symptoms therefore does not necessarily correspond to a high burden on the healthcare system.

Studies have shown that the prevalence of moderate (IPSS 8–19) to severe (IPSS > 19) LUTS ranges from 16% to 56% and increases with age.^{7–11} The overall prevalence of male LUTS, defined as the presence of at least one symptom, varies between 47% and 89% (**TABLE 1**). Nocturia is generally the most frequently reported storage

symptom, while terminal dribble is the most common voiding symptom. Post-voiding symptoms are reported less frequently than either voiding or storage symptoms. These symptom patterns remain consistent across different countries.¹²

Urinary incontinence

Recent community-based studies report lower prevalence rates of urinary incontinence (UI) in men than in women at a ratio 1:2, with prevalence ranging from 1% to 40%. This wide prevalence range may be explained by the same methodological factors proposed to explain LUTS prevalence variation.

The prevalence of UI in community-dwelling men over the age of 40 years is 11% (at least one episode during the prior year), and daily incontinence may be present in as many as 9% of men over 60 years of age.¹³ One longitudinal population-based study observed a high UI prevalence (24%) in octogenarian men.¹⁴

A recent systematic review evaluating UI prevalence included 69 studies, and pooled analysis of these studies detected a clear pattern of increased prevalence of UI (all subtypes) in aging men, from 4.8% in those aged 19 to 44 years (11 studies) to 11.2% in those aged 45 to 64 years (27 studies), to 21.1% in men older than 65 years (41 studies). The highest prevalence of UI (32.2%) was reported in elderly men (17 studies). Urge UI was the most prevalent type of UI in men among all age categories, increasing from 3.1% in those aged 19 to 44 years (7 studies) to 11.7% in those older than 65 years (20 studies).¹³ Prevalence distribution of UI subtypes differs from women to men; in men, urge incontinence predominates (5%–21%), followed by mixed (1%–5%), and stress UI (< 1%–6%).¹⁵

Terminal or post-void dribble is considered as a subtype of UI in some studies, while others classify it as a voiding or post-void symptom. Prevalence of terminal dribble ranges from 14% to 46% and of post-void dribble from 6% to 63% (**TABLE 1**).

There are limited data on the incidence of male UI. The 1-year incidence rate was found to be 3.8% to 10%.^{15,16} In a longitudinal study, Malmsten *et al.* found a 6% increase in the prevalence of UI in a cohort of 3257 men assessed over an 11-year period.¹⁷ Substantial remission rates have been found in several studies, ranging from 27% to 47.8%.^{15,16,18}

Overactive bladder (OAB)

Overactive bladder is defined symptomatically by the International Continence Society (ICS) as urinary urgency, with or without urinary incontinence, usually with frequency and nocturia.¹⁹ It has been the focus of numerous epidemiological studies in recent years. Reported prevalence rates range from 5% to 84%, varying by geography and age (**TABLE 2**). The prevalence of OAB in men is estimated to range between 10% and 25% in most studies, with a tendency to increase with age, particularly in those over 60 years. A recent systematic review encompassing 35 epidemiological studies on OAB in men included 256,470 individuals and reported an overall prevalence of 16.1%.²⁰

TABLE 1 Population-Based Prevalence (%) of LUTS Among Men

Symptom	Sweden 1992 ¹⁸	Finland 1994 ¹⁹¹	Scotland 1995 ¹⁹²	Japan 2002– 2003 ¹⁹³	Sweden, Italy, UK, Germany, and Canada 2005 ^{12,194}	Korea+ 2006 ¹⁹⁵	Sweden, UK, and USA 2007– 2008 ^{6,196}	Brazil 2018 ¹⁹⁷	Poland 2020 ¹⁹⁸	Taiwan, China, South Korea (LUTS Asia study) 2022 ^{199–203}	Iran, Egypt, Bangladesh, Brazil, and Cameroon 2025 ²⁰⁴
Sample size (n)	7763	4256	1177	2100	7210	888	14,139	2433	2612	4076	1477
Any LUTS (at least 1 symptom)	NR	89	NR	NR	47	54	72	69	66	63	NR
Storage symptom	NR	NR	NR	NR	27	27	46	NR	54	13	NR
Nocturia ^a	13	56 ^d	12 ^c	17 ^b	21	10	29	27	31	35	39 ^e
Urgency	16	34	22	16	11	10	22	19	18	15	65
Frequency	NR	47	NR	52	7	14	21	28	28	27	24
Urinary incontinence (UI)	5	NR	NR	NR	5	3	NR	14	NR	17	33
Urge UI	2	17	NR	7	1	1	9	9	4	4	18
Stress UI	NR	9	NR	3	1	1	1 ^f	3	2	5	11
Mixed UI	NR	NR	NR	NR	1	NR	NR	NR	2	10	3
Other UI	NR	10	NR	NR	3	1	6	5	2	8	NR
Voiding symptoms	NR	NR	NR	NR	26	29	57	NR	NR	7	NR
Intermittency	NR	NR	10	NR	9	8	19	13	11	23	50
Slow/weak stream	27	NR	13	37	9	18	27	17	17	25	NR
Straining	NR	NR	3	NR	7	10	8	6	7	19	52
Terminal dribble	NR	NR	23	NR	14	19	46	25	21	31	NR
Split stream	NR	NR	NR	NR	NR	NR	20	17	10	26	NR
Hesitancy	7	46	3	NR	NR	NR	20	6	10	19	52
Post-voiding symptoms	NR	NR	NR	NR	17	16	40	NR	NR	2	NR
Incomplete emptying	23	30	8	26	14	14	23	13	12	29	NR
Post-void dribble	32	63	NR	NR	6	8	30	17	7	10	NR
Other symptoms	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Bladder pain	NR	NR	NR	2	NR	NR	5	NR	NR	NR	NR
Dysuria	NR	22	3	NR	NR	NR	3	NR	NR	NR	NR

Abbreviations: LUTS, lower urinary tract symptoms; NR, gender-specific prevalence not reported; SUI, stress urinary incontinence.

^a Nocturia 2 or more times per night unless otherwise specified.

^b Nocturia greater than 3 per night.

^c Nocturia frequency not defined.

^d Nocturia defined as mild, moderate, or severe.

^e Nocturia 1 or more times.

^f Prevalence defined as “at least sometimes,” SUI due to laughing, sneezing, coughing: 1.2%; SUI due to physical activity: 1.3%, other UI: leak for no reason; some prevalence numbers extrapolated from graphs.

TABLE 2 Population-Based Prevalence (%) of OAB Among Men

Country	Sample size (n)	OAB total	OAB without UI	OAB with UI
Europe and the Americas				
France, Germany, Italy, Spain, Sweden, and UK (survey year not stated) ²⁰⁵	7048	16	NR	NR
Austria (survey year not stated) ²⁰⁶	1199	10	8	2
Canada (survey year not stated) ²⁰⁷	1566	15	13 ^a	2
Sweden 1992 ¹⁸	7763	16	14	2
USA 2000–2001 ⁵	2469	16	13	3
Canada 2002 ²⁰⁸	475	13	9 ^a	4
Brazil 2003–2004 ²⁰⁹	399	14	NR	NR
Finland 2003–2004 ²¹⁰	1649	7	6	1
Spain 2004 ²¹¹	824	15	5 ^a	10
Italy, Germany, UK, Sweden, and Canada 2005 ¹²	7210	11	8	3
Italy ³⁰		9	3	
Germany ³⁰		9	3	
UK ²⁰⁶		6	3	
Sweden ¹⁵		9	5	
Canada ²¹²		5	4	
USA 2005 ²¹³	73,145	24	15 ^a	9
Portugal 2008 ²¹⁴	451	35	NR	NR
Sweden, UK, and USA 2007–2008 ²¹⁵	14,139	NR	NR	NR
Sweden ²¹⁶		22	NR	NR
UK ¹⁹⁴		NR	NR	NR
USA ²¹⁵		NR	NR	NR

Abbreviations: NR, gender-specific prevalence was not reported; OAB, overactive bladder; UI, urinary incontinence; UK, United Kingdom; USA, United States of America.

^a Inputted from published data.

TABLE 2 Population-Based Prevalence (%) of OAB Among Men (*continued*)

Country	Sample size (n)	OAB total	OAB without UI	OAB with UI
Asia				
Asia 1998 ²¹⁷	2369	30	13	17
China		30	NR	NR
Hong Kong		84	NR	NR
India		14	NR	NR
Indonesia		43	NR	NR
Malaysia		27	NR	NR
Pakistan		24	NR	NR
Philippines		20	NR	NR
Singapore		29	NR	NR
Taiwan		23	NR	NR
Thailand		63	NR	NR
Taiwan 2000 ²¹⁸	902	16	NR	NR
Korea 2000 ²¹⁹	1000	21	13	8
Japan 2002–2003 ¹⁹³	2100	14	8	6
Japan 2003 ²²⁰	414	18	NR	NR
Korea 2006 ¹⁹⁵	888	10	9	1
China 2009–2010 ²²	7359	6	4	2
Brazil 2018 ¹⁹⁷	5184	25	16	9

Abbreviations: NR, gender-specific prevalence was not reported; OAB, overactive bladder; UI, urinary incontinence; UK, United Kingdom; USA, United States of America.

^a Inputted from published data.

In a nested case-control analysis of data from the EPIC study—a population-based, cross-sectional survey of adults in five countries—bother and healthcare-seeking among individuals with OAB and control cases were explored. Among men with OAB, 54% reported bother; 77% of those had urinary incontinence, but only 51% used coping techniques.⁵

Underactive Bladder (UAB)

According to the ICS definition, underactive bladder (UAB) is characterized symptomatically by a slow urinary stream, hesitancy and straining to void, with or without a feeling of incomplete bladder emptying, sometimes accompanied by storage symptoms.²¹

Detrusor underactivity (DU), in contrast, is a urodynamic diagnosis requiring pressure-flow studies (PFS), defined by a detrusor contraction of reduced strength and/or duration, resulting in a prolonged bladder emptying and/or failure to achieve complete bladder emptying in a normal timespan.²¹ The prevalence of DU in community-dwelling men remains unknown, as available data are derived from PFS conducted in patients with LUTS. The wide variation in the urodynamic definitions of DU limits inter-study comparisons, and may explain the wide range in DU prevalence in LUTS populations (15%–48%).²²

Jeong *et al.* found a prevalence of detrusor overactivity with impaired contractility of 18.8%, and a prevalence of DU alone of 57.5%, in a retrospective cohort of 2571 men aged over 65 years who had been referred for urodynamic investigation of non-neurogenic LUTS.²³ Abarbanel and Marcus studied 181 community-dwelling LUTS patients aged ≥ 70 years and observed detrusor contractile dysfunction in 48% of men and 12% of women.²⁴ In addition, two-thirds of men and half of women with impaired detrusor contractility were also found to have involuntary detrusor contractions, and 10% of the corresponding patients with involuntary contraction had BOO. The investigators also reported that almost 10% to 20% of men who were confirmed to have a decreased flow rate by PFS exhibited DU. In a long-term follow-up study (13.6 years), Thomas *et al.* reported that two-thirds of institutionalized elderly patients with incontinence had symptoms of UAB.²⁵ Ameda *et al.*, using a definition of presence of DU based on the maximum isometric detrusor pressure of < 60 cmH₂O or unsustained isometric contraction, identified DU in 41.9% of their male cohort.²⁶ Gammie *et al.* found that 25.4% of men undergoing PFS for LUTS met the diagnostic criteria for DU defined as Bladder Contractility Index (BCI) < 100 , Abrams-Griffith number < 20 , and bladder voiding efficiency $< 90\%$.²⁷

The prevalence of DU in community-based populations is unknown because it is impractical to perform this invasive test at a community level; hence, no epidemiological data exists on the true prevalence of DU in the community. Most of the epidemiological data we have are derived indirectly from large epidemiological studies assessing LUTS.²⁸ The Epidemiology of LUTS (Epi-LUTS) study included 30,000 participants over 40 years of age. It found that storage LUTS were present in 45.7% of men and 66.8% of women.²⁹ Voiding LUTS were reported by 57.1% of men. It is possible that DU contributed to the development of LUTS in some of these individuals, but this remains uninvestigated.²⁸

An online survey of individuals aged 20 to 99 years (including 3122 men)¹⁴ found a UAB prevalence of 9.3% (using the ICS definition), increasing with age. In addition, storage symptoms including OAB were more frequent in the UAB group than in the non-UAB group ($P < .0001$). Frailty and several comorbidities were independently associated with UAB.³⁰

Valente *et al.* carried out a questionnaire survey, finding a higher prevalence of bladder emptying disorders in men compared to women (26.1% vs. 20.0%).³¹ Osman *et al.*'s review included several retrospective studies and reported that rates of DU were between 9% and 28% in men aged 18 to 50 years, which rose to 48% in elderly men (aged > 70 years); prevalence of DU was dominant among institutionalized patients.³² A likely explanation is that contractility of the bladder becomes impaired with age, resulting in the development of DU in both sexes in an age-related fashion. However, Ameda *et al.* also showed no significant association between age and impaired detrusor contractility in their study of 193 men with LUTS.²⁶

Future research should adopt standardized definitions of LUTS and ensure consistent measurement of symptom burden to facilitate more reliable comparisons across different populations and settings. There is limited population-based research on the incidence of individual LUTS, with most available data coming from cross-sectional studies rather than longitudinal ones. As longitudinal studies offer stronger evidence, they are essential for gaining a clearer understanding of LUTS progression, burden, and risk factors. Identifying these risk factors will help determine potential targets for preventing symptom development and improving patient outcomes.

LUTS and the prostate

The identification of men with LUTS related to anatomical or functional prostate pathology is challenging, as the complex relationship between prostate histology (benign prostatic hyperplasia; BPH), gland size (benign prostatic enlargement; BPE), and outlet function (benign prostatic obstruction; BPO) thwarts a simple definition. Differences in prevalence and treatment outcomes may actually result from disparate definitions rather than clinical differences among study populations. About 50% of men with LUTS have voiding dysfunction associated with prostate enlargement.³³ However, as BPH is a pathologic and not a clinical diagnosis, it is essential to demonstrate whether male LUTS are caused by an anatomic problem (BPE) or a functional problem (BPO).

Definition of BPH

BPH is a diagnosis pertaining to the proliferation of epithelial cells and smooth muscle within the prostate.³⁴ This, strictly speaking, is a histological diagnosis characterized by the nonmalignant proliferation of stromal connective tissue, smooth muscle, and glandular epithelium within the prostate gland. This proliferation often occurs in the periurethral and transitional zones of the prostate, leading to an increase in gland size. BPH may cause compression of the urethra, resulting in anatomical bladder outlet obstruction (BOO). BOO can manifest clinically as LUTS, which include urinary frequency, urgency, nocturia, weak stream, and incomplete bladder emptying. Additionally, BOO may predispose patients to urinary tract infections, acute urinary retention, and, in severe cases, renal insufficiency due to chronic obstruction.^{35,36}

As histology is only available via biopsy, surgery, or autopsy, clinicians use surrogates to define which patients have BPH, and in particular, LUTS mainly related to prostate. These surrogates are clinical, anatomic, biochemical, and physiological.

Clinical

Patients will typically present for care when they experience bothersome urinary symptoms. It is this clinical surrogate that usually starts the conversation between patient and provider. The effects of BPH on quality of life include lack of sleep, anxiety, reduced mobility, interference with leisure activities and usual daily activities, and a compromised sense of well-being.

A complete medical history regarding urinary symptoms, sexual function, and prior urologic interventions is necessary. The validated IPSS is the most prevalent questionnaire used for male patients in urology practice. Available in 53 languages, it can be used for 60% of the world's male population.³⁷

Anatomic

Prostate size is important in determining the proper pharmacological and surgical treatment for LUTS mainly due to prostate.³⁸ The presence of an obstructing intravesical (median) lobe may also affect treatment response.³⁹ Digital rectal examination (DRE) is the simplest initial test for prostate size, and does indeed correlate (although only moderately) with sonographic size on transrectal ultrasound.⁴⁰ However, imaging techniques such as ultrasound, magnetic resonance imaging (MRI), and computed tomography (CT) scans, or direct visualization via cystourethroscopy provides a more precise measurement of prostatic volume.⁴¹

Biochemical

While more often used as a screening test for prostate cancer, prostate-specific antigen (PSA) has demonstrated a high level of utility for the evaluation of BPH. Due to significant underestimation of prostate size using DRE, accuracy of assessment of prostate volume by physical exam alone is generally suboptimal.^{40,42} However, it has been shown that prostate volume and serum PSA both increase with age and specifically have a log-linear relationship. PSA can estimate prostate enlargement and is therefore a useful tool for the evaluation and therapeutic management of BPH. Roehrborn *et al.* reviewed data from Merck's BPH clinical trials, and by using receiver operating characteristic curves, concluded that age-specific criteria for predicting prostate size > 40 mL (considered "large") are PSA > 1.6 ng/mL, > 2.0 ng/mL, and > 2.3 ng/mL for men with BPH in their 50s, 60s, and 70s, respectively.⁴³ In a similar analysis, a study from the Netherlands found optimal PSA cutoff values (independent of age) of 2.0 ng/mL and 2.5 ng/mL for predicting prostate volumes > 30 mL and > 40 mL, respectively.⁴⁴

Physiological

Assessing the ability of the patient to efficiently empty the bladder is helpful to evaluate the presence, absence, and/or degree of urinary retention. Although a high post-void residual urine volume is neither diagnostic of, nor necessarily characteristic of, LUTS, high volume retention can exacerbate urinary symptoms and may adversely affect renal function. Uroflowmetry is another physiologic parameter that can assess voiding function and be measured noninvasively. In general, a normal uroflow rules out the presence of high-grade bladder outlet obstruction. While maximum flow rate is used to identify benign prostatic obstruction, the test lacks specificity as low flow may also signal detrusor underactivity or extraprostatic urethral obstruction.⁴⁵

Epidemiology of BPH

Based on histology

Histological analyses and prostate size measurements from autopsy data involving 925 human prostates demonstrate that the prevalence of BPH clearly increases with age.⁴⁶ BPH is found in only 8% of men in their 30s, increasing to 50% in their 50s and 80% in their 80s.⁴⁶ This corresponds to a prostate growth rate of 2% to 4% per year in men over age 40 years.^{47–51}

Based on symptoms

While not all men with an enlarged prostate develop bothersome symptoms, BPH remains the most common etiological factor for LUTS in men.^{52–55} When considering symptoms—defined as moderate-to-severe LUTS based on an IPSS of > 8—prevalence increases with age: 26% of men in their 40s, 33% in their 50s, 41% in their 60s, and 46% in their 70s are affected.⁵⁶ In the United States in 2015, approximately 38.1 million men were estimated to have BPH based on prostate size or histologic examination.⁵⁷ However, not all of those men have bothersome LUTS. Of those who did, 12.2 million men were actively managed for BPH: 54.8% were taking pharmacotherapy; 35% were managed expectantly (plus an additional 9.1% who stopped their pharmacotherapy); and 1.1% underwent surgical or office-based intervention.⁵⁷ The 2019 Global Burden of Disease Study—based on international clinical administrative data (including claims data and hospital inpatient admissions data)—reported that the age-standardized prevalence of BPH was 2480 per 100,000 men aged ≥ 40 years, peaking at approximately 25,000 per 100,000 in men aged 75 to 79 years.⁵⁸

Risk Factors Associated with Male LUTS Mainly Related to Prostate

The epidemiology of LUTS mainly related to prostate is changing, with overall case prevalence rising worldwide.⁵⁸ This increase has been associated with various modifiable and nonmodifiable risk factors, which can be categorized as demographic, behavioral, dietary, and medical/metabolic. Because many studies use male LUTS as a surrogate to identify patients with suspected BPH, risk factors for male LUTS and BPH are discussed together below.

Demographics

Age/frailty

According to the World Health Organization, the proportion of the world's population over 60 years will nearly double from 12% to 22% between 2015 and 2050,⁵⁹ meaning that the overall prevalence of all age-related conditions is likely to increase dramatically.

The prevalence of BPH is known to increase with age, and it is estimated that 45% of men will ultimately develop LUTS by age 75 years.^{60–62} Between the ages of 45 and 49 years, BPH incidence is approximately 3 cases per 1000 man-years, which increases to 38 per 1000 man-years between ages 75 and 79 years.^{60–62} For every 1-year increase in patient age, the incidence of BPH increases by 4%.⁵⁰ This increase in incidence appears to plateau after age 80 years, likely due to the “healthy survivor effect,”⁶³ combined with the phenomenon of underreporting of LUTS by the extreme elderly who may face barriers to care.

The relationship between BPH and age is similar for all ethnic and racial groups. And while African American men generally have a larger transition zone and total prostate volume,^{64,65} the prevalence of clinically symptomatic LUTS associated with prostate does not differ between Black and White men.⁶⁶ On the other hand, Hispanic men have been shown to have a higher likelihood of experiencing moderate-to-severe LUTS,⁶⁷ whereas Asian American men may have a lower risk for bothersome LUTS compared to White men.⁸

Frailty is a biologic syndrome characterized by decreased reserve and resistance to stressors, resulting in increased adverse health outcomes, including disability and mortality. The estimated prevalence of frailty ranges from 36% to 88% of older individuals.⁶⁸ Although there are multiple definitions of frailty and numerous tools have been developed for assessment, most conceptualizations are based on the frailty phenotype or the accumulation of deficits model. In 2001, Fried *et al.* proposed that frailty is separate from chronologic age, disability, and comorbidity, and instead involves a distinct biologic process with a cyclical nature that predisposes to vulnerability and adverse outcomes.⁶⁹ Fried *et al.* coined the frailty phenotype and operationalized this into a set of criteria that includes slow gait speed, low grip strength, reduced physical activity, self-reported exhaustion, and unintended weight loss. The presence of these deficits can be used to determine frailty status and, importantly, predict a range of adverse outcomes including decreased activities of daily living, increased hospitalizations, and 3-year mortality.⁶⁹ Alternatively, the accumulation of deficits model, initially published by Mitnitski *et al.*, includes 96 symptoms, signs, deficits, and laboratory abnormalities that make up a frailty index. The number of deficits present correlates with likelihood of adverse health outcomes.⁷⁰

Urinary incontinence is a highly prevalent urinary complaint among the frail elderly population. The presence of urinary incontinence is associated with an elevated risk of hospitalization and nursing home admission, independent of gender, age, and other comorbid conditions.^{71,72}

The pathophysiology of urinary incontinence in frail individuals is multifactorial, and the etiology is likely similarly diverse between impaired and unimpaired elderly individuals. In a prospective study conducted among institutionalized elderly individuals, Resnick *et al.* performed multichannel video urodynamic studies on 94 individuals with incontinence. The majority of patients exhibited detrusor overactivity (61%), and half of these patients had concurrent impaired detrusor contractility.⁷³ At least two likely causes of incontinence were identified in 35% of cases, suggesting that the etiology of incontinence is often just as multifactorial in frail individuals.

Other demographic factors

Between 1990 and 2017, there was an 80% increase in years lived with LUTS worldwide. Incidence increased from 24.94 to 31.77 per 100,000 over the same time period.⁷⁴ Reasons for this increase are likely to be multifactorial: growth of the older male demographic, increased life expectancy, improvement in access to care and diagnosis of BPH, and increase in risk factors associated with the rising rates of obesity and metabolic syndrome occurring in these same countries. This trend is particularly strong in China, where there are 111 million people over the age of 65 (8.2% of the population).⁷⁵ By 2050, this is expected to balloon to 400 million, representing 26.9% of the population, including 150 million greater than 80 years old.⁷⁶ Outside the United States, low- and middle-income countries have witnessed the greatest increases in BPH cases.^{58,74}

Urbanization is associated with an increased prevalence of LUTS, with men who reside in rural China experiencing a rate of LUTS due to prostate at only 67% of those in urban areas.⁷⁷ Similarly, in a study of Greek men, urban living was strongly associated with a higher BPH risk compared to country living. The authors believe that access to care was similar, and the difference was more likely due to environmental factors.⁷⁸ Another study supporting a strong environmental influence specifically on BPH showed that Chinese men living in China had smaller prostates than Chinese men who had emigrated to Australia, whose prostate volumes were similar to those of Caucasian Australians.⁷⁹

While marital status does not affect the prevalence of BPH, men with higher levels of education exhibit greater BPH prevalence—more than 23% in Chinese men with a college education or higher, compared to only 10% in those with no formal education.^{77,80}

Behavioral

Moderate to vigorous exercise reduces the risk of LUTS due to prostate by 25% versus men with a sedentary lifestyle.⁸¹ Unlike OAB, smoking in general does not increase the risk of LUTS due to prostate. In fact, several large studies have shown that smokers, especially heavy tobacco users, had a 50% lower rate of LUTS and a lower chance of progression to surgery.^{82–86} A similar inverse relationship exists between alcohol intake and LUTS.⁷⁷ Moderate alcohol consumption similarly reduces the risk for LUTS by 30% to 40%, and this has been shown in the US,^{84,87} Europe,⁸⁸ and South Korea.⁸⁹ However, a recent multivariable analysis that adjusted alcohol intake for smoking and body mass index (BMI) demonstrated no association between alcohol consumption and BPH.⁵¹

Dietary

Eating habits certainly contribute to metabolic syndrome, obesity, and diabetes, which may play a role in the development of LUTS (see “Systemic disease” below). Increased vegetable consumption, and reduced intake of fat, red meat, and total calories have been shown to lower the risk for LUTS.^{50,90,91} In a case-control study in Greece, dairy products, saturated fats, meats, fish, and eggs increased the risk of LUTS, while fruit intake reduced it.⁹² A higher prevalence of LUTS due to prostate was noted to correspond with increased zinc intake,^{92,93} but in contrast, elevated serum levels of selenium, lycopene, and vitamin E were found to be protective against LUTS.⁹⁴

Systemic disease

LUTS are becoming increasingly recognized for their relationship with non-urologic conditions and systemic diseases, including, but not limited to, cardiovascular disease, hypertension, diabetes, obstructive sleep apnea, non–health-promoting lifestyle choices, and the closely related metabolic syndrome. This evolving perspective is reflected in recent urologic societal guidelines. The European Association of Urology (EAU) guidelines published in 2019 and 2024 assert that all cases of LUTS warrant consideration of etiologies unrelated to lower urinary tract dysfunction.^{95,96} Similarly, the 2018 and 2024 American Urological Association (AUA) guidelines on the management of LUTS attributed to BPH assert that with a more thorough investigation, a proportion of men will be found to have conditions other than BPH that are either causing or contributing to their LUTS.^{97,98}

Nocturia and obstructive sleep apnea

Among the group of symptoms that comprise male LUTS, nocturia is a symptom that illustrates the relationship between LUTS and systemic disease particularly well. This connection is highlighted in a 2017 EAU guideline panel's systematic review of nocturia, in which the authors contend that, “. . . there may be a significant medical cause, potentially an opportunity to screen for undiagnosed or suboptimally managed disease”.⁹⁹

A prime example of this can be seen in the case of obstructive sleep apnea (OSA). OSA is defined by repeated episodes of upper airway obstruction during sleep caused by partial or complete collapse of the pharynx.¹⁰⁰ There are a variety of OSA-screening questionnaires available; however, one of the most frequently used tools is the STOP-BANG questionnaire,¹⁰¹ which is now recommended in a new AUA update on OSA and urological health.¹⁰² The STOP-BANG questionnaire consists of eight questions where each positive response is worth 1 point for a maximum score of 8. A total score of 0–2 corresponds to low risk, 3–4 to intermediate risk, and 5–8 indicates a high risk of moderate-to-severe OSA.¹⁰¹ The STOP-BANG questionnaire detects at least mild OSA with a sensitivity of 84% and moderate-to-severe OSA with a sensitivity of 93%, with corresponding specificities of 56.4% and 43%, respectively. The gold standard for diagnosis of OSA remains an overnight polysomnogram in a sleep laboratory.¹⁰¹

Several chief risk factors for OSA include male sex, older age, obesity, and smoking¹⁰³—all of which notably may increase the likelihood of other medical comorbidities that may be involved in LUTS—further underscoring the frequency with which urologists will encounter patients with these conditions. OSA is strongly associated with cardiovascular disease, including hypertension, coronary artery disease, atrial fibrillation, and myocardial ischemia, and may predispose patients to stroke, pulmonary hypertension, and cognitive impairment. Proposed mechanisms include increased sympathetic nervous system activity, metabolic dysregulation, increased oxidative stress, and systemic inflammation.¹⁰⁴

In OSA, a narrowed oropharynx results in abnormally high negative pressures created during inspiration, which overcome the ability of the oropharyngeal muscles to maintain airway patency. Subsequent pharyngeal collapse produces apneic events, which are often followed by hyperventilation and hypocapnia, decreasing respiratory drive and potentially perpetuating a pro-apneic cycle.^{100,103–105}

Though incompletely understood, several mechanisms are thought to be responsible for the relationship between OSA and nocturia. One involves increased arousal secondary to hypoxia-induced sympathetic overactivity, which leads to awakening and then awareness of the urge to urinate. Another potential mechanism relates to elevations in atrial natriuretic peptide (ANP). In OSA, increased negative intrathoracic pressure results in increased venous return to the right atrium. Concurrently, increased sympathetic activity leads to elevated pulmonary arterial vasoconstriction. Both alterations result in increased atrial stretch and release of ANP. Elevated ANP leads to nocturia through increased urine production by increasing the glomerular filtration rate, inhibiting sodium channels in the kidney, reducing antidiuretic hormone release, and inhibiting renin and aldosterone secretion.¹⁰⁶ Management of OSA with continuous positive airway pressure (CPAP) therapy prevents nighttime arousal, decreases ANP levels, and can decrease nocturia episodes in these patients.¹⁰⁷

Metabolic syndrome and LUTS mainly related to prostate

The metabolic syndrome (MetS) encompasses a group of risk factors for cardiovascular disease and type 2 diabetes, including central obesity, hypertension, dyslipidemia, and impaired glucose tolerance.¹⁰⁸ Eating and exercise habits affect the development of metabolic syndrome, obesity, and diabetes, which are themselves risk factors for BPH. Based on the Baltimore Longitudinal Study of Aging, there was a 0.41 mL increase in prostate volume for every 1 kg/m² increase in BMI. Additionally, with each 0.05 increase in waist-to-hip ratio, men had a 10% increased risk of BPH.^{50,51} At the extremes, obese men (BMI > 35) has a 3.5 times higher risk of prostate enlargement than non-obese men (BMI < 25).¹⁰⁹

It is hypothesized that obesity can lead to oxidative stress and systemic inflammation, secondarily causing immune infiltration into the prostate, mediating hyperplasia and tissue remodeling.^{110,111} While some studies show a higher rate of LUTS in those with high blood pressure (especially with increased diastolic pressure), others show no effect.^{112–115} Additionally, the confounding association with metabolic syndrome and obesity makes it difficult to assess whether isolated hypertension is an important risk factor.^{82,116}

Another risk factor for LUTS mainly due to prostate is diabetes mellitus. Elevated serum insulin and fasting blood glucose levels are both associated with larger prostate volume and worse LUTS, as well as increasing the need for BPH-related surgery.^{117,118} Compared to men with normal fasting blood sugar, men with elevated fasting glucose had a three times higher risk of LUTS,¹⁰⁹ and those with diabetes were twice as likely to have BPH compared to those without a diabetes diagnosis. Similarly, LUTS increased with diabetic severity, correlating positively with glycosylated hemoglobin levels.¹¹² While glucose in the urine can clearly cause polyuria, diabetes also causes prostatic growth, as elevated serum IGF-1, insulin, and IGF-binding protein levels cause prostate hyperplasia.^{119,120}

Multiple studies have described the association between MetS and OAB. For example, data from the National Health and Nutrition Examination Survey (NHANES) found that men with MetS had an elevated risk of certain LUTS, including hesitancy, incomplete emptying, weak stream, and nocturia.¹¹² Although the two syndromes may seem unrelated, it is understood that MetS and OAB share common pathologic mechanisms.¹²¹ One proposed mechanism linking the two syndromes is overactivity of the autonomic nervous system. Interestingly, several studies have demonstrated that the selective alpha-1-adrenoceptor blocker doxazosin, which targets bladder neck dysfunction, also improves insulin sensitivity in patients with diabetes.^{122,123} In another study, MetS was induced in a group of rats, and found that compared to controls, the MetS group exhibited detrusor overactivity and increased the expression of M2,3-muscarinic receptor mRNA in the bladder urothelium and muscle.¹²⁴ Additional pathophysiologic mechanisms thought to link MetS and OAB include chronic bladder ischemia, chronic low-grade proinflammatory state, and dysregulated nutrient-sensing pathways, all of which are discussed in a review by Hsu *et al.*¹⁰⁸

Natural History of Male LUTS and BPH

Progression of male LUTS

LUTS in men have been extensively studied over the decades, with the 2012 International Consultation on Male LUTS providing a comprehensive synthesis of the epidemiology and natural history of these symptoms.¹ This section aims to build upon the 2012 report, presenting an updated analysis that incorporates more recent findings to provide a refined perspective on the natural history of male LUTS and their age-related trajectories.

Despite much work in the area, the progression of male LUTS remains insufficiently explored, with most available data being cross-sectional and focused on clusters of symptoms within specific time frames. For example, a 2022 systematic review and meta-analysis of 74 population-based, cross-sectional, observational studies across 43 countries confirmed the high prevalence of LUTS in men.¹²⁵ The prevalence of moderate-to-severe LUTS in the male population was reported to be 35.2%, with a marked increase among those aged 60 years and older, where the prevalence reached 39%. Among male LUTS subtypes, storage symptoms were the most common, affecting 30.6% of men, followed by voiding symptoms (19.5%) and post-voiding symptoms (16.9%).

Despite its widespread prevalence, longitudinal studies assessing the lifetime progression and remission of LUTS remain scarce, leaving gaps in understanding the evolutive nature of these symptoms. A recently published Delphi process discussed an evolving model of LUTS as a waxing and waning condition, characterized by symptom exacerbation and remission.³ By framing LUTS within a life course epidemiology perspective, we can explore how early-life exposures, cumulative risks, and key transitions interact to shape symptom trajectories over time.¹²⁶

Evidence from childhood demonstrates the importance of early exposures. Lebl *et al.* followed up 43 children (14% male; mean age, 7.9 years) with symptoms of OAB for a mean period of 4.7 years and found a 68% resolution rate for daytime incontinence, suggesting the potential for improvement in some cases.¹²⁷ Conversely, Fitzgerald *et al.* demonstrated that adults with OAB symptoms are more likely to have had a history of childhood urgency or incontinence, indicating a continuity of symptoms across the lifespan.¹²⁸ Additionally, urodynamic studies have observed that childhood urgency may progress to detrusor underactivity in some cases, with long-term changes such as post-void residual urine emerging later in life.¹²⁹ It is also unclear whether this might be the only possible link between the two conditions. Combined detrusor overactivity with underactivity has been noted in adult men of all age groups including young men, suggesting that there might be a basal level of prevalence of this condition in the general population.¹³⁰

Transitioning to adulthood, research highlights how LUTS continue to impact quality of life, often progressing subtly over time. The natural history of male LUTS reveals significant variability in progression and regression rates across populations, with findings from longitudinal studies conducted between 2012 and 2024 summarized in **TABLE 3**. Progression was typically defined in the included studies as an increase in symptom scores, such as a ≥ 3 -point rise in the American Urological Association Symptom Index (AUASI) or a ≥ 4 -point increase in the IPSS, while regression involves a corresponding decrease. Importantly, these definitions are rooted in numerical

changes in symptom scores rather than patient-reported outcome measures, which assess the subjective impact of symptoms on quality of life. As such, a numerical increase in scores may not always justify the initiation of treatment, while in other cases, even a modest score change may reflect a significant clinical impact necessitating intervention.

Progression of BPH

There is a limited amount of information on the natural history of BPH, and most of it was published some years ago. The pathological signs of BPH typically begin to appear in men aged 31 to 40 years, with an estimated prevalence of 8% in this age group.⁴⁶ As discussed, the prevalence of BPH increases significantly with age. By the seventh decade of life, over 70% of men are affected, demonstrating the progressive nature of this condition. By the ninth decade, the prevalence has risen to approximately 90%.⁴⁶ This trend highlights the significant burden of BPH in older populations and underscores the importance of understanding its progression for effective management.

It is possible to analyze prostate growth by measuring prostate weight. As discussed earlier, an autopsy study confirmed that the organ grows across different age groups.⁴⁶ Prostate weight increases rapidly during adolescence and early adulthood, growing at an average rate of 1.6 grams per year in individuals aged 10 to 20–30 years. However, the growth rate significantly decreases after this period, averaging 0.4 grams per year in men aged 31 to approximately 90 years. The growth trajectory of most human prostates can be categorized into two distinct phases: a rapid growth phase occurring between birth and 30 years and a slower growth phase spanning from 31 years to over 90 years. Interestingly, in this study, 3.7% of prostates (5 of 135) in men over 70 years reached a large weight exceeding 100 grams, indicating notable variability in prostate size among elderly individuals.⁴⁶

In the Olmsted county study, which followed a randomly selected cohort of 2115 men aged 40 to 79 years over 12 years, prostate size increased from 31.3 mL to 33.7 mL, then to 36.1 mL, and to 43.1 mL per 5-year increment.¹³¹ In the subgroup of men aged 50 to 77 years who had BPH, untreated men experienced mean growth rates of 2.5 mL, 4.9 mL, 6.4 mL, and 7.2 mL from baseline each year over a 4-year period.¹³² These findings provide valuable insights into the physiological development of the prostate and its variations in aging populations.

Linear regression analysis of age versus the logarithm of BPH tumor weight is a valuable method for estimating the doubling time and growth rates of BPH. During the early phase of growth, typically observed in men aged 31 to 50 years, BPH tumors requiring surgical intervention exhibit an almost exponential growth pattern, with a doubling time of approximately 4.5 years.⁴⁶ In the mid-phase of growth, which occurs between the ages of 55 and 70 years, the doubling time increases to around 10 years, indicating a slower progression. These findings provide insight into the natural history of BPH growth, which can help inform clinical decision-making and timing for intervention.⁴⁶ The exponential growth in younger men underscores the importance of early detection and monitoring, while the slower growth in older men may suggest a more conservative approach to management in some cases.

TABLE 3 Summary of Longitudinal Studies on the Progression and Regression of Male LUTS (2012–2024)

Study	Country	Size	Follow-up duration (y)	Symptom definition	Progression	Regression
Maserejian <i>et al.</i> (2014) ¹³⁸	United States	1610 (total, 4144)	5	AUASI	Progression ($\geq$ 3-point increase in AUASI), 21%–33%	Regression ($\geq$ 3-point decrease in AUASI), 30%–44%
Wallner <i>et al.</i> (2014) ²²¹	United States	19,505	4	AUASI	Progression ($\geq$ 4-point increase in AUASI), 30.2%	Regression ($\geq$ 4-point decrease in AUASI), 11.4%
Martin <i>et al.</i> (2014) ¹⁵⁶	Australia	780	5	AUASI	39.8% progressed in storage LUTS ($\geq$ 2-point increase); 32.3% in voiding LUTS ($\geq$ 3-point increase)	33.1% regressed in storage LUTS ($\geq$ 2-point decrease); 23.4% in voiding LUTS ($\geq$ 3-point decrease)
Fukuta <i>et al.</i> (2012) ¹³⁶	Japan	91	15	IPSS	Progression ($\geq$ 4-point increase in IPSS), 38.5%	Regression ($\geq$ 4-point decrease in IPSS), 13.2%
Liu <i>et al.</i> (2016) ¹⁵¹	Hong Kong	2000 (baseline); 1564 at follow-up	4	IPSS	Progression ($\geq$ 3-point increase in IPSS), 31%	Not applicable (regression data not reported)
Choo <i>et al.</i> (2015) ¹⁵³	Korea	224	3	IPSS	LUTS prevalence increased by 13.1% (from 55.4% to 68.3%); mean IPSS increased by 2.6 points	Physical activity was protective for voiding symptoms
Fu <i>et al.</i> (2016) ¹⁶⁸	China	525	3	IPSS	Overall progression ($\geq$ 4-point increase in IPSS), 21.1%	Not applicable (regression data not reported)
Rohrmann <i>et al.</i> (2016) ¹³⁹	Germany	7821	3	IPSS	Worsening symptoms, 54.8%	Improvement in symptoms, 27.1%
Åkerla <i>et al.</i> (2024) ²²²	Finland	2480	11	DAN-PSS	43% had persistent mild urgency; 5% progressed to persistent moderate/severe urgency; 10% new onset of moderate/severe urgency	27% had resolution of urgency ($\geq$ 2-point decrease in urgency scores); 35% regression in mild urgency symptoms
Bauer <i>et al.</i> (2023) ¹⁴³	United States	3235	7	AUASI	Mean increase of 4.1 points in the moderately frail group and 7.3 points in the severely frail group	Not applicable (focus was on frailty-driven progression)

Abbreviations: AUASI, American Urological Association Symptom Index; DAN-PSS, Danish Prostatic Symptom Score; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms.

Progression of LUTS associated with prostate

BPH is a progressive condition characterized by the deterioration of several clinical parameters, including LUTS, health-related quality of life, peak urinary flow rate, and prostate enlargement. Additionally, unfavorable outcomes such as acute urinary retention (AUR) and the need for BPH-related surgery are considered markers of disease progression.¹³³

The natural history of BPH and LUTS is best analyzed through longitudinal studies of community-dwelling men. The Olmsted County study revealed that the incidence of active treatment was age dependent, with a rate of 3.3 per 1,000 person-years in men aged 40 to 49 years, increasing significantly to 30 per 1,000 person-years in men over 70 years. Other data from the study demonstrated a mean annual increase in the IPSS of 0.18 points, with variations ranging from 0.05 points per year in men in their 50s to 0.44 points per year in those in their 70s.⁴¹ Furthermore, peak urinary flow rate decreased by approximately 2% per year, and median prostate volume exhibited an annual growth rate of 1.9%.¹³⁴ Despite these changes, the cumulative incidence of AUR remained relatively low, at 2.7% over 4 years.¹³⁴

A limitation of the Olmsted County study was that the participants were not necessarily representative of the general population. The study targeted mainly middle-class North American men, all of whom were Caucasian and who had access to excellent healthcare. Moreover, baseline selection criteria (exclusion of men aged ≥ 80 years and those with a history of prostate surgery), may have contributed to the selection of men at lower risk of disease progression. Nevertheless, this study, which looks at events occurring in the general population rather than in patients, showed that serious outcomes such as AUR occurred uncommonly.¹³⁵ The prevalence of LUTS in men varies across countries, potentially due to cultural and linguistic differences in translated questionnaires and the responses they illicit.¹³⁶

Regarding asymptomatic men with prostate enlargement, the REDUCE trial examined a cohort of more than 3000 men with mild or no LUTS.¹³⁷ In the group who did not receive pharmacotherapy for BPH, men with larger prostates were indeed at a higher risk for bothersome symptoms. Specifically, for every 10 mL increase in prostate size, there was a 17% increase in developing incident LUTS. Men with prostate size 40 mL to 80 mL were 67% more likely to experience LUTS compared to men with prostate size < 40 mL.¹³⁷

Risk factors for clinical progression in male LUTS

BPH, together with the associated LUTS, is a chronic, progressive disease. Men with BPH typically experience a gradual increase in prostate size and symptom severity over time. This rate of progression is not uniform, with some men showing a greater propensity for disease progression. Identifying such individuals may allow for early initiation of therapies aimed at modifying disease progression. This approach could help reduce disease morbidity in men at higher risk of progression while avoiding the adverse effects of such therapies in those at lower risk who may not require intervention. More importantly, addressing modifiable risk factors may favorably alter the natural history of progression. A better understanding of these risk factors, along with advances in medical

therapeutics, may eventually allow for the modification of currently nonmodifiable risk factors. Progression can be measured by direct changes in prostate volume or histology, or through surrogate markers such as the progression of LUTS or the need for prostate surgery. This section examines new evidence related to the subject published since the previous iteration of this ICUD in 2012.¹

Age

The impact of age has been well documented earlier in this chapter and elsewhere,^{138,139} with an increase in IPSS score of 0.18 points per year, an increase of prostate volume of 1.9% per year, and a decrease in maximum flow rate of 2% per year noted in a large community-based study.¹⁴⁰ A secondary multivariable analysis of the MTOPS data examined 3047 men who were followed for 4.5 years and noted an age-associated hazard ratio for progression of 1.33 (95% confidence interval [CI], 1.15–1.53) per decade.¹⁴¹ A cross-sectional study of 4706 men suggested that the risk might be nonlinear. In this study, age became a risk factor independent of other factors such as PSA, prostate volume, or IPSS score above a threshold of 61 years of age.¹⁴² Recent evidence suggests that age alone does not predict progression. Key transitions, such as the onset of frailty in older age (see earlier), represent critical turning points. Bauer *et al.* demonstrated that progression in LUTS, as measured by AUASI scores, was closely linked to increasing frailty. Men who became moderately frail over a 7-year period experienced a mean AUASI score increase of 4.1 points, while those with severe frailty showed a mean increase of 7.3 points ($P < .01$).¹⁴³

While chronological age is a nonmodifiable factor, individuals can age at different rates, a concept captured by biological age. Biological age has been estimated by various methods using physical, biochemical, hormonal, and other markers. An additional measure, accelerated age, captures the difference between chronological age and biological age. Data from the UK Biobank Cohort Study involving 135,933 men without BPH followed for 13 years showed that chronological age, biological age, and accelerated age were all associated with BPH progression in a nonlinear manner. Accelerated age risk was independent of underlying genetic factors and appeared to enhance the overall risk of progression. This introduces a unique modifiable element to aging, allowing individuals control over some aspects of the aging process and, consequently, the risk of BPH progression.¹⁴⁴

Clinical presentation

Baseline clinical characteristics—including the IPSS score, maximum flow rate, post-void residual urine, and PSA—have been shown to predict BPH progression.^{140,141} Higher baseline symptom severity is a strong predictor; men with moderate-to-severe symptoms are at significantly higher risk for progression than those with mild symptoms.¹³⁹ The duration of symptoms has also been shown to be an independent risk factor for LUTS progression.¹⁴⁵ In a community-based survey, each 1-year increase in self-perceived duration of LUTS was associated with an increase in IPSS of 0.3 points ($P < .001$).¹⁴⁵

Baseline prostate size can likewise predict the development and progression of LUTS. In the REDUCE study, this risk was highest in men with a prostate size between 40 mL and 80 mL and was not seen in men taking dutasteride.¹³⁷ Configuration of the prostate may also be associated with progression. Anterior lobe thickness

of ≥ 0.65 cm was associated with clinical progression of BPH and the need for prostate surgery.¹⁴⁶ In another study, prostatic urethral length > 4.53 cm and transitional zone urethral length > 3.35 cm predicted the need for prostatic surgery.¹⁴⁷ In contrast, baseline circulating androgen levels did not predict BPH progression in the REDUCE study.¹⁴⁸

Lifestyle, education, and psychosocial factors

A healthy diet and lifestyle, including regular physical activity, protects against progression of LUTS and BPH.¹⁴⁹ A diet rich in red meat and fat has been shown to increase the risk of BPH, while flax seed and its extract, fruits, and vegetables have been shown to mitigate the risk.¹⁵⁰ In a 4-year longitudinal study of 2000 Chinese men, consuming a diet rich in fruits and dark, leafy vegetables reduced the progression of BPH and LUTS.¹⁵¹ Increased physical activity and reduced sedentariness have been shown to reduce the risk of progression of LUTS in a long-term follow-up of health professionals.¹⁵² Choo *et al.* found that storage subsymptoms significantly worsened in heavy smokers, with an odds ratio of 5.13 (95% CI, 2.25–11.67), while physical inactivity was linked to worsened voiding subsymptoms (OR, 2.25; 95% CI, 1.04–4.87).¹⁵³

On the contrary, an analysis of 5495 German men in the EPIC-Heidelberg cohort showed no association between LUTS progression and smoking, alcohol consumption, or physical activity.¹⁵⁴ However, men with more years of education had greater odds of LUTS progression than men with only primary education, whereas men who were very satisfied with life at baseline were less likely to report progression.¹⁵⁴ Quality of sleep and presence of obstructive sleep apnea have also been correlated with LUTS progression.^{155,156} Sleep quality can also serve as a marker for healthy men who are more likely to develop LUTS.¹⁵⁵ Psychosocial factors, including delayed recognition of symptoms and lower health literacy, also exacerbate progression.¹⁵⁷

Genes

Genetic factors have been estimated to be important in the causation of BPH in 39% to 72% of patients.¹⁵⁸ A large number of genes have been shown to be associated with BPH, including variants related to vitamin D receptors, sex hormones (testosterone, progesterone, estrogen), inflammation, cytokines, and growth factors.¹⁵⁸ It is unlikely that a single gene is responsible for BPH. It is uncertain whether these genes merely mark a predisposition for BPH or have a specific impact on disease progression. The glutathione S-transferase P1 (GSTP1) gene has been shown to increase the risk of progression of BPH.¹⁵⁹ CCL5 and CCR2 genes associated with chronic inflammation might be important in both the development and progression of BPH.¹⁶⁰ Polymorphism of another inflammation-associated gene, the COX-2 (rs2745557), has been shown to increase the risk of BPH progression.¹⁶¹ Genes associated with sex steroid pathways might be important in disease progression. Polymorphisms in the gene coding for 5 α -reductase 2 (SRD5A2), an enzyme associated with testosterone-dihydrotestosterone conversion, have been noted to be associated with BPH progression,¹⁶² while another study found an association with the estrogenic receptor-related GATA3 gene.¹⁶³

Metabolic syndrome

MetS is common in men with LUTS and BPH and might impact the risk of progression. An association has been noted between components of MetS and markers of BPH progression such as prostate volume.^{164–168} BMI is also critical, with Maserejian *et al.* reporting a positive association with symptom progression ($P < .01$).¹³⁸ A systematic review noted that men with MetS showed a higher prostate growth rate than controls, with a weighted mean difference of 0.79 mL per year (95% CI, 0.36–1.2; $P < .001$).¹⁶⁴ Levels of TNF α might identify men at risk for progression.¹⁶⁶ An association has also been noted with other markers of BPH progression such as IPSS score¹⁶⁵ and maximum flow rate.¹⁶⁴ Circulating levels of high-density lipoprotein (HDL) were found to be inversely associated with the risk for BPH in a study of two large population-based databases.¹⁶⁹ Targeting metabolic syndrome could reduce the risk for BPH progression in addition to having other well-established health benefits.¹⁷⁰ A systematic review of the effect of statins found no reduction in the development of BPH, except for a subgroup of men > 60 years, but did note a reduction in the progression of LUTS.¹⁷¹ A nationwide population study from South Korea showed reduction in BPH progression in men on metformin, based on a reduced risk of prostate surgery over an 8-year follow-up.¹⁷²

More interventional studies are needed to determine the therapeutic value of interventions.

Prostatic inflammation

Incidental histological inflammation is commonly noted in the prostate. Some patients show biochemical evidence of inflammation, with elevated serum markers of inflammation or PSA. The impact on prostate growth seems to be small, although such men possibly carry a higher risk of acute retention.¹⁷³ Torkko *et al.* examined inflammatory markers in prostatic tissue of 859 men who participated in the MTOPS trial.¹⁷⁴ In those who showed elevated CD45, CD4, and CD68 markers in transitional zone biopsies, the risk of progression of BPH was higher, with the strongest association noted with CD4 (hazard ratio [HR], 2.03; $P < .001$ for the highest tertile of moderate/severe inflammation versus the lower two tertiles).¹⁷⁴ Molecular tissue biomarkers such as cysteine-rich protein 61 (CYR61) and vascular endothelial growth factor (VEGF) have also shown an association with BPH progression.¹⁷⁵ Luo *et al.* developed a nomogram that could be used to predict tissue inflammation on a prostatic biopsy. The nomogram was based on prostate volume, fasting blood glucose, and prostatic calcification.¹⁷⁶ Such nomograms might help identify men at risk of progression without the need for biopsy.

Systemic inflammation

Circulating markers of inflammation have shown an association with prostatic inflammation. Plasma interleukin 2 (IL-2) levels have been shown to predict the risk of developing BPH and, when already present, its progression, in young and middle-aged men.¹⁷⁷ Furthermore, a systemic immune inflammation index (defined as [neutrophil x platelet]/lymphocyte) identified men at risk of progression of LUTS and the development of retention.¹⁷⁸ There also appears to be an association between apparently distant inflammation and the development of BPH. Correlation has been noted between prostatic growth and intrahepatic inflammation in patients with non-alcoholic steatohepatitis (NASH),¹⁷⁹ and studies suggest an association between periodontal pathogens such

as *Porphyromonas gingivalis* and BPH in men, and between these pathogens and BPH progression in animal models.¹⁸⁰ It is thought that periodontitis may affect the progression of BPH through IL-6/IL-6R inflammation and Akt signaling pathways.¹⁸⁰ A systematic review noted association between SARS-COVID infection and progression of BPH and surmised a possible role for systemic inflammation, androgen receptors, and angiotensin-converting enzyme-2 pathways.¹⁸¹ The therapeutic implications of these findings remain uncertain. Few studies have examined interventions. In a longitudinal study of 1670 men over 7 years, the use of dietary antioxidants failed to impact progression of LUTS.¹⁸²

Implications for Prognosis and Management

Findings in the literature highlight the slow but progressive nature of BPH and underscore the importance of longitudinal monitoring for the early identification of patients at risk of significant clinical deterioration. Future research should focus on identifying predictive markers for disease progression to optimize therapeutic interventions and improve patient outcomes.

For much of the 20th century, our understanding of natural history was largely based on small observational studies. The decision to adopt watchful waiting traditionally relied on a combination of patient preference and a physician's clinical judgment regarding the patient's prognosis, and there were no well-defined criteria to determine which patients were optimal candidates for this approach. However, the introduction of large, randomized, placebo-controlled trials, along with extensive longitudinal studies, has helped to advance our knowledge of the natural history of BPH. This progress has, in turn, enabled more accurate identification of patients eligible for watchful waiting.¹⁸³ It has been observed that the risk of requiring surgical intervention increases with age. Among the predictive factors for eventual surgery, a progressively diminished urinary stream and the sensation of incomplete bladder emptying stood out as particularly significant.¹⁸³

Other authors consider that the progression of BPH can be predicted based on baseline variables. Studies have identified age, severe LUTS, low peak flow rate, high post-void residual volume, enlarged prostate, and elevated serum PSA levels as risk factors for acute urinary retention and BPH-related surgery.¹⁸⁴ Although nonmodifiable risk factors—such as age, genetics, and geographic variation—play significant roles in the etiology of BPH and BOO, recent research has highlighted several modifiable risk factors that offer new avenues for treatment and prevention. These include alterations in sex steroid hormones, metabolic syndrome, cardiovascular disease, obesity, diabetes, dietary habits, physical activity, and inflammation.^{185–187}

Further research into these and other predictive factors continues to shape management strategies, ensuring that patients are better informed and that treatment decisions align with their individual risks and preferences. However, despite numerous studies published on BPH, its natural history remains incompletely understood due to the absence of a uniform definition of the disease and the lack of well-designed, longitudinal studies. A comprehensive understanding of BPH's progression would require the longitudinal follow-up of a large cohort of men from the general population, employing standardized symptom scores, transrectal ultrasonography,

and pressure-flow urodynamic studies. Such studies would help identify the key factors influencing disease progression and provide more accurate prognostic models.^{36,188} However, the high cost and invasive nature of such a study present significant challenges to its feasibility and implementation.

Plasticity—the capacity for regression and recovery—emerges as a critical component of male LUTS management, whether prostate related or not. Younger age, milder symptoms, and structured interventions such as physical activity promote regression. Maserejian *et al.* demonstrated that younger men exhibit higher rates of symptom improvement compared to older cohorts.¹³⁸ Milder baseline symptoms also strongly correlate with higher chances of regression. Regression of storage LUTS tends to be more frequent than voiding LUTS, a pattern noted in studies like that by Martin *et al.*, reflecting differences in symptom pathophysiology and responsiveness to lifestyle or natural changes.¹⁵⁶ The prospective study by Mondul *et al.* demonstrated that men with higher levels of physical activity (≥ 63 MET-hours per week, equivalent to 3 or more hours of walking per day at a moderate pace) were significantly less likely to experience LUTS progression, though progression and regression rates showed no association with sedentary behavior or inactivity in already symptomatic men (HR for LUTS progression to severe: 0.91; 95% CI, 0.79–1.04).¹⁵² While physical activity has a stronger established link to preventing LUTS incidence, its role in promoting symptom regression may involve physiological mechanisms such as improved vascular function, reduced systemic inflammation, and metabolic regulation. Similarly, Matsumoto *et al.* observed that elderly men participating in a structured exercise program showed significant improvements in LUTS, including urgency, storage symptoms, and nocturia ($P < .05$).¹⁸⁹ Participants in this program also reported enhanced quality of life, likely due to better circulation and activation of the nervous system, which supports bladder and pelvic floor function.

The evolutive nature of male LUTS may be best understood through an accumulation model characterized by the clustering of risks and their cumulative impact over time.¹⁹⁰ This approach posits that LUTS arise not from isolated exposures but from a lifetime of connected factors that build upon one another. Early-life urinary symptoms, such as childhood LUTS, may create a foundation of vulnerability that predisposes individuals to symptom progression later in life. As men age, these early susceptibilities are compounded by modifiable lifestyle behaviors, such as smoking and physical inactivity, and systemic health conditions like metabolic syndrome and obesity. These factors cluster together, amplifying each other's effects and contributing to worsening symptom severity. This model also explains the heterogeneity in LUTS trajectories, where men with fewer risks or healthier behaviors may experience slower progression or even regression, while those with multiple risks face more rapid symptom escalation. Importantly, the accumulation model highlights critical intervention points. Addressing childhood urinary symptoms early or modifying lifestyle factors in midlife—such as increasing physical activity or promoting weight loss—can disrupt the compounding effects of risk accumulation and reduce the likelihood of severe LUTS in later life.

Conclusion

Male LUTS, whether due to prostate pathology or not, are strongly related to age, and difficult to distinguish from one another. However, they are likely independent conditions with very similar underlying causes and risk factors, including metabolic syndrome, cardiovascular disorders, diabetes, obesity, inflammation, and physical inactivity. While not all men with an enlarged prostate develop bothersome symptoms, anatomic or functional BPO is the most common etiological factor for LUTS in men. However, not all LUTS are attributable to BPO, and they are becoming increasingly recognized for their relationship with non-urologic conditions and systemic diseases.

Early-life urinary symptoms, such as childhood LUTS, may create a foundation of vulnerability that predisposes individuals to symptom progression later in life. As men age, these early susceptibilities are compounded by modifiable lifestyle behaviors, such as smoking and lack of exercise, and by systemic health conditions including metabolic syndrome and obesity. These factors tend to group together, intensifying risk and symptom severity. This model also helps explain the heterogeneity in LUTS trajectories and is exemplified by obstructive sleep apnea syndrome: several major risk factors for OSA may also increase the likelihood of other medical comorbidities implicated in LUTS.¹⁰³ As a result, urologists are liable to encounter patients with a range of non-urological conditions within their practice and must ensure that they are equipped to take a holistic approach to LUTS diagnosis and management.

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COMMITTEE

02

PATIENT ASSESSMENT

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Table of Contents

History and Examination by Marcus J. Drake, DM, FRCS (Urol)	52
Conclusion	52
Symptom Scores by Hiroki Ito, MD, PhD	52
Conclusion	54
Bladder Diaries by Paulina Bueno-Garcia-Reyes, MD	54
Conclusion	56
Flow Rate Testing by Tufan Tarcan, MD, PhD	57
Conclusion	59
Urinalysis by Alex Ciudin, MD, PhD, FEBU	59
Conclusion	60
Prostate-Specific Antigen by Filipe Abadesso Lopes, MD	60
Conclusion	61
Prostate Size and Shape Assessment by Qi-Xiang Song, MD, PhD	62
Conclusion	63
Cystoscopy by Alex Ciudin, MD, PhD, FEBU	63
Conclusion	64
Urodynamics by Ricardo Pereira e Silva, MD, FEBU	64
Videourodynamics by Ricardo Pereira e Silva, MD, FEBU	67
Ambulatory Urodynamics by Ricardo Pereira e Silva, MD, FEBU	67
Conclusion	68
Frail Older Men by William Gibson, MBChB(MD), PhD, FRCP	68
Conclusion	69
Suspected Neurological Mechanism by Marcio A. Averbeck, MD, MSc, PhD	70
Conclusion	72
Experimental Methods by John E. Speich, PhD	73
Electronic bladder diaries	73

Table of Contents

Urodynamic pressure measurement	73
Near-infrared spectroscopy	74
Imaging methods	74
Artificial intelligence	74
Experimental uroflowmetry	75
Conclusion	75
Summary of Recommendations <i>by Marcus J. Drake, DM, FRCS (Urol)</i>	76
References	78

Lower urinary tract symptoms (LUTS) can be classified into storage, voiding, and post-micturition symptoms. Symptom types, their impact on quality of life (QoL),¹ and the underlying mechanisms are key requirements of LUTS assessment. Precise symptom assessment, based on suitable pathways with accurate equipment available, is crucial for diagnosis, treatment planning, and monitoring therapeutic response. Furthermore, specific values and preferences of each individual patient must be established.²

History and Examination

Assessment begins with the patient's history to identify type(s) of LUTS experienced, their individual impact, and any potential causes of LUTS.³ Relevant comorbidities should be identified, such as medical (e.g., diabetes mellitus or insipidus, renal disease, heart failure, sleep apnea) and neurological diseases (e.g., Parkinson's disease, multiple sclerosis, or cerebrovascular disease). It is also recommended to review current medications and assess lifestyle habits, as well as emotional and psychological factors.^{2,3} Physical examination should be undertaken to rule out bladder distention, and conditions affecting the external genitalia that may cause or contribute to LUTS (e.g., phimosis, meatal stenosis, penile cancer).³ Neurological assessment of the perineum and lower limbs should evaluate motor and sensory function. Digital rectal examination (DRE) may help determine the coexistence of prostate cancer and abnormalities in anal sphincter tone.³

Conclusion

The medical history in men with LUTS should cover symptom type(s) and their individual impact, lifestyle, potential causes, and current medications. Physical examination is needed to assess for bladder distension, external genitalia abnormalities, neurological status, and signs of prostate cancer.

Symptom Scores

Patient-reported outcome measures (PROMs) are essential for patient-centered assessment, offering tools designed to measure both the severity and types of LUTS present. Some PROMs also capture bother—either the overall impact of LUTS or the bother contribution of the component LUTS. PROMs are questionnaires that directly gather health baselines or outcomes from patients, including aspects such as symptoms, health-related QoL, and functional status.⁴ In recent decades, healthcare systems have increasingly acknowledged the importance of incorporating patients' perspectives.⁵ Symptom scores are essential in diagnosing and managing LUTS, as they provide a standardized measure of symptom severity. For individual patient management, these scores facilitate communication between patients and healthcare providers, and a scrutiny of item responses in the clinic can reveal the most severe and bothersome symptoms, allowing for targeted interventions. Sometimes, the scores assist in determining appropriate treatments such as medications, behavioral therapy, or surgical intervention.⁶ Additionally, these tools enable the longitudinal monitoring of symptom progression or improvement following

interventions and allow for comparisons in clinical research and epidemiological studies. For research, overall scores and subscores offer a way to quantify key parameters and the change associated with intervention.

Various validated symptom scoring tools have been developed to quantify the severity of LUTS. These generally consist of a series of short, simple questions (items) with a fixed number of response options (scored 0 to 4, for example).

Several standardized symptom assessment tools are available for LUTS, each with specific applications. Some of the key tools are:

1. International Consultation on Incontinence Questionnaires (ICIQ) Male LUTS module (ICIQ-MLUTS). The ICIQ has developed a set of validated PROMs designed to assess urinary and bowel symptoms in a standardized and high-quality manner.⁷ Developed over the past 22 years, the modules have undergone rigorous validation, ensuring their reliability and clinical utility. ICIQ-MLUTS⁸ evaluates male LUTS by identifying both severity and bother of each of the key symptoms, and has voiding and incontinence severity subscores. The ICIQ has also developed the ICIQ overactive bladder (ICIQ-OAB) tool.
2. The International Prostate Symptom Score (IPSS)⁹ is an extensively used tool for assessing LUTS in men, particularly those with benign prostatic enlargement (BPE). It comprises seven questions addressing voiding, storage, and post-micturition symptoms, along with an additional QoL question. Scores range from 0 to 35, with higher scores indicating more severe symptoms.
3. The Danish Prostate Symptom Score (DAN-PSS)¹⁰ was developed to assess LUTS with a focus on both symptom severity and bother. It differentiates between storage and voiding symptoms, providing a more detailed assessment.
4. The Overactive Bladder Symptom Score (OABSS)¹¹ is designed to assess overactive bladder syndrome (OAB), a common subtype of LUTS. It evaluates frequency, nocturia, urgency, and urgency urinary incontinence (UUI) and is instrumental for treatment planning and monitoring response to therapy.
5. The Urinary Symptom Profile (USP)¹² assesses voiding, storage, and incontinence symptoms and is applicable in both men and women for research and clinical settings.
6. The Bladder Control Self-Assessment Questionnaire (B-SAQ)¹³ is a brief screening tool designed for the self-assessment of LUTS severity and potential need for medical consultation.

The IPSS has long been the dominant PROM in male LUTS. However, symptoms affecting QoL are not fully identified by IPSS, because two key symptoms (urinary incontinence and post-micturition dribble) are not measured by IPSS.¹⁴ ICIQ-MLUTS does measure these and so is advantageous in assessment of key aspects of LUTS at baseline. ICIQ-MLUTS also discerns the differential between bother and severity, addressing the issue that bother of some lower urinary tract symptoms is disproportionately high. Severity banding scores for ICIQ-MLUTS have recently been proposed.¹⁴

Sexual function assessment is an important aspect for therapy decision-making, and symptom tools can capture this systematically. Examples include:

1. International Index of Erectile Function (IIEF) exists as a 15-item PROM (IIEF-15) and a shortened 5-item version (IIEF-5). While widely used, further research on the validity of these questionnaires in clinical research and clinical practice is needed.¹⁵
2. ICIQ-MLUTSsex is a useful adjunct to the ICIQ-MLUTS tool.
3. Male Sexual Health Questionnaire (MSHQ) assesses key areas, including erections, ejaculation, and overall sexual satisfaction, particularly in older men with LUTS.^{16,17}
4. Sexual Health Inventory for Men (SHIM) questionnaire is widely used, including in prevalence studies for erectile dysfunction and efficacy of erectile dysfunction treatment.¹⁸

Symptom scores have certain limitations. They rely on self-reporting, which is subjective and affected by individual perception and psychological factors, and there is a risk of incomplete responses.¹⁹ They lack specificity regarding underlying mechanism(s), as some symptoms are phenotypically similar, yet may reflect diverse underlying conditions, potentially including urinary tract infections (UTIs) or neurological disorders. There is also variability in different populations, requiring culturally adapted versions of symptom scores. In complex cases, such as those with neurological conditions or multifactorial LUTS, additional diagnostic tools may be required for a more comprehensive assessment.

Advancements in tools for assessing LUTS focus on improving precision and clinical relevance. Digital health technologies such as mobile applications and wearable devices are being developed to monitor LUTS symptoms in real time. The adoption of personalized medicine is increasing, enabling treatments to be customized based on symptom score trends and patient-reported outcomes. Ongoing refinement of scoring systems aims to enhance the sensitivity and specificity of these tools through rigorous research and validation studies.

Conclusion

Symptom assessment using validated scoring tools is an essential aspect of evaluating and managing LUTS, though they have some limitations. The ICIQ-MLUTS has important advantages over the longer-established IPSS.

Bladder Diaries

Bladder diaries (BDs) semi-objectively assess a patient's urinary symptoms by systematically recording voiding events and associated details. They provide insights into toileting and drinking habits, reducing reliance on patient recall and improving diagnostic accuracy. BDs are a key prospective and self-administered tool available to assess the nature and severity of LUTS.

These records can be kept in varying levels of detail:

- A micturition chart logs voiding times alone.
- A frequency-volume chart (FVC) expands on this by including voided volumes.
- Additional information such as fluid intake, pad usage, incontinence episodes, severity of leakage, and its circumstances, and other factors assessed as relevant for the individual make for a comprehensive BD.

In each type of record, bedtime and waking up times should be recorded.^{20,21}

The [2012 International Consultation on Urological Diseases on Male LUTS](#) recommended the development of a validated tool. In 2014, Bright *et al.* published the first and, to date, only validated BD as part of the ICIQ project,²² marking a significant advance in standardized urinary assessment.

Key parameters that can be derived include:

- 24-hour fluid intake
- Types and timing of beverages ingested
- Daytime and nighttime voiding frequency
- Total voided volume
- Nighttime urine production
- Volume of each void
- Maximum voided volume (functional bladder capacity)
- Bladder sensation
- Incontinence episodes
- Number of pads used

From this data, additional calculations can be made, such as:

- Mean voided volume = total voided volume ÷ number of voids
- Nocturnal polyuria index (NPI) = (nocturnal urine volume ÷ 24-hour urine volume) × 100. The NPI represents the percentage of total urine production that occurs during sleep, starting from the time the individual goes to bed and including the first void upon waking.

Completing the BD for a longer recording period helps capture daily variations, reduces sampling errors due to situational influences or individual fluctuations, and provides more clinically useful data. However, the duration should be balanced to avoid patient noncompliance.^{20,23,24} A study by Elmer *et al.* comparing 24-hour and 72-hour BDs found that 1-day diaries led to a significant increase in invasive diagnostic tests and other treatment recommendations when compared with the longer version.²⁵ Similarly, when comparing 3-day and 7-day BDs, the shorter-duration BD showed better compliance with record-keeping.²⁶ Overall, a duration of 3 days is generally employed.

Currently, no studies have determined whether BDs must be completed on consecutive days or whether including weekdays versus weekends is preferable. However, since fluid intake and output typically self-regulate within a few hours, consecutive days are likely to provide more accurate overall information. Additionally, nocturnal voided volume includes the first morning void, which could be lost if recordings are scattered across nonconsecutive days.

Several factors influence patient compliance when completing BDs, beyond just the duration of the recording. Younger individuals are more likely to either not submit a diary at all or submit one that is unusable. Lower education levels have also been associated with a higher likelihood of incomplete entries. The most common missing data point is voided volume, where patients acknowledge voiding but fail to record the amount. This may be explained by the fact that over half of the studied population reported urgency, making it difficult to measure urine volume accurately.²⁷

Unfortunately, incomplete or unusable BDs are common in both clinical and research settings. In a research setting, Ito *et al.* found that only 25% of men with LUTS fully completed a 3-day BD,¹⁹ though useful data was generally retrievable from the partly completed diaries. Other studies reported completion rates ranging from 50% to 65%.²⁸ Moreover, compliance issues are not limited to patients—physicians also face challenges in using bladder diaries effectively.²³

BDs are considered the cornerstone of nocturia evaluation.²⁹ Only through a detailed BD can clinicians accurately classify each case into global polyuria, nocturnal polyuria, reduced bladder capacity, or mixed causes.^{30,31} To ensure accuracy, the diary should clearly document waking and bedtimes, alongside a complete record of voided volumes.

BDs also play a critical role in guiding lifestyle modifications for conservative management. They help provide targeted advice, such as fluid restriction before bedtime, avoiding beverages that may worsen OAB, or implementing bladder training programs. Identifying exacerbating factors and triggers enables a personalized treatment approach. Additionally, the process of completing and analyzing a BD can enhance patient engagement, as individuals gain valuable insight into their symptoms.

Beyond diagnosis and lifestyle interventions, BDs serve as a baseline reference for tracking symptom progression and evaluating treatment outcomes in both clinical practice and research. Agreement between the ICIQ-BD and ICIQ-MLUTS questionnaires shows low correlation in daytime frequency and nocturia, such that both tools are necessary in LUTS assessment.³²

Conclusion

BDs are an essential tool in the evaluation and diagnosis of LUTS, particularly storage symptoms, and are fundamental for nocturia assessment. They provide a semi-objective, prospective measure that complements the retrospective, subjective recall of patient history.

Flow Rate Testing

Uroflowmetry is a noninvasive urodynamic test strongly recommended by the European Association of Urology (EAU) Guidelines prior to medical or invasive treatment in male LUTS, with a weak recommendation for use in the initial assessment.³³ Uroflowmetry is widely used, generally with measurement of post-voiding residual (PVR) urine. The International Continence Society (ICS) has determined standards for good urodynamic practices (ICS-GUP2016), which include recommendations about uroflowmetry.³⁴ A recent ICS educational module advised best practices in uroflowmetry testing for adult patients.³⁵

Uroflowmetry measures flow rate of the urinary stream as volume per unit time in milliliters per second (mL/s). Modern flow meters enable a continuous graphic record of the urinary flow and include data on the main parameters, such as maximum flow rate ($Q_{\max}$), voided volume (VV), flow time, average flow rate (Q_{ave}), and time to maximum flow. However, their software currently cannot distinguish physiological flow features from artifacts. Therefore, direct interpretation is still mandatory to ensure diagnostic accuracy.³⁵ The ICS GUP recommendations indicate to check that the voiding was representative, based on the patient's description and other observations (notably bladder diary).³⁴ Correction of the results is needed where the parameters given from the machine do not plausibly derive from the patient's actual flow performance, such as manual correction of the site taken as $Q_{\max}$ by the machine, if that point is a spike in the flow rate most likely resulting from an artifact (such as a “knock artifact,” where a body part contacted the flow meter or its support stand).

Low bladder volume affects detrusor muscle performance, meaning that even a largely normal lower urinary tract may appear to suffer from poor flow performance at low volume. Hence, a minimum VV of 150 mL has been subjectively specified as a threshold for meaningful interpretation of uroflowmetry results.³⁵ Accordingly, if VV was voided and flow was poor, retesting could be warranted to see whether a higher volume does achieve a better flow rate. Logically, however, it is the bladder volume that affects bladder performance, so the PVR should also be considered when deciding whether a slow flow is due to an underfilled bladder. Overfilling of the bladder can also be detrimental to performance. Hence, the average or maximum void volumes, seen on the patient's bladder diary, can be used as a guide for whether the voided volume indicates a flow study representative of their general voiding performance. If the trace is not representative, or the test was technically unreliable, or if the result indicates an abnormality (VV and/or flow rate unexpectedly low or PVR unexpectedly high), the test should be repeated.^{34,35} The uroflowmetry report should at least include the $Q_{\max}$, VV, and PVR. An elevated PVR can be a causative factor in all forms of LUTS (storage, voiding, and post-micturition). Other characteristics such as flow pattern and other parameters may be added, but should be specified.^{34,35}

If a flow/volume nomogram is used, this should be stated and referenced (e.g., Siroky Nomogram for men under 55 years and the Bristol Nomogram for men over 55 years).^{35,36} Routine use of nomograms in the decision-making process has not been specifically recommended by guidelines or international organizations. Nomograms are not diagnostic tools but may be used to compare flow rates at different volumes (e.g., after therapy).

Bladder outlet obstruction (BOO) is formally diagnosed with pressure-flow studies. The EAU guidelines strongly recommend that noninvasive tests should not be offered as an alternative to urodynamics or pressure-flow studies for diagnosing BOO. Nonetheless, several studies have investigated the value of the $Q_{\max}$ in predicting BOO during pressure-flow studies and attempted to identify the most accurate $Q_{\max}$ cutoff for this purpose. The diagnostic accuracy of uroflowmetry in predicting BOO varies considerably and is substantially influenced by the threshold values used. A threshold $Q_{\max}$ of 10 mL/s has a specificity of 70%, a positive predictive value (PPV) of 70%, and a sensitivity of 47% for BOO. In contrast, a threshold $Q_{\max}$ of 15 mL/s yields a specificity of 38%, a PPV of 67%, and a sensitivity of 82%.³⁷ If $Q_{\max}$ is > 15 mL/s, physiological compensatory processes may mask the presence of BOO, meaning that BOO cannot be excluded. A low $Q_{\max}$ can arise as a consequence of BOO, detrusor underactivity (DU) or an under- or over-filled bladder.^{38,39} Hence, uroflowmetry is limited as a diagnostic test, as it is unable to discriminate between the underlying mechanisms. Instead, it is better suited for monitoring treatment outcomes and correlating symptoms with objective findings.^{40,41}

Some studies have proposed distinguishing DU from BOO based on uroflowmetry parameters—not only $Q_{\max}$ but also flow patterns and combinations of scores.^{42,43} However, the diagnostic accuracy of the developed models remains to be established and external validation is lacking. The ICS educational module defined five patterns of the flow curve: bell-shaped, plateau, interrupted, staccato, and tower-shaped curves, which are derived from the curve.³⁵ However, distinguishing such patterns is not clear-cut—notably, tower- and bell-shaped curves. The value of this flow pattern subcategorization in predicting urodynamic findings such as BOO, DU, or detrusor overactivity (DO) has not been established.

The predictive value of $Q_{\max}$ in determining the outcome of prostate surgery has also been assessed. For example, observations from an ICS study reported a mean $Q_{\max}$ of 9.7 mL/s in men with BOO and 12.6 mL/s in men without BOO.⁴⁴ That study also revealed that among patients with BOO, 53% had a $Q_{\max}$ > 10 mL/s and 18% had a $Q_{\max}$ > 15 mL/s. An initial evaluation of the UPSTREAM trial established that a $Q_{\max}$ of up to 9.8 mL/s at baseline was a favorable uroflowmetric parameter for predicting the success of prostate surgery in treating LUTS.⁴⁵ Although that study did not establish a threshold for recommending urodynamics (UDS), further analysis identified a $Q_{\max}$ of 13 mL/s as a clear threshold above which UDS should be recommended to reduce the risk of experiencing symptom deterioration.⁶ The authors concluded that outcomes of prostate surgery can be predicted preoperatively using age, total IPSS, and uroflowmetry data, with prognostic thresholds of 16 for IPSS and 13 mL/s for $Q_{\max}$. Qualitative data from the UPSTREAM trial also suggested that UDS for men should be discussed with patients to explore individual preferences.⁴⁶

Analysis of the relationship between free uroflowmetry curve features and their urodynamic correspondence indicated that a fluctuating or intermittent curve shape (compatible with the use of Valsalva maneuver) is suggestive of DU.⁴⁷ A few pre-urodynamic nomograms using symptom scores and uroflowmetry characteristics have been developed for predicting and differentiating the presence of BOO and DU, with encouraging results, although only applicable to men with non-neurogenic LUTS and not previously submitted to surgery for LUTS.⁴⁸

Conclusion

The technique and application of uroflowmetry must be in accordance with the standardization and recommendations of the ICS. Uroflowmetry can predict but cannot diagnose BOO. Findings of uroflowmetry should be combined with other preoperative parameters such as age, PVR urine, and symptom score to reach the best prediction of prostate surgery outcome in male LUTS. A $Q_{max} \geq 13$ mL/s mandates preoperative UDS if interventional treatment is planned.

Urinalysis

Urinalysis is a noninvasive, widely available diagnostic tool relevant for the initial evaluation of LUTS. It can involve a rapid dipstick test or microbiological laboratory evaluation (microscopy and culture)—**TABLE 1**. It is particularly important in cases presenting with storage LUTS, given the potential contribution of inflammatory processes to symptoms such as increased voiding frequency. It can serve as an initial screening test for UTI by detecting leukocytes, nitrites, and bacteriuria. Additionally, it can identify hematuria, which may indicate relevant underlying mechanisms (malignancy,⁴⁹ urolithiasis, or inflammatory). Urinalysis also helps in screening for metabolic disorders, such as diabetes mellitus and kidney disease, by detecting glucosuria and proteinuria.^{50,51} Microscopic examination can identify red blood cells (RBCs), white blood cells (WBCs), bacteria, and casts.^{52,53} When abnormal findings are present, further evaluation with urine culture, cytology, or cystoscopy may be required for a definitive diagnosis.^{52,54}

TABLE 1 Urinalysis Tests

Component	Findings	Clinical relevance
Dipstick testing	Leukocytes, nitrites	Indicates urinary tract infection
Microscopy examination	RBCs, WBCs	Suggests malignancy, inflammation, or infection
Urine culture	Bacterial growth	Confirms infection and guides therapy

Abbreviations: RBCs, red blood cells; WBCs, white blood cells.

Advantages

- Noninvasive, widely available.
- Provides immediate clinical insights, guiding further testing.

Limitations

- Potential for false positives due to contaminated samples, or false negatives.
- Limited sensitivity in detecting low-grade infections.

Recommendations

- Perform urinalysis as an initial diagnostic test in all storage LUTS cases.
- Confirm abnormal findings with urine culture for precise infection diagnosis.
- Integrate urinalysis findings with clinical history and other evaluation results for accurate diagnosis.

Conclusion

Urinalysis serves as an important initial screening tool for inflammation and malignancy, determining whether further diagnostic evaluations are necessary.

Prostate-Specific Antigen

Prostate-specific antigen (PSA) is a glycoprotein enzyme produced primarily by the epithelial cells of the prostate gland. PSA is considered an organ-specific, but not disease-specific, protein. This means that many conditions affecting the prostate can lead to an elevation in serum PSA, such as prostate cancer, benign prostatic hyperplasia (BPH), urinary tract infections (especially prostatitis), urethral or rectal instrumentation, and even ejaculation. Therefore, interpretation of a PSA measurement should be undertaken in the context of the individual patient.

An important diagnostic consideration is the trajectory of PSA changes over time. A “bouncing PSA” pattern, characterized by fluctuations without a consistent upward trend, is often indicative of benign conditions, such as prostatitis or other inflammatory processes, rather than malignancy. Monitoring PSA kinetics can provide valuable insights and help differentiate between benign and malignant prostate pathology.⁵⁵

The production of PSA by benign prostatic cells follows a relatively predictable pattern. In the absence of prostate cancer, PSA levels correlate directly with prostate volume, as confirmed by multiple population-based studies.⁵⁶ This relationship allows PSA to serve as a rough surrogate marker for prostate size. However, its practical utility in clinical settings is limited, as imaging techniques, such as transrectal ultrasound (TRUS) and multiparametric magnetic resonance imaging (mpMRI), provide much greater precision in assessing prostate volume.⁵⁷

Despite the limitations of PSA in estimating prostate size, the role of PSA in clinical decision-making cannot be overlooked. When evaluating men with LUTS, an elevated PSA level may prompt further investigations to differentiate between benign and malignant causes of prostate enlargement. While BPH is the most common explanation for increased PSA levels in aging men, the possibility of coexisting prostate cancer must always be considered, particularly when PSA levels rise disproportionately to prostate volume.

Another emerging concept in prostate evaluation is the role of inflammatory processes in PSA elevations. Studies suggest that chronic inflammation within the prostate may contribute to both gland enlargement and fluctuations in PSA levels.⁵⁸ This may help explain why some men with significant LUTS exhibit PSA variability, even in the

absence of cancer. Furthermore, conditions such as acute or chronic prostatitis can cause transient PSA spikes, potentially leading to unnecessary biopsies if results are not interpreted properly in the context of the patient's overall clinical picture.⁵⁹

In addition to prostate size, several studies have demonstrated a strong correlation between PSA levels and prostate growth.⁶⁰ One such study—the Medical Therapy of Prostatic Symptoms (MTOPS) study, a longitudinal observational survey—demonstrated that prostate growth can be reliably predicted using a combination of prostate size and PSA levels.⁶¹ Another study found that serum PSA is a stronger predictor of prostate growth than prostate size alone.⁶⁰ Furthermore, baseline PSA has been shown to predict changes in symptoms and alterations in urinary flow rate after 4 years of follow-up, highlighting its utility in long-term disease monitoring.⁶² Beyond its predictive value for prostate growth, PSA levels are also associated with the risk of acute urinary retention (AUR).⁶³

While elevated PSA levels are often associated with BPH and BPO, PSA is not a disease-specific marker, which complicates its interpretation. One of its primary limitations is the lack of specificity in distinguishing between benign and malignant prostate conditions. This nonspecific elevation may lead to unnecessary anxiety, further diagnostic testing, and potential overtreatment. Moreover, PSA levels may fluctuate naturally, making a single measurement less reliable for informed clinical decision-making.

Another limitation of PSA is its variability based on prostate size and individual patient characteristics. While PSA generally correlates with prostate volume, there is significant interpatient variability. Some men with large prostates may have relatively low PSA levels, whereas others with smaller prostates may exhibit higher PSA values. This inconsistency limits the utility of PSA as a sole determinant for therapeutic decisions in LUTS management.⁶⁴ Moreover, PSA does not directly correlate with symptom severity in men with LUTS. Some individuals with elevated PSA levels may experience only mild urinary symptoms, whereas others with lower PSA values may report severe LUTS. This weak correlation between PSA and symptom burden limits its role as a standalone tool for assessing treatment response and disease progression.

The impact of 5 α -reductase inhibitors (5-ARIs) on PSA levels complicates the utility of 5-ARIs in LUTS management. These agents can reduce PSA levels by approximately 50% after 6 months of therapy, potentially masking the presence of underlying prostate cancer. Failure to adjust PSA values in patients on 5-ARI therapy can lead to delayed cancer detection and misinterpretation of disease progression. Although PSA can help stratify patients for specific treatments, such as 5-ARI therapy, it should not be the sole criterion for clinical decision-making.⁶⁵

Conclusion

PSA is a useful biomarker in the evaluation of prostate conditions, but has several limitations in the management of LUTS. Its lack of specificity, variability among individuals, and influence by medications like 5-ARIs necessitate a cautious and multifaceted approach to patient evaluation.

Prostate Size and Shape Assessment

Assessment of prostate size and morphology is proposed to aid treatment selection and outcome prediction. Dimensions can be obtained by imaging (transrectal ultrasound [TRUS], transabdominal ultrasound [TAUS], CT, MRI), and volume can be derived by calculation—for example, using an ellipsoid formula ($\text{height} \times \text{length} \times \text{width} \times \pi/6$). TRUS gives more precise dimensions than TAUS, but it is uncomfortable.⁶⁶ TAUS can provide accurate measurement, especially in patients with prostate volume less than 30 mL and with a bladder volume less than 400 mL during testing.^{67–71} MRI may offer the highest accuracy and can be a suitable choice when PSA is elevated, as it provides additional information relevant to assessing potential malignancy.^{72–74}

The basic parameter of prostate size alone does not correlate reliably with LUTS severity,^{75,76} though it may predict development of LUTS in the longer term.⁷⁷ Imaging features based on prostate zonal anatomy may be more discriminatory for LUTS. The transitional zone (TZ) is the major site for hyperplasia, associated with a compressed peripheral zone (PZ).⁷⁸ Several studies suggest that the TZ volume or TZ index (the ratio of TZ volume to total prostate volume) is more strongly correlated with LUTS and $Q_{\max}$ than total prostate volume, and could be useful in preliminary screening for BOO.^{79–83} Thinner PZ thickness measured by TRUS is significantly associated with various symptom measures, though with borderline correlation with reduced $Q_{\max}$ ($P = .055$).⁸⁴

Further morphologic parameters of the prostate have also been investigated:

1. Presumed circle area ratio (PCAR)

PCAR is based on the premise that prostate enlargement stretches the capsule to approach a circular shape. As PCAR approaches 1, it indicates a more circular shape (measured by TRUS in a horizontal section). A PCAR > 0.9 has been associated with elevated symptom scores and voiding subscores in multivariable logistic regression analysis.⁸⁵ Urodynamic studies have demonstrated that PCAR correlates better with BOO compared with TZ index, with a sensitivity and specificity of 77% and 75%, respectively, for PCAR > 0.8.^{86,87}

2. Resistive index

Prostatic glandular proliferation and increased intraprostatic pressure may compress the blood vessels within the prostate, thereby raising vascular resistance.⁸⁸ An elevated resistive index of the capsular arteries has been associated with symptoms, reduced $Q_{\max}$, and higher probability of BOO.^{89–91} It also predicts the risk of developing acute urinary retention and clinical response after minimally invasive procedures of the prostate.^{88,92}

3. Intravesical prostatic protrusion (IPP)

IPP is measured from the tip of the protruding prostate to the bladder neck in the midsagittal plane on TAUS, with bladder volume at 150 mL to 250 mL.^{93–96} It can be graded based on protrusion length (grade I, < 5 mm; grade II, 5–10 mm; grade III, > 10 mm), with higher grades potentially signifying worse $Q_{\max}$ and more severe

BOO.^{93,94,97} A systematic review of 11 studies with 1478 patients suggested that IPP > 10 mm predicts BOO.⁹⁸ Additional analysis suggested that the same cutoff also predicts failure of trial without catheter after acute urinary retention.⁹⁸ Patients with higher IPP grades also had lower $Q_{\max}$, more pronounced detrusor overactivity (DO), reduced bladder compliance, elevated PVR volume, and poorer response to medical treatment.^{95,99}

4. Prostatic urethral angle (PUA)

A fluid dynamic rationale suggests that increased angulation of the prostatic urethra leads to energy loss during voiding—similar to the resistance encountered when bending a hose—which contributes to BOO.^{100,101} PUA can be measured on the midsagittal plane during TRUS. It has been associated with reduced $Q_{\max}$, increased maximal urethral closure pressure, higher detrusor pressure at maximum flow rate, and raised BOO index.^{100,102}

In terms of treatment selection, medical therapy with 5-ARIs is not indicated for patients with prostate volume below a threshold of 40 mL. The selection of type of interventional therapy also involves size and configuration assessment.¹⁰³ Some of the recommendations in this context have emerged from consensus and expert opinion, with limited robust data relating to the technical feasibility of procedures or therapy outcomes in other situations.

Conclusion

Assessment of prostate size and morphology by various imaging modalities is proposed to aid treatment selection in terms of medical therapy or choice of minimally invasive surgical therapy; this may contribute to outcome prediction, but more data is needed.

Cystoscopy

Cystoscopy provides direct visualization of the urethra, bladder, and bladder neck, facilitating diagnosis of structural abnormalities such as strictures, tumors, inflammation, and bladder stones that may not be detected through noninvasive methods like urinalysis or imaging. In cases of persistent hematuria, cystoscopy allows targeted biopsy and cytology sampling to enhance diagnostic accuracy. Additionally, it enables immediate interventions, such as urethral stricture dilation or tumor resection, optimizing procedural efficiency.¹⁰⁴

Cystoscopy for LUTS is indicated in the following clinical scenarios:

1. Unexplained hematuria—persistent hematuria requires cystoscopic evaluation to exclude malignancy, particularly in high-risk populations such as smokers or individuals with occupational exposure to carcinogens.^{105–107}
2. Past history of bladder cancer or urological trauma—to exclude recurrence or strictures.
3. Presurgical planning—cystoscopy may be performed prior to surgical procedures, potentially guiding procedure selection.

Flexible cystoscopy is preferred for diagnostic purposes, due to lower patient discomfort and reduced risk of complications compared with rigid cystoscopy.¹⁰⁸ It is typically performed under local anesthesia in an outpatient setting. It potentially allows for additional aspects if indicated, such as urethral stricture dilation or biopsy when suspicious lesions are identified. Routine antibiotic prophylaxis is not required for diagnostic cystoscopy in low-risk patients; however, consideration of prophylaxis is recommended in cases with a high risk of UTI (recurrent infections or immunosuppression¹⁰⁹). Cystoscopy is invasive and may cause discomfort or pain. Potential complications include UTI and urethral trauma. Conventional water cystoscopy may have reduced visibility in cases of active bleeding, leading to potential diagnostic limitations.

Advanced imaging technologies, such as photodynamic diagnosis and narrow band imaging, have been introduced with a view to enhancing sensitivity to detect visually subtle or early lesions.¹¹⁰ Innovations such as confocal laser endomicroscopy and optical coherence tomography are being explored to improve real-time bladder assessment.^{111,112} However, further studies are required to validate their clinical utility in LUTS management.

Conclusion

Cystoscopy provides direct visualization of bladder and urethral pathologies where indicated (hematuria, history of bladder cancer, surgical planning), and allows for real-time assessment and biopsy of suspicious lesions.

Urodynamics

Urodynamics is an overarching term describing various evaluations of lower urinary tract function. For the purposes of this section, UDS refers to filling cystometry and pressure-flow studies (PFS). These evaluations can identify DO during the filling phase, and BOO and/or DU during voiding. Urodynamic stress incontinence could also be identified, but this is a rare symptom in an otherwise healthy man, and is not considered in this section. Neither physical examination nor uroflowmetry with PVR can confidently distinguish between BOO and DU.¹¹³ PFS measure detrusor pressure and urinary flow during voiding. A high detrusor pressure with low urinary flow suggests BOO, whereas a low-pressure, low-flow pattern is indicative of DU. The BOO Index (BOOI) is derived from the equation:

$$\text{BOOI} = P_{\text{det}} Q_{\text{max}} - 2Q_{\text{max}}$$

in which $P_{\text{det}} Q_{\text{max}}$ is the detrusor pressure observed at the time of Q_{max} . Based on this calculation, men can be categorized as having BOO if their BOOI is > 40 .

The Bladder Contractility Index (BCI) is an evaluation of the detrusor function during voiding phase, represented

by the following formula:

$$BCI = P_{\text{det}} Q_{\text{max}} + 5Q_{\text{max}}$$

Normal contractility is denoted by $BCI > 100$.

The quality of the data is vital, in that inaccurate pressures and flow data can lead to misinterpretation of results and wrong diagnosis. This can have clear-cut implications for the risk of undertaking irreversible interventions inappropriately (such as performing surgery to relieve BOO in somebody wrongly diagnosed with the condition). A recent study examined the quality of UDS-derived data and interpretation from 25 large centers, reporting important errors in standardization, testing, and interpretation.¹¹⁴ Some units fail to calibrate their equipment regularly and perform maintenance checks according to manufacturer requirements. The need for quality assurance in UDS was the stimulus for the recently published UK Continence Society certification program, which supports governance-led practice.¹¹⁵ Key professional organizations have published a series of guidelines and support materials for healthcare professionals performing UDS, which have been updated.^{116,117}

Many men with LUTS experience bothersome storage symptoms, including urgency, frequency, and nocturia. OAB can be ascribed based purely on symptoms.¹¹⁸ However, empirical therapy based on symptoms alone often fails to achieve adequate symptom improvement. Consequently, filling cystometry may be undertaken, leading to identification of DO in some, based on the presence of contractions that may be spontaneous or provoked. Detecting DO is often considered important in patients with persistent urgency symptoms, as it prompts the use of specific therapy. Furthermore, UDS can differentiate DO from other causes of urgency, such as impaired bladder compliance due to chronic BOO or neurological disorders. However, confirmation that therapy selection based on a urodynamic diagnosis achieves better outcome is lacking, with only low-quality indicative studies. Indeed, in women with OAB, UDS has not been shown to improve outcomes overall when compared with a standard comprehensive clinical assessment.¹¹⁹

DO may manifest in different forms during UDS. The most common finding in non-neurogenic LUT dysfunction is a characteristic elevation of detrusor pressure during filling cystometry, which may or may not lead to urinary incontinence, depending on the efficiency of sphincteric mechanisms. This is usually referred to as a phasic contraction. A terminal contraction occurs at the end of a filling cystometry, when the bladder reaches capacity, and a contraction of the detrusor is initiated and persists until the bladder is emptied. A third form of DO is manifested by detrusor after-contractions (or post-terminal contractions), which consist of elevations in detrusor pressure after voiding.¹²⁰ Also relevant in the study of DO are the maximum detrusor pressure originated by involuntary contractions, the bladder volume at first contraction, and the total time of contractions. These parameters may provide an indication of the severity of DO, although their clinical correlation remains uncertain.

Bladder compliance refers to the ability of the bladder to accommodate increasing volumes of urine at low intravesical pressures during the storage phase. It is calculated as the change in bladder volume divided by the change in detrusor pressure ($\Delta V/\Delta P_{det}$) and is expressed in mL/cmH₂O. Normal bladder compliance is an important aspect of urine storage, reducing risk of upper urinary tract damage and maintaining continence.¹²¹

A reduction in bladder compliance indicates structural changes in the bladder, including increased wall stiffness. In men with LUTS, poor compliance signifies increased detrusor pressure at low bladder volumes, which can ultimately compromise the upper urinary tract through vesicoureteral reflux or ureteral obstruction. This may be associated with chronic urinary retention. Notably, men with impaired compliance may not respond well to standard pharmacological therapies like α -blockers. This may lead to recommendations for more invasive therapies, yet a definite association between bladder compliance and surgical outcomes has not been established.²⁴

A key use of UDS is in the preoperative assessment of men considering surgical interventions to relieve BOO. Implicitly, procedures for BOO, such as TURP, adenectomy, or minimally invasive therapies, have a greater chance of improving symptoms if BOO is actually present. An otherwise healthy man with voiding LUTS and prostatic enlargement is likely to have BOO, meaning that proceeding to surgery without urodynamic confirmation of obstruction has a good prospect of improving voiding symptoms. However, the characteristics of voiding symptoms resulting from DU are largely indistinguishable from those due to BOO. Hence, selecting patients for UDS becomes a legitimate consideration where patients have clinical risk factors for DU, such as advanced age, comorbidities (notably chronic diabetes mellitus), or a history of chronic urinary retention. Logically, this facilitates making recommendations tailored to the individual patient, helping to set realistic expectations regarding surgical outcomes.¹²²

In the Urodynamics for Prostate Surgery Trial: Randomised Evaluation of Assessment Methods (UPSTREAM) study, detailed analysis of baseline assessments was used to identify men who had a good symptom outcome from surgery, and those who failed to improve or experienced symptomatic deterioration (an important minority).^{6,45} This was used to generate an algorithm to help identify men with a high chance of symptom improvement, based on nonurodynamic parameters (medical history, symptom score, and flow rate). Specifically, these were the men with relatively severe LUTS overall (ICIQ-MLUTS > 18 or IPSS > 16), significant voiding LUTS (ICIQ-MLUTS voiding subscore > 8), QoL severely affected by LUTS (IPSS QoL score > 4), slow maximum flow rate ($Q_{max} < 10$ mL/s), and low severity of comorbidities. If any of these parameters did not apply, the chance of a good symptomatic outcome was lower. For those individuals, UDS was able to provide information predictive of outcome. Specifically, if BOOI was ≥ 48 and BCI ≥ 123 , a man could anticipate a good symptomatic outcome despite having suboptimal features in other noninvasive baseline parameters.⁶ Overall, UDS was considered necessary for those individuals for whom voiding LUTS are not affecting QoL, Q_{max} is ≥ 13 mL/s, if symptoms are present that have poor response rate to surgical treatment (nocturia, incontinence, post-micturition dribble) or if there is extensive comorbidity.⁶ Furthermore, the presence of DO reduced the improvement obtained with surgery, independently of obstruction and contractility. In the absence of DO, BOOI and BCI were better predictors of outcome, with higher obstruction and preserved contractility resulting in more successful surgery—these are, in theory, the best candidates for BOO surgery.

In general, UDS is not undertaken prior to recommending pharmacological therapy for LUTS in men. Implicitly, patients with significant BOO would be more likely to benefit from α -blockers and 5-ARIs, whereas those with DU may experience limited improvement.¹²³ However, the comparatively rapid response to medication and the ability to stop drugs if they are not providing benefit make the clinical and cost justification for diagnosing BOO with an invasive test less supportive. Likewise, filling cystometry can confirm the presence of DO, yet whether this translates into worthwhile approaches to prescribing anticholinergics and β 3-agonists is currently doubtful. PVR assessment prior to botulinum toxin injections may indicate risk of voiding difficulty, yet such information can be derived by noninvasive bladder scanning.¹²⁴

In general, men are willing to tolerate the short-term discomfort of UDS when they stand to benefit over the longer term from improved decision-making about their care.⁴⁶ Nonetheless, some patients, especially younger individuals, report physical and emotional discomfort, particularly during urethral catheterization.¹²⁵ When this is the case, urodynamic parameters may be impaired by the embarrassment and pain felt by the person undergoing the test, leading to the potential for misinterpretation and misdiagnosis. The presence of the urethral catheter can sometimes affect flow rate performance.¹²⁶ Furthermore, recent studies have demonstrated a failure to reproduce symptoms in a considerable proportion (up to 46%) of patients undergoing UDS.¹²⁷

Videourodynamics

Videourodynamics (VUDS) integrates standard UDS with fluoroscopic imaging, which allows for simultaneous visualization of the bladder, bladder neck, and urethra during filling and voiding phase, additionally permitting detection of vesicoureteral reflux (VUR). This is at the cost of radiation exposure for the patient, and greater investment on the part of healthcare services. In general, use of VUDS is typically restricted to patients with a more complex functional background, such as previous urinary tract surgery, suspected VUR, or a neurogenic cause for LUTS.¹²⁸ As a result, its application is in complex or refractory cases where standard UDS does not provide sufficient diagnostic clarity.¹²⁹ There is limited research evidence relating to outcomes.

Ambulatory Urodynamics

Ambulatory urodynamic studies involve continuous bladder pressure monitoring over an extended period, usually between 2 and 24 hours, allowing for the assessment of lower urinary tract function during normal daily activities. Unlike conventional UDS, which is conducted in a controlled setting with patients sitting or lying down, ambulatory UDS enables dynamic assessment during routine activities in a more natural environment. It uses conventional UDS catheters connected to a small portable recording device that records vesical and abdominal pressure data over time. Voiding information is captured with a remotely linked flowmeter, allowing incorporation of pressure and flow data. Electronic buttons permit the patient to indicate the timing of events such as urgency or urinary incontinence.¹³⁰ This test is somewhat more physiological, as bladder filling occurs

via the patient's own urine output rather than through an extrinsic pump. However, the test is more complex, resource intensive, and somewhat prone to artifacts and catheter displacement.¹³¹ The technology has not been widely adopted in urology departments worldwide, and there is no large-scale research evidence.

Conclusion

Selective use of urodynamics for men considering surgery to relieve BOO is indicated in those individuals with an increased risk of detrusor underactivity (older age, comorbidities) or a lower chance of outlet obstruction (flow rate faster than 13 mL/s or low severity of voiding symptoms).

Frail Older Men

All LUTS rise in prevalence in association with increasing age,¹³² and older people with frailty have a notably high prevalence of urinary incontinence.¹³³ Age-related changes to the bladder, brain, and prostate are associated with the development of LUTS in older men.¹³⁴ OAB, in particular, is strongly associated with frailty,¹³⁵ most likely due to age-related changes in the brain leading to failure of suppression of urgency.¹³⁶

Frailty is the age-related, multidimensional state of increased vulnerability to external stressors,¹³⁷ and represents the culmination of numerous changes that occur with aging, including muscle loss (sarcopenia), cognitive decline, decreased functional reserve, increased comorbidity, and polypharmacy. While frailty is associated with comorbidity, the presence of comorbidity is not synonymous with frailty, and it is possible for an individual to have numerous comorbidities without being frail, and for an individual with frailty to have few or no other medical conditions.

It is well recognized that the risks of interventions to treat LUTS are also higher in those with frailty. As such, assessing the presence or absence of frailty in older adults is crucial to allow appropriate, frailty-informed care to be delivered—to avoid harms from both under- and over-intervening. Following surgical intervention, those with preexisting frailty are more likely to experience complications, major complications, and mortality. Older people with frailty are also more likely to experience side effects of medications,¹³⁸ and there are increasing concerns around the use of anticholinergics, including those for OAB, in older adults and those with frailty.¹³⁹

There are two main conceptual models of frailty described in the medical literature. In the Fried phenotypic model,¹⁴⁰ frailty is defined by the presence of at least three of unintentional weight loss, slow gait speed, reduced grip strength, exhaustion, and reduced physical activity. In Rockwood's accumulation of deficits model, frailty is quantified as a Frailty Index, defined as the number of deficits identified during a Comprehensive Geriatric Assessment, divided by the number of deficits looked for. The Fried and Rockwood models of frailty are both useful in the research setting but are limited in clinical practice. This is especially true in practices without experience in frailty, as the models require lengthy, often specialist assessment, and equipment, such as a dynamometer, that are not usually available in the urology clinic.

To effectively operationalize the assessment of frailty, several assessment tools have been developed to allow it to be identified and quantified in the general setting. The Clinical Frailty Scale (CFS)¹⁴¹ assigns a value between 1 (very fit) and 8 (living with severe frailty), based upon a routine assessment of function and required assistance (**FIGURE 1**). The CFS does not require any specific equipment and can be accurately used by healthcare staff without special training in geriatrics.¹⁴² The CFS correlates well with adverse outcomes from cardiac¹⁴³ and urologic¹⁴⁴ surgery.

The Edmonton Frail Scale (EFS; <https://edmontonfrailscale.org/>) assesses 9 domains, with a total possible score of 17.¹⁴⁵ Those scoring over 5 are defined as vulnerable, with scores of 8 to 9, 10 to 11, and 12 or higher representing mild, moderate, and severe frailty, respectively. The EFS includes a measure of gait speed and, therefore, requires a stopwatch. However, no specialist equipment is needed, and it can be completed in around 5 minutes following only brief training. The EFS also includes an assessment of incontinence.

Older men with frailty will commonly experience challenges with mobility, sensation, and cognition. As such, factors outside the lower urinary tract—such as slow gait speed, visual impairment, and cognitive impairment—may have an impact on their continence. For example, a man with dementia may struggle to identify and plan his route to toileting facilities, or visual impairment may make it difficult to distinguish the bathroom from other doors. An assessment of this in the clinic can be easily performed by watching the patient go from the consulting room to the toilet.¹³³ An assessment by an occupational therapist may also be of benefit to evaluate the need for walking aids, grab bars, or improved lighting.

Frailty is strongly associated with disability, polypharmacy, and comorbidity—older men living with frailty often face multiple competing demands on their health, and frailty is associated with increased healthcare service use.¹⁴⁶ When managing LUTS in frail men, it is essential to consider the individual's priorities about their health and weigh the burden of their LUTS against the potential burden of any proposed treatment.¹⁴⁷ While there are risks associated with urinary urgency and incontinence in older people, including falls and fractures,¹⁴⁸ there are also harms associated with pharmacological and surgical management of LUTS, and, as such, these competing risks should be balanced against each other in conjunction with the patient, their partners, and their support network to provide care that acknowledges the complex challenges associated with frailty.¹⁴⁹ This approach allows urologists to avoid the harms of agism, therapeutic nihilism, and undertreatment of distressing and harmful symptoms, as well as the unacceptable risks from overly aggressive treatment.

Conclusion

Frailty is the age-related state of increased vulnerability to stressors. Frailty is strongly associated with LUTS. Older adults with frailty are at greater risk of both under- and over-treatment of urological disease. Frailty may be assessed in the clinic by nonexperts using validated tools.

FIGURE 1 Clinical Frailty Scale

 1 Very Fit—People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.	 7 Severely Frail—Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~6 months).
 2 Well—People who have no active disease symptoms but are less fit than category I. Often, they exercise or are very active occasionally, e.g., seasonally.	 8 Very Severely Frail—Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.
 3 Managing Well—People whose medical problems are well controlled, but are not regularly active beyond routine walking.	 9 Terminally Ill—Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.
 4 Vulnerable—While not dependent on others for daily help, often symptoms limit activities. A common complaint is being “slowed up,” and or being tired during the day.	Scoring frailty in people with dementia The degree of frailty corresponds to the degree of dementia. Common symptoms in mild dementia include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal. In moderate dementia, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting. In severe dementia, they cannot do personal care without help. *1. Canadian Study on Health & Aging, Revised 2008. 2. K Rockwood <i>et al.</i> A global measure of frailty in elderly people. <i>CMAJ</i>. 2005;73:489–495. © 2007–2009. Version 1.2 All rights reserved. Geriatric Medicine Research, Dalhousie University, Halifax, Canada. Permission granted to copy for research and educational purposes only.  DALHOUSIE UNIVERSITY <i>Inspiring Minds</i>
 5 Mildly Frail—These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.	
 6 Moderately Frail—People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.	

Suspected Neurological Mechanism

The diagnostic approach for men with diagnosed or suspected neurological disease and neurogenic lower urinary tract dysfunction (NLUTD) is comparable to that for non-neurological individuals. Depending on the underlying disease, patients with known neurological conditions frequently require evaluation to rule out or prove NLUTD, both when symptoms are already present and as a standard diagnostic approach in specific cases. Comorbidities such as BPE can also cause LUTS in men with neurological diseases.

Sometimes men may present with LUTS as an initial feature prior to the recognition of the underlying disorder. These conditions often involve pathophysiological mechanisms such as demyelination, neurodegeneration, or congenital abnormalities.¹⁵⁰ In some cases, LUTS may precede neurological symptoms (e.g., urgency in Lewy body dementia), coincide with neurological disease onset (e.g., multiple system atrophy), or emerge later in disease progression (e.g., unawareness of incontinence in Alzheimer's disease).¹⁵¹ Hence, LUTS may serve as an early clinical manifestation, with the LUTS presentation potentially preceding identification of the presence of a neurological disease.¹⁵⁰ As a result, cases may arise in which urology referral has been made while the underlying neurological pathology remains undiagnosed. Failure to recognize an undiagnosed neurological etiology presents two significant risks: the potential progression of the neurological disorder (which may be preventable with prompt diagnosis), and suboptimal LUTS management outcomes. The latter may stem from inappropriate surgical interventions or exacerbation of symptoms. Therefore, an accurate neurological assessment and targeted management of the underlying condition are essential to optimize patient outcomes.¹⁵⁰

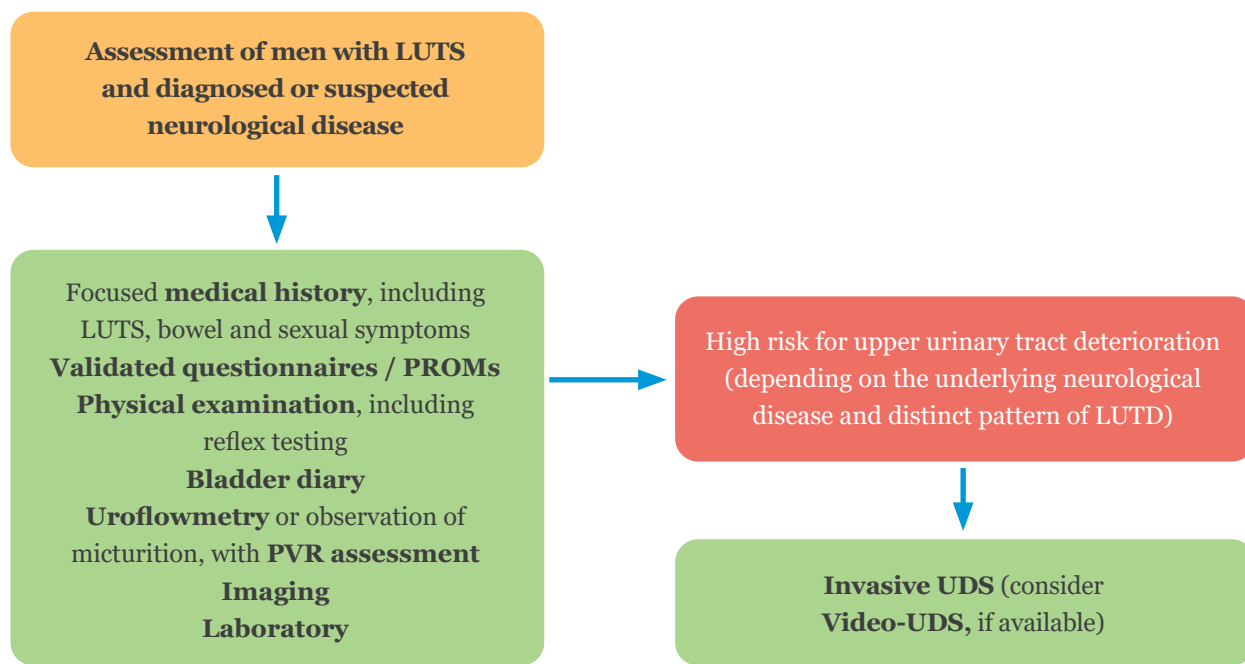
A thorough evaluation of patients with suspected or diagnosed neurological disease is essential for appropriate management (**FIGURE 2**). This assessment includes detailed patient history, physical examination, laboratory investigations, and specific diagnostic tests. The objective is to identify symptoms, determine their impact on QoL, and detect potential risk factors for upper urinary tract (UUT) deterioration.¹⁵² In neurological patients, altered sensory nerve function means that some sensations and symptoms may be atypical and unreliable. Patients should be asked about their sensation of bladder fullness and the presence of an urge to void. Altered sensory nerve function can affect UTI features, in which dysuria may not be reported, so the presence of infection may have been overlooked. UTI in overt neurological disease can instead lead to nonspecific symptoms, such as increased spasticity or autonomic dysreflexia.¹⁵³ Distinguishing between these sensations may offer diagnostic insights, particularly in cases where neurological damage affects bladder afferents.

Bowel history should always be included in the assessment.¹⁵⁴ Sexual dysfunction is prevalent in patients with neurological conditions. A structured history should cover orgasmic function, and erectile and ejaculatory dysfunction in men.¹⁵⁵ Review of ongoing medications is necessary. For instance, cholinesterase inhibitors, commonly prescribed for cognitive disorders, may exacerbate urgency symptoms and interact with antimuscarinic agents used for overactive bladder treatment.¹⁵¹

A general assessment of the patient's physical and cognitive status is crucial in determining further investigations and therapeutic options. Factors such as severe mobility impairment, spasticity, psychiatric disorders, or general weakness should be considered.¹⁵⁶ A dedicated neurourological examination should include:

- Sensory evaluation in sacral dermatomes.
- Digital rectal examination to assess anal sphincter tone, perianal sensation, along with prostate examination.
- Reflex testing, including the bulbocavernosus reflex.

FIGURE 2 Flowchart of assessment of men with diagnosed or suspected neurological disease.



Abbreviations: LUTD, lower urinary tract dysfunction; LUTS, lower urinary tract symptoms; PROMs, patient-reported outcome measures; PVR, post-void residual urine volume; UDS, urodynamics; Video-UDS, videourodynamics.

A bladder diary recorded over at least 2 to 3 days provides valuable insight into micturition patterns, including frequency and voided volumes.^{157,158} The choice of additional tests depends on the type of NLUTD, underlying neurological disease, associated risk factors, and planned interventions. UDS remains the gold standard for evaluating LUT function. VUDS is standard of care in neurological disease, by providing additional morphological insights into bladder and outlet function, and identifying risk factors that may affect upper urinary tract function over time.

Conclusion

A structured and multidisciplinary approach to the assessment of NLUTD is critical. Comprehensive history-taking, targeted physical examination, laboratory screening, and advanced diagnostic modalities allow for early identification of risk factors and personalized management strategies. As NLUTD is a progressive condition, initial assessment and ongoing surveillance need to consider prevention of irreversible complications and preservation of urinary tract and renal function.

Experimental Methods

Electronic bladder diaries

Electronic bladder diaries have been developed to improve the collection, storage, and analysis of patient fluid intake, voiding activity, and LUTS. One study found that electronic diaries may improve reliability and accuracy.¹⁵⁹ Other studies found that 83% to 88% of participants would choose an electronic diary over a paper diary,^{160,161} with a good correlation between electronic and paper data.¹⁶¹

Urodynamic pressure measurement

The penile cuff test is a noninvasive method for diagnosing BOO in men,^{162–164} which may provide less discomfort and procedure time than an invasive pressure-flow study.¹⁶⁵ A systematic review reported median sensitivity and specificity values for diagnosing BOO of 0.89 and 0.70, respectively, based on 7 studies with 546 patients.¹⁶⁶ A more recent meta-analysis of 17 studies reported sensitivity and specificity values of 0.85 and 0.78, respectively,¹⁶⁷ and another meta-analysis of 10 studies with 806 patients reported sensitivity and specificity values of 0.87 and 0.78, respectively.¹⁶⁸ This method is becoming established within standard clinical pathways in some centers.

A condom catheter method for noninvasive pressure measurement has also been developed.^{169–172} Maximum pressures measured using this technique are relatively reproducible.^{170,171} This technique correctly identified BOO in 75% of participants in one study,¹⁶⁹ but did not outperform free uroflowmetry in a subsequent study.¹⁷³ The approach requires a sufficiently high flow rate¹⁷² and may be affected by abdominal straining.¹⁶⁹ There were no recent studies using the condom catheter method identified in the literature, and this technique is not part of current clinical practice.

Wireless bladder pressure sensors and wearable devices are being developed to continuously monitor bladder activity without the restrictions of conventional UDS.¹³¹ Efforts to develop a catheter-free wireless bladder pressure sensor for ambulatory UDS are ongoing.¹⁷⁴ In a pilot study, pressures measured using the catheter-free sensor correlated well with simultaneous urodynamic pressure measurements.¹⁷⁵

Implantable bladder sensors are small, biocompatible devices that can be placed inside the bladder to continuously measure intravesical pressure and transmit data wirelessly. This allows for long-term monitoring of bladder function, particularly in patients with refractory LUTS or NLUTD.¹⁷⁶ A study in animals describes the development of a wireless pressure monitor, implanted in the bladder submucosa, connected to a neuromodulation generator that could provide real-time data on bladder function and optimize neuromodulation impulses. These developments are still in animal tests, and further studies are necessary before their use in patients.¹⁷⁷

Alongside pressure recording, wearable electromyography (EMG) devices can provide supplementary information. External sensors can assess pelvic floor muscle activity, which might give information about

pathophysiological mechanism, or presence of reflexes to oppose overactive detrusor contractions. However, EMG interpretation and clinical correlation may be difficult.¹⁷⁸

Near-infrared spectroscopy

Near-infrared spectroscopy (NIRS) is a noninvasive imaging technique that has been used to quantify bladder hemodynamics for male LUTS.^{179–182} This is a noninvasive optical technique using infrared light to detect oxygenation status of various organs. This technology has the potential to noninvasively assess urodynamic information, such as intravesical pressure, by measuring infrared penetration into the bladder wall. The information obtained from NIRS can be used to calculate relative concentrations of tissue components, such as total, oxygenated, and deoxygenated hemoglobin. A systematic review reported median sensitivity and specificity values for diagnosing BOO of 0.86 and 0.88, respectively, based on 5 studies with 282 patients.¹⁶⁶

Other studies have focused on using NIRS to detect DO, with mixed results.^{183,184} Additional studies with more advanced NIRS technology, artifact removal, and refined metrics are needed to determine whether NIRS can be a suitable approach to identifying the presence of DO.¹⁸⁵

Imaging methods

Bladder sonomorphological parameters have been used to gauge structural features, such as detrusor wall thickness (DWT) and ultrasound-estimated bladder weight (UEBW). These parameters suggest that functional changes, such as BOO or DO, causes secondary structural changes. Hence, noninvasive sonography could be used to derive urodynamic information. Analysis of 10 studies with 1204 participants reported a sensitivity of 0.68 (95% CI, 0.56–0.78) and a specificity of 0.91 (95% CI, 0.82–0.96) for BOO diagnosis by DWT.¹⁸⁶ Diagnostic accuracy of UEBW for BOO gave a sensitivity of 0.88 (95% CI, 0.78–0.93) and a specificity of 0.81 (95% CI, 0.67–0.90), derived from 6 studies including 643 patients.¹⁸⁶

Recent studies have evaluated bladder shape parameters derived from ultrasound images as diagnostic tools for overactive bladder. One study identified increased bladder sphericity as being associated with DO in women.¹⁸⁷ Another study found that bladder shape irregularities were associated with overactive bladder in women.¹⁸⁸ These techniques have yet to be studied in men.

Artificial intelligence

Artificial intelligence (AI) has potential utility in the interpretation of UDS. This task remains complex and time-consuming, requiring expertise to analyze pressure-flow relationships, detrusor activity, and voiding efficiency. AI offers promising solutions to enhance accuracy, reduce variability, and improve clinical decision-making in UDS.¹⁸⁹ Machine learning and AI algorithms are being applied to improve data analysis for the diagnosis of BOO and DU in men, including the analysis of urodynamic data,¹⁹⁰ uroflowmetry data,¹⁹¹ or combinations of noninvasive¹⁹² and/or invasive parameters.¹⁹³

AI-based models can assist in:

- Automated pattern recognition: AI algorithms can identify characteristic pressure-flow patterns associated with BOO, DO, DU, and neurogenic bladder dysfunction (with detrusor-sphincter dyssynergia, for instance).⁵³
- Reduction of subjective interpretation bias: Machine learning models can standardize UDS interpretation, improving diagnostic consistency across different clinicians and institutions.
- Prediction of treatment outcomes: AI can analyze large datasets to predict which patients are more likely to benefit from interventions such as α -blockers, 5-ARIs, or surgical therapies.¹⁸⁹

However, and despite its potential, AI in UDS faces challenges, including data standardization, as UDS datasets must be harmonized across different centers to improve algorithm training and generalizability. Moreover, AI tools should seamlessly integrate with existing electronic health record systems to facilitate real-time decision support. Finally, clinicians must understand how AI reaches conclusions to ensure transparency and clinical trust, otherwise the implementation of these technologies in clinical practice may face skeptical resistance.

Experimental uroflowmetry

At-home uroflowmetry devices have been developed for patient assessment and monitoring, and have demonstrated utility in the assessment of uroflow variability¹⁹⁴ and the identification of patients with abnormal voiding curves in the clinic but normal curves at home.¹⁹⁵ The availability of daily uroflow data may enable the development of AI-based algorithms for optimizing treatments.

Systems have been developed that use AI algorithms to measure and analyze the sound of voiding to estimate flow rate, eliminating the need for standard uroflow equipment.^{196–198} One system demonstrated sensitivity and specificity values of 0.87 and 0.78, respectively, for the identification of abnormal flows.¹⁹⁷ Another study used the sound of voiding to distinguish patients with normal flow from those with other forms of lower urinary tract dysfunction.¹⁹⁶

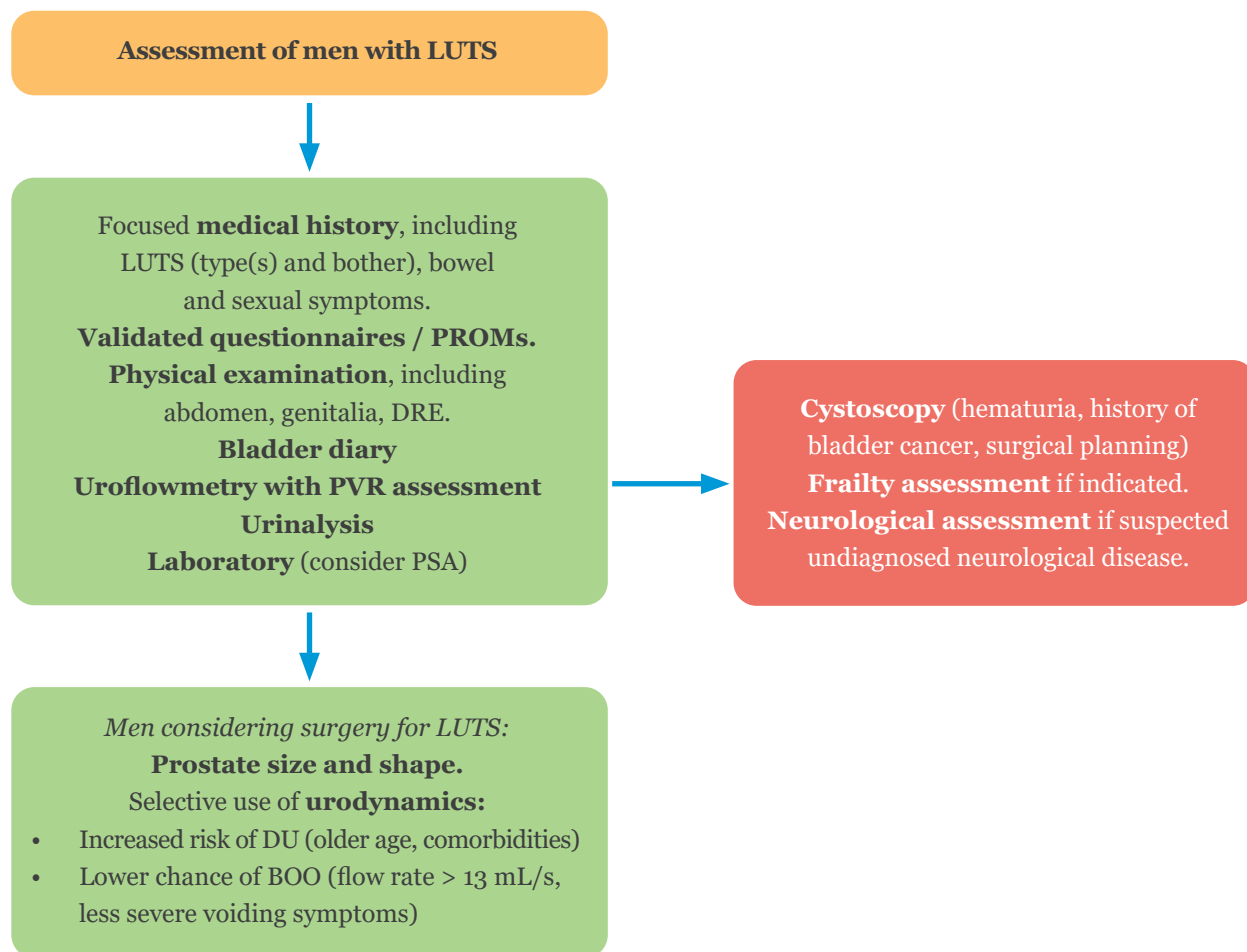
Conclusion

Electronic bladder diaries are widely used but not standardized. Systematic reviews have identified detrusor wall thickness, NIRS, and the penile cuff test as the non-invasive assessment methods most comparable to standard UDS for measuring bladder pressure, with the penile cuff test being the closest to clinical adoption. AI is likely to influence diagnostic practice in the foreseeable future through automated pattern recognition, reduction of interpretation bias, and prediction of treatment outcomes.

Summary of Recommendations

The overall assessment of male LUTS is summarized in **FIGURE 3** and in the boxed **table** below.

FIGURE 3 Summary of recommendations for assessment of Male LUTS



Abbreviations: BOO, bladder outlet obstruction; DU, detrusor underactivity; PROMs, patient-reported outcome measures; PSA, prostate-specific antigen; PVR, post-void residual.

Recommendation	LoE	GoR
The medical history in men with LUTS covers type(s) of symptoms and their separate impact, lifestyle, potential causes, and medications. Examination is needed for bladder distension, conditions affecting the external genitalia, neurological assessment, and prostate cancer.	IV	B
Symptom assessment using validated scoring tools is an essential aspect of evaluating and managing LUTS.	III	B
Bladder diaries are an essential tool in the evaluation and diagnosis of LUTS, particularly storage symptoms, and are fundamental for nocturia assessment.	III	B
Uroflowmetry can predict but cannot diagnose BOO. Raised PVR can be causative for all forms of LUTS. Uroflowmetry must be assessed in accordance with the standardization and recommendations of the International Continence Society.	II	B
Urinalysis serves as an important initial screening tool for inflammation and malignancy, determining whether further diagnostic evaluations are necessary.	III	C
PSA is a useful biomarker in the evaluation of prostate conditions, but has several limitations in the management of LUTS. Its lack of specificity, variability among individuals, and influence by prior medications necessitate caution for LUTS evaluation.	I	A
Assessment of prostate size and morphology by various imaging modalities is proposed to aid treatment selection in terms of medical therapy or choice of minimally invasive surgical therapy.	III	B
Cystoscopy provides direct visualization of bladder and urethral pathologies where indicated (hematuria, history of bladder cancer, surgical planning)	III	C
Selective use of urodynamics for men considering surgery to relieve BOO is indicated in those individuals with an increased risk of detrusor underactivity (older age, comorbidities) or a lower chance of outlet obstruction (flow rate faster than 13 mL/s or low severity of voiding symptoms)	I	A
Older adults with frailty are at greater risk of under- and over-treatment of urological disease. Frailty may be assessed in the clinic by the nonexperts using validated scores.	III	C
Assessment of known or suspected neurogenic lower urinary tract dysfunction requires comprehensive history-taking, targeted physical examination, laboratory screening, and advanced diagnostic modalities to identify risk factors and personalized management strategies.	III	C

Abbreviations: BOO, bladder outlet obstruction; LUTS, lower urinary tract symptoms; LoE, Level of Evidence; GoR, Grade of Recommendation; PSA, prostate-specific antigen; PVR, post-void residual.

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COMMITTEE

03

**LIFESTYLE
INTERVENTION AND
PHARMACOLOGICAL
TREATMENTS**

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Table of Contents

Introduction	99
Watchful Waiting and Lifestyle Interventions <i>by Souhil Lebdai, MD, PhD</i>	99
Alpha1-Adrenoceptor Antagonists (α1-Blockers) <i>by Yoshihisa Matsukawa, MD, PhD</i>	100
Mechanisms of action of α 1-adrenoceptor antagonists (α 1-blockers)	100
The α 1-blockers	101
Clinical efficacy of α 1-blockers	101
Factors contributing to treatment resistance to α 1-blockers	102
Prostatic volume and intravesical prostatic protrusion (IPP)	102
Presence of detrusor underactivity (DU)	102
Baseline severity of symptoms and duration of LUTS	102
Tolerability and safety	102
Orthostatic hypotension and dizziness	102
Ejaculatory dysfunction	103
Nasal congestion and fatigue	103
Real-world tolerability and discontinuation rates	103
Practical considerations and future perspectives	104
Conclusions	104
5-Alpha-Reductase Inhibitors (5-ARIs) <i>by Petros Sountoulides, MD, PhD, MSc, FEBU</i>	104
Mechanism of action	104
5-ARI monotherapy	105
The ideal patient for combination therapy	105
Combination therapy from the start versus add-on therapy	108
Withdrawal of α -blocker	109
Impact of 5-ARIs on progression	109
Safety and adverse events	110
5-ARIs in prostate cancer prevention	111
Additional risks associated with 5-ARIs	112
Conclusion	112
Phosphodiesterase Type 5 Inhibitors (Monotherapy and in Combination) <i>by Souhil Lebdai, MD, PhD</i>	113

Table of Contents

Mechanism of action	113
Efficacy and safety	113
PDE5Is as part of combination therapy	114
Phytotherapy for Male LUTS by Prof. Stavros Gravas, MD, PhD, FEBU	115
Mechanism of action	115
Efficacy and safety	116
Phytotherapy and guidelines	117
Conclusions—Future directions	118
Muscarinic Receptor Antagonists (Monotherapy and in Combination) and β-3 Agonists (Monotherapy and in Combination) by Mélanie Aubé-Peterkin, MD; Sender Herschorn, MD	119
Muscarinic receptor antagonists (antimuscarinics)	119
Monotherapy	119
Combination with α -blockers	120
Side effects and long-term risks	121
Patient and drug selection, dose escalation	121
Beta-3 adrenoceptor agonists	122
Monotherapy	122
Combination with α -blockers	123
Side effects	123
Patient and drug selection, dose escalation	124
Combination therapy: Antimuscarinics and β -3 agonists	124
Special considerations: Subpopulations and real-world challenges	125
Challenges in Medical Treatment of LUTS	
by Marcus J. Drake, DM, FRCS (Urol); Ferdinando Fusco, MD, PhD	126
The challenge of intravesical prostatic protrusion (IPP)	126
The challenge of treatment adherence	127
The challenge of nocturia and nocturnal polyuria	128
Strategy in treatment selection	130
Follow-up	131
References	133

Introduction

Incidence of lower urinary tract symptoms (LUTS) increases with age. The cause of LUTS can be multifactorial and prostatic enlargement, with or without obstruction, is not the only suspect. Management of LUTS should start with differential diagnosis among the different possible causative conditions. Different symptoms may be triggered by diverse conditions, and the most bothersome symptoms should be first addressed knowing that treatment rarely results in their complete clearance. The difference between subjects indexed in epidemiological studies and patients seeking medical advice is often due to bother of the reported symptoms and deterioration of quality of life. Guidelines suggest that pharmacological treatment should be initiated only when quality of life is impaired by the impending symptoms and mild symptoms are better managed conservatively.

Watchful Waiting and Lifestyle Interventions

Patients may experience different degrees of LUTS severity, with variable impact on quality of life (QoL). Management of LUTS ranges from watchful waiting (WW) to medical treatment, minimally invasive therapies, and surgery.

Lifestyle modifications including weight loss, reduction of fluid intake, physical exercise, limitation of excess consumption of caffeine and alcohol, bladder retraining, treatment of constipation, review of comedications, and dietary modifications are effective in limiting LUTS, and they are part of the initial management irrespective of the need for medical or surgical treatment.¹ It is also important to reassure patients that cancer is not the cause of their LUTS, as this is a major cause of patient referral to our clinics.^{1,2}

Different factors have been associated with an increased risk of LUTS/BPO such as metabolic syndrome and low levels of physical activity, but evidence that reversal of syndrome X and increased physical activity may improve LUTS remains weak.^{3,4} The natural history of LUTS is variable in the individual patient. In one study, approximately 81% of men with mild LUTS remained stable on WW at 1 year,⁵ suggesting conservative management is a viable option in selected cases. A randomized controlled trial (RCT) comparing WW with transurethral resection of the prostate (TURP) in a population of 556 patients with moderate LUTS reported a significant improvement in all outcomes in favor of surgery. However, only 36% of patients with moderate LUTS crossed over from WW to surgery over 5 years, leaving 64% doing well in the WW group. After crossover, bother from LUTS was similar to that of the resection group. Predictors of WW failure were initial symptom severity and post-void residual urine (PVR).⁶ Another RCT reported a 24% crossover to surgery within 3 years and greater efficacy of surgery among patients who were most bothered by LUTS at baseline.⁷

Self-management, lifestyle modifications, and behavioral changes were compared with simple monitoring in an RCT involving 140 patients.⁸ Therapeutic failure was defined as the initiation of medication or surgery, an

increase in the International Prostate Symptom Score (IPSS) score of > 3 points, or the occurrence of acute urinary retention. At 1 year, the rate of therapeutic failure was significantly lower in the self-management group (32% vs. 64%, respectively), with a significantly lower IPSS score (10.7 vs. 16.4, respectively).

A meta-analysis of eight studies involving 1006 patients (moderate-quality evidence) showed no difference between self-management and medication in IPSS improvement within 6 to 12 weeks, but demonstrated greater efficacy of the combination of self-management and medication compared with medication alone at 6 weeks,⁹ suggesting this form of combination treatment should always be considered.

Topic	Recommendation	LoE	GoR
Watchful Waiting (WW)	Offer WW as an option in men with mild-to-moderate LUTS who are not too bothered by their symptoms.	III	C
	Advise men with LUTS to change their lifestyle advice and apply self-management prior to, or concurrent with, treatment.	III	C

Abbreviations: GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms.

Alpha1-Adrenoceptor Antagonists (α 1-Blockers)

Mechanisms of action of α 1-adrenoceptor antagonists (α 1-blockers)

Alpha1-blockers competitively inhibit the binding of norepinephrine to α 1 receptors, leading to relaxation of smooth muscle fibers in the prostate and bladder neck. This action reduces dynamic obstruction and facilitates urine flow. Unlike 5 α -reductase inhibitors (5-ARIs), α 1-blockers do not reduce prostate volume; their therapeutic effect is attributed primarily to functional rather than anatomical changes.

In addition to improving voiding symptoms, α 1-blockers have also been shown to improve storage symptoms through several mechanisms: (a) blockade of α 1D receptors located in the bladder mucosa, resulting in reduced adenosine triphosphate (ATP) release and suppression of afferent nerve activity; (b) improvement of urethral afferent signaling secondary to the resolution of bladder outlet obstruction (BOO); and (c) enhancement of bladder blood flow via relaxation of the bladder vasculature, which predominantly expresses α 1A receptors.²⁻⁴

The α1-blockers

Currently available α1-blockers include alfuzosine, doxazosin, naftopidil^a, silodosin, tamsulosin, and terazosin. Although the different formulations result in varying pharmacokinetic and tolerability profiles, the overall differences in clinical efficacy among these formulations appear to be negligible. The pharmacologic characteristics of these drugs are summarized in **TABLE 1**.

TABLE 1 Pharmacologic Characteristics of α1-Blockers

Drug	Receptor selectivity	Onset of action	Major adverse effects	Clinical notes
Tamsulosin	α1A > α1D >> α1B	Rapid (days)	Ejaculatory dysfunction, dizziness	Commonly used; cataract surgery caution (IFIS)
Silodosin	Highly α1A-selective	Rapid (days)	High incidence of ejaculatory dysfunction	Potent urinary symptom relief, commonly used; cataract surgery caution (IFIS)
Naftopidil	α1D > α1A >> α1B	Rapid (days)	Mild hypotension, dizziness	Particularly effective for storage symptoms
Terazosin	Nonselective (α1A, α1B, α1D)	Slower (weeks)	Hypotension, dizziness	Requires dose titration; older generation
Doxazosin	Nonselective (α1A, α1B, α1D)	Slower (weeks)	Hypotension, fatigue	Requires dose titration; older generation
Alfuzosin	α1A-selective	Rapid (days)	Hypotension, dizziness	Commonly used, slow-release tablets, lower IFIS risk.

Abbreviation: IFIS, intraoperative floppy iris syndrome.

Clinical efficacy of α1-blockers

Meta-analyses have confirmed the efficacy of α1-blockers in patients with LUTS. Several systematic reviews have shown that α1-blockers improve IPSS score by an average of 4 to 6 points (30%–40%) and increase maximum urinary flow rate by 1.5 to 2.5 mL/sec (20%–25%) compared with placebo.^{5–11} Most patients experience symptomatic improvement within 2 to 4 weeks after treatment initiation.^{2–4}

Large RCTs such as the MTOPS and CombAT studies have also supported the efficacy of α1-blockers, albeit showing that these agents do not significantly reduce the long-term risk of disease progression compared with 5-ARIs.^{12,13} Comparison between placebo and α-blocker arms of the MTOPS study suggests they delay the natural history of the disease by an average of 1 year.

^a Not registered in all countries.

Alpha1-blockers improve BOO in men with LUTS. A systematic review and meta-analysis of urodynamic studies indicated that α 1-blockers improve the bladder outlet obstruction index (BOOI) by an average of 14.2 points.^{14,15} Notably, silodosin demonstrated greater improvement, with an increase of more than 30 points in BOOI.^{14,15} Previous studies have also reported that silodosin exhibits superior efficacy in relieving LUTS and BOO compared with other α 1-blockers at the cost of more frequent ejaculation disorders.^{15,16}

Factors contributing to treatment resistance to α 1-blockers

Prostatic volume and intravesical prostatic protrusion (IPP)

Patients with significantly enlarged prostate volume (typically > 40 mL) or pronounced IPP (typically > 10–12 mm) are less likely to respond adequately to α 1-blocker monotherapy.^{17–19} These anatomical factors contribute to persistent mechanical obstruction, which is not sufficiently relieved by smooth muscle relaxation alone.

Presence of detrusor underactivity (DU)

Detrusor contractility may be impaired in elderly men or those with long-standing BOO.²⁰ In such cases, symptom improvement due to reduced outlet resistance is limited by intrinsic bladder dysfunction. In clinical practice, the presence of DU should be considered in older patients and those with excessive residual urine volume and patients consulted consequently about the risk of reduced improvement upon treatment.

Baseline severity of symptoms and duration of LUTS

Patients with long-standing, severe LUTS may develop irreversible bladder changes that reduce their responsiveness to pharmacotherapy.¹⁷ Delayed intervention can also contribute to poor therapeutic outcomes. In effect, in most registration trials of drugs for LUTS due to BPO, a maximum flow rate lower than 5 mL/s was considered an exclusion criterion.

Tolerability and safety

The most frequent adverse events associated with α 1-blockers are orthostatic hypotension, dizziness, ejaculatory dysfunction, nasal congestion, and fatigue.^{2–4}

Orthostatic hypotension and dizziness

Nonselective agents (e.g., doxazosin and terazosin) are more frequently associated with orthostatic hypotension, leading to dizziness, syncope, and falls (actually, doxazosin is a registered drug for the treatment of arterial hypertension). In contrast, selective agents (e.g., tamsulosin and silodosin) demonstrate a reduced risk.^{5,21} The frequency of hypotension with the α 1A-selective blocker silodosin is comparable to that observed with placebo.¹¹

Cardiovascular safety is a major consideration, particularly in elderly patients, in those with concurrent cardiovascular diseases, and in patients taking multiple medications. A large population-based study reported an increased risk of cardiac failure associated with long-term α -blocker use (hazard ratio [HR], 1.22), with a higher risk observed for nonselective α -blockers.²²

Ejaculatory dysfunction

Ejaculatory dysfunction was previously attributed to retrograde ejaculation; however, more recent data has suggested a decrease or an absence of seminal fluid during ejaculation because of ejaculatory duct dysfunction, with young age being an apparent risk factor. In a meta-analysis, ejaculatory dysfunction was significantly more common among patients receiving α_1 -blockers than among those receiving placebo (odds ratio [OR], 5.88).²³ Highly α_1A -selective agents, particularly silodosin, are associated with higher rates of ejaculatory dysfunction (reported in up to 28% in some studies).^{23,24} Tamsulosin demonstrates a lower but still significant rate (approximately 8%–10%), whereas both doxazosin and terazosin (ORs, 0.80 and 1.78, respectively) are associated with a low risk of ejaculatory dysfunction.²³ Alfuzosin treatment is associated with a lower risk of ejaculatory dysfunction when compared to uroselective α -blockers.²⁵ These adverse events have significant implications for patient adherence, but they are reversible upon discontinuation of therapy.

Nasal congestion and fatigue

These two events have been reported with all α_1 -blockers, but they are generally mild and do not commonly lead to treatment discontinuation.

The use of α_1 -blockers in elderly populations, naturally hypotensive subjects, or patients receiving concomitant antihypertensive therapies requires careful monitoring to prevent falls and syncope. A large, retrospective cohort analysis of men aged > 66 years treated with α_1 -blockers reported that the risk of falling (OR, 1.14) and of consequent fractures (OR, 1.16) was increased.²⁶

Urologists should also be aware of intraoperative floppy iris syndrome (IFIS), which can complicate cataract surgery. A meta-analysis examining IFIS after exposure to alfuzosin, doxazosin, tamsulosin, or terazosin showed an increased risk with all α_1 -blockers.²⁶ However, the OR for IFIS was significantly higher for tamsulosin.^{27,28} It appears prudent not to initiate α_1 -blocker treatment before scheduled cataract surgery, and ophthalmologists should be informed of any α_1 -blocker use. Several studies have also reported that silodosin is associated with a higher incidence of IFIS compared with other α_1 -blockers.^{2,3,29}

Real-world tolerability and discontinuation rates

Observational studies and pharmacovigilance databases indicate that tamsulosin and silodosin are associated with relatively low discontinuation rates due to adverse events, typically < 10% in large patient cohorts.^{2–4} Discontinuation is most commonly driven by ejaculatory dysfunction in younger patients and by hypotension in elderly patients treated with nonselective agents.

Practical considerations and future perspectives

- α_1 -blockers are typically considered the first-line treatment for LUTS owing to their rapid onset of action, favorable efficacy, and low rate and severity of adverse events. However, they do not alter the natural history of benign prostatic hyperplasia (BPH), including its progression to acute urinary retention or need for surgery.²⁻⁴
- If adequate improvement in subjective symptoms is not achieved after 4 to 12 weeks of treatment, combination therapy could be considered. In cases where the prostate volume exceeds 40 mL, the addition of a 5-ARI is recommended. For men with persistent storage symptoms suggestive of overactive bladder (OAB), the use of a β_3 -adrenoceptor agonist or an anticholinergic agent may be beneficial.²⁻⁴ Combination therapy with phosphodiesterase type 5 inhibitors may also be considered a therapeutic option.
- The development of novel agents with enhanced selectivity profiles or ongoing research into the genetic polymorphisms of adrenergic receptors may pave the way for precision medicine in the field of LUTS. In the future, personalized medicine approaches will likely be required for optimizing treatment strategies.

Conclusions

Alpha1-blockers remain a cornerstone in the pharmacological management of LUTS associated with BPO, offering rapid symptom relief and a favorable safety profile. Tailoring agent selection according to individual patient characteristics, comorbidities, and comedications is critical to maximize therapeutic outcomes and minimize adverse events.

Topic	Recommendation	LoE	GoR
α_1 -Adrenoceptor Antagonists (α_1 -Blockers)	Offer α_1 -blockers to men with bothersome LUTS.	I	A
	Discuss with the patients with large prostates or middle lobe, that response is less likely to be adequate.	II	B

Abbreviations: GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms.

5-Alpha-Reductase Inhibitors (5-ARIs)

Mechanism of action

The primary drivers of BPH and benign prostatic enlargement (BPE) are age and the presence of androgens. The androgenic effects on the prostate are primarily mediated by dihydrotestosterone (DHT), which is converted from testosterone by the enzyme 5 α -reductase.¹ Two isoforms of this enzyme exist: type 1, mainly expressed in the skin and liver, and type 2, predominantly expressed in the prostate.

5-ARIs promote apoptosis of prostate epithelial cells,² leading to a prostate volume reduction of 18% to 28% and an approximate 50% decrease in serum PSA after 6 to 12 months of treatment. These effects may be more pronounced with long-term use.³ Two 5-ARIs are approved: finasteride, which selectively inhibits type 2, and dutasteride, which inhibits both isoforms.^{4,5}

5-ARI monotherapy

5-ARIs as monotherapy are effective in reducing prostate volume (by 18%–28%), improving LUTS (by 5%–30%), lowering the risk of acute urinary retention (AUR) and the need for surgery in men with BPE, particularly in those with larger prostates.^{6–9} **TABLE 1** presents the key studies on 5-ARIs.

In the MTOPS study, the first long-term study on an 5-ARI, finasteride monotherapy was shown to reduce the risk of long-term clinical progression compared with placebo (17% vs. 10%, $P < .001$).⁷ Similarly, the CombAT study confirmed that dutasteride alone provides sustained improvements in symptom scores and reduces the risk of AUR and surgery over a 4-year period.⁸ These outcomes highlight the disease-modifying potential of 5-ARIs, making them the first-line option for patients with risk of BPH progression.

Although the onset of symptom relief with 5-ARIs is significantly slower than that observed with α -blockers, their long-term benefits and impact on BPH natural history support their use in patients with prostate-specific antigen (PSA) of level of 1.5 ng/mL or higher or prostate volume of 40 mL or larger. 5-ARI monotherapy offers a well-tolerated treatment option in men at risk of disease progression.⁹

The ideal patient for combination therapy

The MTOPS⁷ and CombAT⁸ studies and the earlier PLESS study,¹⁰ have defined the ideal candidate for combination therapy with an α -blocker and an 5-ARI as a man with moderate-to-severe LUTS due to BPH, who is at risk for disease progression. Disease progression was defined as worsening of LUTS, urinary retention or need for surgery, with an increase in symptom score of at least 4 points being the most common event of progression.⁷

Risk factors for progression include a prostate volume of > 40 mL and a PSA level of > 1.5 ng/mL, both indicative of a substantial androgen-dependent prostatic component. An important consideration is the treatment duration of at least 12 months, as the benefits of combination therapy, particularly in reducing the risk of AUR and BPH-related surgery, are most evident with sustained treatment. In this context, dual therapy offers superior outcomes compared to monotherapy for symptoms and maximum flow rate (Q_{max}), and superior to α 1-blocker alone in reducing the risk of AUR or need for surgery.^{7,8} **TABLE 1** presents the key studies on combination therapy.

TABLE 1 Key Studies on the Use of 5-ARIs

Author/Year	Type of study	Patients (n)	Outcome searched	Result	Comment
Andriole <i>et al.</i> (2004) ¹	Review	n/a (Review)	Scientific rationale for 5-ARIs in BPH	DHT plays key role; 5-ARIs mechanistically justified	Foundational rationale for therapy
Naslund, Miner (2007) ³	Review	n/a (Review)	Efficacy and safety of 5-ARIs	5ARIs reduce symptoms, prostate volume, and risk of AUR/surgery	Summarizes available data up to 2007
Pirozzi <i>et al.</i> (2015) ⁴	Review	n/a (Review)	Comparison dutasteride vs. finasteride, risk of surgery/AUR	Both effective, dutasteride may provide greater suppression	No large head-to-head outcome RCTs
McConnell <i>et al.</i> (2003) ⁷	RCT (MTOPS trial)	3047	Progression of BPH with doxazosin, finasteride, or both	Combination more effective than monotherapy; finasteride reduces risk of AUR and surgery	Landmark trial in the medical management of BPH
Roehrborn <i>et al.</i> (2010) ⁸	RCT (CombAT trial)	4844	Dutasteride + tamsulosin vs. monotherapy, time to first AUR or BPH-related surgery. BPH clinical progression, symptoms, Q _{max} , prostate volume, safety, and tolerability.	Combination superior to either monotherapy for symptom relief and BPH progression	Supports combination therapy in large (> 40 mL) prostates, in men with moderate-to-severe LUTS
Kim <i>et al.</i> (2018) ⁹	Meta-analysis	23 RCTs (~27,000)	5-ARI monotherapy efficacy and safety	Significant improvement in LUTS, reduced prostate volume, acceptable safety	Up-to-date pooled evidence, need for more head-to-head comparisons
Roehrborn <i>et al.</i> (1999) ¹⁰	RCT (PLESS study)	3040	Finasteride vs. placebo, 4 years	Reduced risk for AUR and surgery, PSA > 1.4 ng/mL and prostate volume predicted outcomes	Key long-term evidence
Naslund <i>et al.</i> (2009) ¹²	Observational	Claims data (~7000 men)	Impact of delayed 5-ARI	Delays ↑ risk of AUR and surgery within 12 months	Supports timely initiation
Barkin <i>et al.</i> (2003) ¹⁴	RCT	327 men	α-blocker withdrawal after dutasteride	Most men maintained symptom control on dutasteride monotherapy	Supports step-down strategy
Nickel <i>et al.</i> (2008) ¹⁵	RCT	395	Finasteride monotherapy 9 mo after α-blocker cessation	Control of LUTS maintained	Supports discontinuation approach

Abbreviations: 5-ARIs, 5α-reductase inhibitors; AS, active surveillance; AUR, acute urinary retention; BPH, benign prostatic hyperplasia; CV, cardiovascular; CVD, cardiovascular disease; DHT, dihydrotestosterone; ED, erectile dysfunction; EjD, ejaculatory dysfunction; FDA, U.S. Food and Drug Administration; mo, months; PCa, prostate cancer; PSA, prostate-specific antigen; Q_{max}, maximum flow rate; RCTs, randomized controlled trials.

TABLE 1 Key Studies on the Use of 5-ARIs (*continued*)

Author/Year	Type of study	Patients (n)	Outcome searched	Result	Comment
Roehrborn <i>et al.</i> (2008) ¹⁶	RCT (CombAT study)	4844	Combination vs. monotherapy	Combination superior at 2 years	Interim results before 4-y data
Roehrborn <i>et al.</i> (2015) ¹⁷	RCT (CONDUCT study)	742	Fixed-dose dutasteride + tamsulosin vs. watchful waiting	Combination reduced risk of progression, improved LUTS	Early intervention beneficial
van der Worp <i>et al.</i> (2019) ¹⁸	Systematic review/meta-analysis	19 studies (~3500)	Discontinuation of α -blockers after combination therapy	Discontinuation feasible in most after combination	Useful practical implication
de la Rosette <i>et al.</i> (2002) ¹⁹	Observational	2200	Retreatment risk in α -blocker monotherapy. Tamsulosin has a markedly lower retreatment percentage than alfuzosin and terazosin.	High long-term retreatment rates	α -blockers do not modify BPH natural history
McConnell <i>et al.</i> (1998) ²⁰	RCT	3040	Finasteride vs. placebo. $Q_{\max}$, BPH progression	Increased $Q_{\max}$, reduced AUR and surgery risk	Foundational efficacy trial
Corona <i>et al.</i> (2017) ²⁵	Systematic review/meta-analysis	17 studies (~17,000)	Sexual dysfunction with 5-ARIs	$\uparrow$ risk of ED, $\downarrow$ libido, ejaculatory issues	Large synthesis, highlights adverse effects
Gacci <i>et al.</i> (2014) ²⁶	Systematic review/meta-analysis	24 studies (~22,000)	Impact of LUTS therapies on ejaculation	Combination therapies 3x risk of EjD compared to monotherapies	Comparative to other treatments
Thompson <i>et al.</i> (2003) ²⁷	RCT (PCPT study)	18,882	Finasteride for PCa prevention	$\downarrow$ overall PCa incidence, $\uparrow$ high-grade tumors	Controversial findings
Andriole <i>et al.</i> (2010) ²⁸	RCT (REDUCE study)	8121	Dutasteride for PCa risk	$\downarrow$ low-grade cancer risk, possible $\uparrow$ high-grade	FDA safety concerns
Belknap <i>et al.</i> (2015) ³¹	Meta-analysis	34 trials (~11,000)	Adverse event reporting in alopecia finasteride trials	Under-reporting suspected	Highlights bias issues
Kaplan <i>et al.</i> (2016) ³⁴	RCT (MTOPS adverse events)	3047	Timing of treatment side effects	Most occur early in treatment	Useful for patient counseling

Abbreviations: 5-ARIs, 5 α -reductase inhibitors; AS, active surveillance; AUR, acute urinary retention; BPH, benign prostatic hyperplasia; CV, cardiovascular; CVD, cardiovascular disease; DHT, dihydrotestosterone; ED, erectile dysfunction; EjD, ejaculatory dysfunction; FDA, U.S. Food and Drug Administration; mo, months; PCa, prostate cancer; PSA, prostate-specific antigen; $Q_{\max}$, maximum flow rate; RCTs, randomized controlled trials.

TABLE 1 Key Studies on the Use of 5-ARIs (*continued*)

Author/Year	Type of study	Patients (n)	Outcome searched	Result	Comment
Thompson <i>et al.</i> (2006) ³⁵	Secondary analysis	18,882	Effect on PSA sensitivity	Finasteride improves PSA specificity	Diagnostic implication
Matsukawa <i>et al.</i> (2024) ⁴⁰	Systematic review/meta-analysis	22 studies (~11,000)	Nonsurgical interventions in AS PCa	5-ARIs may delay progression	Recent evidence, ongoing debate
Hsieh <i>et al.</i> (2015) ³⁷	Cohort study	19,735	CVD risk with 5-ARIs	No increased risk	Supports safety
Skeldon <i>et al.</i> (2017) ³⁸	Cohort study	72,000	CV safety of dutasteride	No excess CV risk	Patient reassurance

Abbreviations: 5-ARIs, 5 α -reductase inhibitors; AS, active surveillance; AUR, acute urinary retention; BPH, benign prostatic hyperplasia; CV, cardiovascular; CVD, cardiovascular disease; DHT, dihydrotestosterone; ED, erectile dysfunction; EjD, ejaculatory dysfunction; FDA, U.S. Food and Drug Administration; mo, months; PCa, prostate cancer; PSA, prostate-specific antigen; Q_{max}, maximum flow rate; RCTs, randomized controlled trials.

Combination therapy from the start versus add-on therapy

The decision of when to initiate 5-ARI therapy in men with LUTS already receiving α -blockers can significantly influence treatment outcomes. Emerging evidence suggests that starting 5-ARI therapy earlier may help reduce the risk of clinical progression, AUR, and prostate surgery.^{11,12} Data from a large health database was used to assess the clinical and economic impacts of early versus delayed initiation of 5-ARI therapy in men already on α -blockers. The results indicated that early addition of 5-ARIs (within 30 days) led to lower rates of clinical progression (12.8% vs. 17.4%), AUR (10.2% vs. 13.8%), and prostate-related surgery (5% vs. 7%) compared to delayed addition (31 to 180 days). Additionally, early combination therapy was associated with reduced BPH-related medical costs.¹¹

Naslund *et al.* compared clinical outcomes between patients who initiated 5-ARI therapy within 30 days of starting α -blocker therapy (early cohort) and those who began 5-ARI therapy more than 30 days after starting α -blocker therapy (late cohort). The study found that each 30-day delay in initiating 5-ARI therapy was associated with an increased likelihood of overall clinical progression (average, 21.1%), AUR (average, 18.6%), and prostate-related surgery (average, 26.7%).¹²

More evidence in favor of early start of combination therapy was provided by a later study by D'Agate *et al.* The authors utilizing a time-to-event model based on pooled data from 10,238 patients included in the dutasteride trials demonstrated significant differences ($P < .001$) when switch to combination treatment occurred ≥ 6 months from initiation of treatment with an α -blocker. The study showed that, at 4-year follow-up, the risks of AUR and

BPH surgery were 4.6% and 11.3%, for patients receiving immediate combination therapy compared with those who switched to combination therapy after 24 months.¹³

Withdrawal of α -blocker

The rationale for α -blocker discontinuation following combination therapy with 5-ARIs is to maintain symptom control while reducing medication burden and minimizing adverse effects. As 5-ARIs begin to exert their therapeutic effect, continued use of α -blockers may become unnecessary, particularly in patients with milder baseline symptoms or those experiencing drug-related side effects.^{14–18}

The effects of discontinuing α -blockers following 6 to 9 months of combination therapy with 5-ARIs have been evaluated in both a randomized controlled trial and an open-label multicenter study.^{14,15} In the first study, patients receiving tamsulosin plus dutasteride were assessed after tamsulosin withdrawal at 6 months; 77% experienced no symptom deterioration. However, among patients with severe baseline symptoms (IPSS, > 20), only 56% experienced no symptom deterioration, indicating that α -blocker discontinuation might not be beneficial in this subgroup.¹⁴

The second trial assessed finasteride monotherapy outcomes at 3 and 9 months following withdrawal of α -blocker after 9 months of combination therapy. Improvements in LUTS persisted at both time points, with IPSS changes of 1.24 and 0.4, respectively. Nonetheless, study limitations included relatively short treatment and duration of follow-up post-discontinuation.¹⁵

The SMART-1 trial investigated the effects of discontinuing tamsulosin after 24 weeks of combination therapy with dutasteride. Results showed that although there was a modest increase in symptom scores after α -blocker withdrawal, the majority of patients maintained acceptable symptom control with dutasteride monotherapy alone.¹⁶ Similarly, the CONDUCT study compared early combination therapy with deferred α -blocker use in patients receiving dutasteride and found that many men did not require long-term α -blocker use, particularly those with less severe baseline symptoms.¹⁷ These findings were further supported by a systematic review, which showed that withdrawal of α -blockers from combination therapy had no clinically significant effect and may be appropriate for the frail, elderly, or those with concomitant illness or polypharmacy.¹⁸

Impact of 5-ARIs on progression

Alpha1-blockers are known to improve LUTS without any effect on the natural history of BPH. A retrospective analysis of 316 patients evaluated the long-term risk of retreatment in patients on α -blockers and the parameters that influence this risk.¹⁹ The percentage of patients who received any form of retreatment during follow-up was 38% after 3 years and 54% after 5 years. Patients with prostates larger than 40 mL were more likely to receive retreatment within 5 years than those with smaller prostates (48% vs. 72%).

5-ARIs significantly reduce the long-term (> 1 year) risk of AUR and the need for surgical intervention.^{7,16,20} The results from the *Proscar*™ Long-Term Efficacy and Safety Study (PLESS) on the risk of AUR according to baseline prostate volume confirmed the findings of the Olmsted community study that showed a 3-fold higher risk of AUR in men with larger (> 30 mL) versus smaller (≤ 30 mL) prostates.²¹

In the PLESS trial, finasteride reduced the relative risk of AUR by 57% and of surgery by 55% over 4 years, with absolute risk reductions of 4% and 7%, respectively.²⁰ Similarly, the MTOPS study showed a 68% relative reduction in AUR risk and a 64% reduction in need for surgery, with absolute reductions of 2% and 3%.⁷

A pooled analysis of three RCTs with 2-year follow-up reported a 57% relative risk reduction for AUR and 34% for surgery in patients with moderate LUTS, with absolute reductions of 2% for both outcomes.²² Dutasteride has also shown similar benefits in lowering AUR and surgery risk, supported by trials demonstrating favorable changes in urodynamic parameters.^{23,24}

Both the MTOPS and CombAT trials demonstrated the superiority of combination therapy over monotherapy in preventing clinical progression, defined by an increase in IPSS ≥ 4 points, AUR, incontinence, or a > 50% rise in serum creatinine. In MTOPS, combination therapy with finasteride and doxazosin reduced the risk of long-term progression, primarily driven by symptom worsening, by 66% versus placebo, outperforming monotherapy with either finasteride (34%) or doxazosin (39%).⁷ Only regimens including finasteride (alone or in combination) significantly decreased the incidence of AUR and BPO-related surgery.

Similarly, the CombAT study showed that combination therapy with dutasteride and tamsulosin significantly lowered the relative risk of AUR by 68%, BPO-related surgery by 71%, and symptom deterioration by 41% compared with tamsulosin alone over 4 years.⁸ Thirteen patients would need to be treated for 4 years to prevent one case of AUR and/or surgery, with an absolute risk reduction of 7.7%.

The CONDUCT trial, an RCT involving 742 men, compared a fixed-dose combination of dutasteride and tamsulosin with a WW strategy plus lifestyle advice and potential tamsulosin initiation. The combination therapy yielded a more substantial and sustained IPSS reduction at 24 months (5.4 vs. 3.6 points). It also reduced the relative risk of clinical progression by 43.1% versus WW, with an absolute risk reduction of 11.3% (number needed to treat [NNT], 9).¹⁶

Safety and adverse events

5-ARI adverse effects are primarily related to sexual function. The most commonly reported adverse events include reduced libido and erectile dysfunction (ED), while ejaculation disorders, such as retrograde ejaculation, anejaculation, and decreased semen volume, occur less frequently.^{3,7,8,25} Their impact on quality of life can be substantial, particularly in younger men or those more concerned by sexual side effects. Furthermore, a meta-analysis evaluating the effects of medical treatments for LUTS on ejaculatory function revealed that combination therapy with α -blockers and 5-ARIs increased the risk of ejaculatory dysfunction by 3-fold compared to either monotherapy.²⁶

Clinical trials have shown that most sexual side effects are reversible upon discontinuation of therapy. In the PCPT and REDUCE trials, sexual dysfunction was reported more frequently in the treatment groups, but most cases resolved either spontaneously or after cessation of the drug, suggesting a primarily dose- and duration-dependent relationship.^{27,28}

However, there is concern regarding a subset of patients who experience persistent sexual dysfunction following discontinuation of 5-ARIs, a condition often referred to as post-finasteride syndrome (PFS). Observational studies and case series of younger men treated with 5-ARIs for androgenic alopecia reported long-lasting symptoms including ED, diminished libido, genital numbness, and psychological distress even months after stopping the medication.^{29,30} While causality remains elusive, a retrospective study found that younger men (< 40 years) with no prior sexual dysfunction were more likely to experience persistent symptoms, with some cases persisting even beyond 12 months.³¹

Importantly, psychological factors, including anxiety and depression, may contribute to or exacerbate perceived sexual dysfunction. Some researchers have proposed a nocebo effect in susceptible individuals, although this does not fully explain the persistence of symptoms in all cases.³¹ Despite ongoing debate, regulatory agencies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have acknowledged reports of persistent sexual adverse effects, and updated product labeling to reflect this possibility.³²

Recent evidence has raised concerns regarding the psychological consequences of treatment with 5-ARIs. A large Swedish cohort study demonstrated an increased risk of depression in men treated with either finasteride (HR, 1.61) or dutasteride (HR, 1.68). However, the same study found no long-term association between the use of 5-ARIs and increased risk of dementia or suicide.³³ These findings highlight the importance of careful patient selection when initiating 5-ARI therapy, particularly in individuals with preexisting psychiatric vulnerabilities or significant concerns about sexual side effects.

Adverse effects associated with both drug classes have been observed in patients undergoing combination therapy.^{7,8,16} These adverse events are generally consistent with the known side effects of α 1-blockers and 5-ARIs. The occurrence of these events was notably more frequent in individuals receiving combination therapy. The MTOPS trial indicated that the incidence of treatment-related adverse events was higher in the first year of combined doxazosin and finasteride therapy.³⁴

5-ARIs in prostate cancer prevention

Two landmark randomized controlled trials—the Prostate Cancer Prevention Trial (PCPT) and the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) study—have provided the most robust data on the potential role of 5-ARIs in prostate cancer (PCa) prevention. In the PCPT, finasteride administration over 7 years resulted in a 24.8% relative reduction in the overall incidence of PCa compared with placebo ($P < .001$), with the majority

of cases prevented being low-grade tumors (Gleason score [GS], ≤ 6).²⁸ Similarly, the REDUCE trial demonstrated a 22.8% reduction in biopsy-detectable PCa over 4 years with dutasteride, primarily affecting the diagnosis of GS 6 tumors.²⁹

However, both studies reported a high detection of high-grade tumors (GS, 8–10) in the treatment arms, raising concerns regarding the benefit of 5-ARI-based chemoprevention. Subsequent analyses have suggested that this apparent increase may be attributable to detection bias. By reducing prostate volume, 5-ARIs may enhance the diagnostic yield of prostate biopsy, thereby increasing the likelihood of sampling higher-grade lesions.³⁵

These findings should however be interpreted with caution given that both studies were concluded in the pre-mpMRI-guided biopsy era. Currently, a clear recommendation on the benefit of 5-ARIs in reducing the risk of PCa cannot be given.³⁶

Additional risks associated with 5-ARIs

Gynecomastia, characterized by breast or nipple tenderness, occurs in 1% to 2% of individuals undergoing treatment. The cardiovascular safety profile of 5-ARIs, especially dutasteride, remains a subject of ongoing discussion.³⁸ Population-based investigations conducted in Taiwan and Ontario found no significant correlation between 5-ARI usage and an increased risk of cardiovascular events.^{38,39} A British-Taiwanese cohort study highlighted an elevated risk of type 2 diabetes in men using 5-ARIs compared with those treated with tamsulosin, although the risk did not differ significantly between dutasteride and finasteride.⁴⁰

Conclusion

When compared to α 1-blockers or 5-ARI monotherapy, combination therapy provides superior improvements in LUTS and uroflowmetry parameters and is more effective in preventing disease progression. However, this treatment regimen is associated with a higher incidence of adverse events. Therefore, combination therapy should primarily be prescribed for men with moderate-to-severe LUTS who are at risk of disease progression. It should be reserved for individuals expected to adhere to long-term treatment (greater than 12 months). Patients at high risk for surgery could be informed about the possibility to reduce the risk of AUR or surgery with 5-ARIs either alone or in combination with α 1-blockers. In cases of moderate LUTS, discontinuation of the α 1-blocker after 6 months may be considered. Given the delayed onset of action and the potential for sexual adverse effects, effective patient counseling is crucial to ensure compliance and appropriate expectations.

Topic	Recommendation	LoE	GoR
5 α -Reductase Inhibitors (5-ARIs)	Offer 5-ARIs alone or in combination with α -blockers to men with bothersome LUTS and risk of disease progression.	I	A

Abbreviations: GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms.

Phosphodiesterase Type 5 Inhibitors (Monotherapy and in Combination)

Mechanism of action

The exact mechanism by which phosphodiesterase type 5 inhibitors (PDE5Is) improve LUTS remains uncertain. Two hypotheses have been proposed: (1) the relaxation of smooth muscle in the bladder, prostate, and urethra by increased intracellular levels of cyclic guanosine monophosphate (cGMP) levels, thereby reducing urethral resistance and improving urinary flow; and (2) improved blood perfusion and oxygenation of the bladder and prostate, which may reduce local inflammation.¹

Efficacy and safety

At least six clinical trials have evaluated the efficacy and safety of various PDE5Is at different doses in patients with BPH-related LUTS.²⁻⁷ Owing to its longer half-life (17.5 hours), tadalafil is currently the only PDE5I recommended for this indication.

Several trials have shown that tadalafil 5 mg once daily over a 12-week period resulted in a significant reduction in IPSS score of -4.8 to -6.3 points from baseline, compared with -2.0 to -3.0 points with placebo ($P < .001$).²⁻⁷ In these different studies, the improvement in quality of life (IPSS-QoL) varied between -0.8 and -1.2 points with tadalafil, compared with -0.4 to -0.6 points with placebo ($P < .01$). In contrast, no significant change in $Q_{\max}$ was reported. Furthermore, tadalafil led to an improvement in erectile function in patients suffering from associated ED, with an increase in the International Index of Erectile Function 5-item (IIEF-5) score of +4 to +6 points compared with placebo ($P < .001$).

A 2018 Cochrane review including 16 randomized clinical trials compared the efficacy of PDE5Is with placebo, α -blockers (AB), and 5-ARIs.⁸ In this review, PDE5Is demonstrated a greater reduction in IPSS compared with placebo (-1.9; $P < .001$), with no statistically significant difference compared with AB. At least four meta-analyses have compared tadalafil with placebo.⁹⁻¹² The results are quite homogeneous, showing a significant improvement in IPSS score (-2.2 to -2.8 points; $P < .001$) and IIEF-5 (+3.5 to +5.0 points; $P < .001$) and no improvement in $Q_{\max}$. Although these meta-analyses included a large number of patients ($n = 3214$),¹² it is important to note that most were limited by a short treatment duration (maximum, 12 weeks).

PDE5Is can cause a variety of adverse effects. The most common include headache, flushing, nasal congestion, dyspepsia, and back pain. Less frequently, visual disturbances or dizziness have been reported.⁹ Hypotension and priapism are rare complications. Because of the limited long-term data, the long-term tolerability of these agents cannot be fully assessed. Tadalafil is contraindicated in combination with a nitrate derivative, as well as in those with unstable angina, uncontrolled arrhythmias or hypertension, myocardial infarction within the previous

3 months, heart failure of New York Heart Association (NYHA) class > 2, or stroke within the previous 6 months. It is also contraindicated in cases of hypotension and anterior ischemic optic neuropathy.

PDE5Is as part of combination therapy

The combination of PDE5Is and α -blockers is poorly documented, with a small number of high-level studies and lack of long-term data. A first RCT including 318 men with BPH-related LUTS compared the combination of tadalafil and AB with AB monotherapy. This study evaluated the occurrence of treatment-related dizziness and orthostatic disorders and found no difference between the two groups.¹³ Another RCT including 140 men showed an improvement in IPSS (-1.69), IPSS QoL score (-0.70), IIEF score (3.8), and $Q_{\max}$ (1.8 mL/s) favoring the combination therapy group.¹⁴ Similar results were reported in four other RCTs, with significant improvement in IPSS with the combination of tadalafil and AB.^{15–18} However, the results were conflicting regarding the improvement in the IIEF score, $Q_{\max}$, and PVR. Finally, published meta-analyses have confirmed these results, showing a significant improvement in IIEF, IPSS, $Q_{\max}$, and PVR favoring the combination compared with AB alone.^{12,19,20} Regarding adverse effects, published data shows that the occurrence of adverse effects with combination therapy is similar to that observed with either treatment used as monotherapy, suggesting that the addition of PDE5Is to α -blockers is well tolerated.^{16,17,21}

The combination of a PDE5I with a 5-ARI has been evaluated in only two clinical studies.^{22,23} Both were randomized, double-blind, placebo-controlled trials evaluating tadalafil (5 mg) with finasteride (5 mg) in men with BPH. In the first study,²² 695 men were treated for 26 weeks, and those receiving tadalafil plus finasteride initially showed greater improvements in LUTS compared with placebo plus finasteride, with IPSS reductions of -4.0, -5.2, and -5.5 at weeks 4, 12, and 26 versus -2.3, -3.8, and -4.5, respectively; there was only a 1-point difference at week 26. Erectile function also improved, with IIEF scores increasing by +3.7 at week 4 and by +4.7 at weeks 12 and 26 compared with minimal or no change with placebo plus finasteride. The second study²³ included 610 sexually active men. The combination of tadalafil and finasteride significantly improved IIEF in men with or without ED, and a higher proportion of men with baseline ED achieved clinically meaningful improvements in erectile function at weeks 4, 12, and 26 compared with placebo plus finasteride. Both studies reported that the combination therapy was well tolerated, with most adverse events being mild to moderate and a low incidence of sexual side effects.

Topic	Recommendation	LoE	GoR
Phosphodiesterase Type 5 Inhibitors (PDE5Is)	Offer tadalafil 5 mg alone or in combination with α -blockers as a treatment option to men with bothersome LUTS and especially those with erectile dysfunction.	I	A

Abbreviations: GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms.

Phytotherapy for Male LUTS

Phytotherapy is defined as the use of plants or plant-derived substances for the treatment of clinical conditions. Phytotherapeutic agents for the treatment of LUTS represent a heterogeneous group of extracts derived from roots, seeds, pollen, bark, or fruits. These preparations may be obtained from a single plant or a combination of two or more plants. The most widely used plants for the treatment of male LUTS are: *Cucurbita pepo* (pumpkin seed), *Hypoxis rooper* (South African star grass), *Pygeum africanum* (bark of the African plum tree), *Secale cereale* (rye pollen), *Serenoa repens* (synonym *Sabal serrulata*; saw palmetto), and *Urtica dioica* (roots of the stinging nettle).¹

The landscape of plant-based therapy for male LUTS is characterized by considerable variability and heterogeneity. **TABLE 1** summarizes the main challenges and limitations of phytotherapy.

TABLE 1 Challenges and Limitations of Phytotherapy

Topic	Limitations	Result
Products	Numerous different products from different plants and plant parts	Difficult to analyze and compare the evidence
Extraction techniques	Extraction techniques can affect the qualitative and quantitative composition of the bioactive compounds	Effects of one brand cannot be extrapolated to others and outcomes must be compared according to the same extraction technique
Studies	Heterogeneity in design, small number of patients, short follow-up, variability in control arms, different endpoints	Difficult to make comparisons and provide evidence-based recommendations
Regulatory framework	Heterogeneity from country to country: available as food supplements, non-prescription medicines, prescription medicines	Different regulatory requirements for quality depending on their status Weaker evidence base compared to chemically defined therapies

Mechanism of action

The mechanisms of action of these products are not fully known or understood in many cases.^{2,3} *In vitro* studies have suggested that plant extracts may have anti-inflammatory activity, inhibit cell proliferation, induce apoptosis, have anti-androgenic and estrogenic effect, and improve smooth muscle relaxation. However, the *in vivo* effects of most of these compounds remain unclear.

Efficacy and safety

Preparations of the same phytotherapeutic agent may differ not only in their extraction method but also in their regulatory form, being available either as nutritional supplements or as registered drugs.

The efficacy of the different phytotherapeutic agents has been reported in many clinical trials, with highly variable results. The main limitations of these studies include heterogeneity in the design of these trials, the use of different endpoints, the low number of patients, the short follow-up, and the variability in the control arms.³

Phytotherapy demonstrates an excellent safety profile, with a low incidence of adverse events, particularly those related to sexual and ejaculatory function—making this treatment appealing to patients concerned about preserving sexual function. The most common adverse events are headache, gastrointestinal disorders, and upper respiratory symptoms.^{2,3}

Hexanic *Serenoa repens* (HESr) is the most extensively researched herbal medical product for LUTS. **TABLE 2** summarizes the systematic reviews of available studies on *Serenoa repens*. Careful analysis of the studies on HESr reveals conflicting findings: although no consistent clinically meaningful benefit in IPSS has been confirmed compared with placebo, improvements have been observed in $Q_{\max}$ and nocturia episodes.^{4–7} Moreover, there is no inferiority of HESr compared to established treatments such as tamsulosin or finasteride. When meta-analyses include data from multiple *Serenoa repens* extracts (hexane, ethanol, CO₂-based), outcomes are very difficult to interpret, as one extract differs from another in the composition and concentration of bioactive compounds, resulting in different clinical profiles, even when derived from the same plant.^{8,9} Therefore, results from different studies should be compared only when based on the same validated extraction technique and/or content of active compounds.^{8,9}

HESr can also be used in combination with α -blockers for the treatment of male LUTS. A review of six studies showed that this combination resulted in greater symptom improvement and fewer adverse events in patients with LUTS compared with α -blocker monotherapy.¹⁰ Patients with specific characteristics, such as a higher body mass index (BMI), larger prostate volume, and diabetes mellitus, appeared to experience a better response to the combination, indicating a potential individualized approach.

TABLE 2 Summary of Systematic Reviews on the Role of *Serenoa repens* in Treating LUTS

Name	Type of study	Year	Comparison arm	Follow-up	Summary of outcomes
Hexanic <i>Serenoa repens</i>	Systematic review and meta-analysis (12 RCTs)	2016	Placebo Tamsulosin Finasteride	1–12 months	-Vs. <i>placebo</i> : Significant improvement in $Q_{\max}$ (+3.37 mL/s) and nocturia episodes (-0.31). -Vs. <i>Tamsulosin and finasteride</i> : Similar improvement in IPSS and $Q_{\max}$. - Well tolerated, with very limited impact on sexual function.
Hexanic <i>Serenoa repens</i>	Systematic review and meta-analysis (15 RCTs and 12 observational studies)	2018	Placebo α -blockers 5-ARIs	1–60 months	-Vs. <i>placebo</i> : Significant improvement in $Q_{\max}$ (2.75 mL/s) and nocturia episodes (-0.64). -Vs. α -blockers: No statistically significant differences in IPSS improvement (MD, -0.57), $Q_{\max}$, and prostate volume. -Vs. 5-ARIs (6 months): No statistically significant differences in IPSS improvement (MD, -0.46). - Well tolerated, with very limited impact on sexual function.
Hexanic <i>Serenoa repens</i>	Systematic review (13 RCTs and observational studies)	2022	Placebo α -blockers 5-ARIs	3–12 months	RCTs: Similar efficacy to α -blockers and/or 5-ARIs (voiding and storage symptoms, $Q_{\max}$) Real-world observational studies: Similar efficacy to 5-ARIs and/or α -blockers (symptoms and QoL).
<i>Serenoa repens</i> : Hexanic and non-Hexanic extracts	Cochrane systematic review (19 RCTs)	2023	Placebo	3–6 months	- <i>Serenoa repens</i> results in little to no difference in symptoms at 3–6 months (MD, -0.90). - <i>Serenoa repens</i> results in little to no difference in QoL at 3–6 months (MD, -0.20).

Abbreviations: 5-ARIs, 5 α -reductase inhibitors; IIEF, International Index of Erectile Function; IPSS, International Prostate Symptom Score; MD, mean difference; NR, not reported; $Q_{\max}$, peak urine flow; QoL, quality of life score; RCT, randomized controlled trial.

Phytotherapy and guidelines

Because of the existing limitations (**TABLE 1**), it is very difficult to compare the various agents and to provide evidence-based recommendations for their use. As a result, the European Association of Urology (EAU) and American Urological Association (AUA) Guidelines have adopted different approaches: AUA does not include any phytotherapeutic agents in their Guidelines. In contrast, the EAU Working Panel on male LUTS follows the opinion of the Committee on Herbal Medicinal Products (HMPC), developed by the European Medicines Agency (EMA). The HMPC evaluates all available nonclinical and clinical data, and the experience from the long-standing use of different herbal substances in the European Union, and recommends them either for well-established use or for traditional use:

- Well-established use applies to herbal medicinal substances that have been used for more than 10 years and for which efficacy and safety have been well established.

- Traditional use applies to herbal medicinal products that do not fulfil the requirements for a marketing authorization but have sufficient safety data and plausible efficacy based on long-standing use and experience.

Among all the available phytotherapeutic agents, only HESr has been recommended for well-established use.¹¹ Therefore, the EAU Guidelines analyzed the evidence from HESr studies and recommend offering HESr to patients with LUTS who want to avoid any potential adverse events, particularly those affecting sexual function (weak recommendation), informing them that the magnitude of efficacy may be modest (strong recommendation).¹²

Conclusions—Future directions

Numerous phytotherapeutic agents are available for the treatment of male LUTS, but they are not supported by the same body of evidence. HESr is the most extensively studied agent and is recommended for well-established use in male LUTS.

There remains a clear need for large-scale, well-designed RCTs with defined entry criteria to identify patients who will benefit from phytotherapy. Within this context, the Prostatic Inflammation Nomogram Study (PINS) was developed to predict prostatic inflammation in men with LUTS, based on baseline parameters (please see [Chapter 6](#) for more details). This nomogram may be used in studies evaluating specific therapies with anti-inflammatory properties, such as phytotherapeutic agents, in the management of LUTS.¹³ Future research should also investigate combination therapies involving phytotherapy and different pharmatherapeutic agents to better define their role in clinical practice.

Topic	Recommendation	LoE	GoR
Phytotherapy	Offer Hexanic <i>Serenoa repens</i> to men with LUTS who wish to avoid adverse events related to sexual function and accept a modest improvement of their symptoms.	II	B

Abbreviations: GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms.

Muscarinic Receptor Antagonists (Monotherapy and in Combination) and β -3 Agonists (Monotherapy and in Combination)

Storage symptoms associated with male LUTS, such as urgency, frequency, nocturia, and incontinence, are often very bothersome and have a significant impact on quality of life. While these symptoms have traditionally been associated with OAB, storage LUTS can occur across a spectrum of pathophysiological contexts in men, including BPE. As previously detailed in this chapter, first-line management consists of lifestyle modifications and mitigation of contributing risk factors, including caffeine reduction, fluid management, bladder training, and treatment of comorbid conditions such as uncontrolled diabetes or sleep apnea.

When these conservative measures fail to sufficiently control bothersome storage symptoms, pharmacologic treatment becomes appropriate. Several classes of medications are available, and these may be used either as monotherapy or in combination, tailored to the individual's symptoms, presence or not of BOO, comorbidities, anticholinergic burden, and risk of adverse effects. The two main categories for addressing storage symptoms are antimuscarinics and β 3-adrenoceptor agonists. Each class offers distinct advantages and limitations, particularly when used in combination with α -blockers and/or 5-ARIs in patients with coexisting BOO. The pathophysiology of urgency remains elusive and multifactorial, and in the individual patient, treatment is initiated empirically and also based on individual comorbidities and comedications.

Muscarinic receptor antagonists (antimuscarinics)

Monotherapy

Antimuscarinics act by inhibiting muscarinic receptors—particularly the M3 subtype on the detrusor muscle, reducing involuntary bladder contractions during the storage phase that underlie urgency and urinary frequency.¹ Commonly used agents in this class include oxybutynin, tolterodine, solifenacin, darifenacin, fesoterodine, and trospium. Multiple randomized controlled trials and meta-analyses have confirmed the efficacy of all these agents in improving symptoms of urgency and frequency in male patients with predominantly storage LUTS.^{2,3}

In men, especially those with underlying BOO or PVR, cautious use is warranted due to the theoretical risk of urinary retention.⁴ However, trials have demonstrated that, with appropriate patient selection (e.g., PVR < 150 mL, preserved detrusor contractility), antimuscarinic monotherapy is safe and effective.^{5,6} Extended-release once-daily formulations and stepwise dose titration can enhance efficacy while mitigating anticholinergic side effects such as xerostomia and constipation.^{7–9}

A summary of key findings of relevant studies regarding antimuscarinic monotherapy is presented in **TABLE 1**.

TABLE 1 Summary of Key Findings: Antimuscarinic Monotherapy

Study	Study type	Patient population	Drugs studied	Key findings
Stoniute <i>et al.</i> (2023) ²	Cochrane review	Adults with OAB	Multiple antimuscarinics vs. placebo/no treatment	Antimuscarinics significantly reduced urgency and frequency; higher rates of xerostomia and constipation.
Chapple <i>et al.</i> (2008) ³	Systematic review and meta-analysis	Adults with OAB	Multiple antimuscarinics vs. placebo	All agents effective vs. placebo; once-daily extended-release formulations improved tolerability; constipation and xerostomia most frequent side effects.
Abrams <i>et al.</i> (2006) ⁴	RCT	Men with BOO and OAB	Tolterodine vs. placebo	Tolterodine safe and well tolerated in men with BOO; no increase in retention.
Herschorn <i>et al.</i> (2010) ⁸	Pooled analysis of 2 RCTs	Men with OAB	Fesoterodine 4 mg and 8 mg vs. placebo	Significant improvement in storage LUTS; less urge incontinence with fesoterodine 8 mg; low risk of retention in treatment group; constipation and xerostomia most frequent side effects.
Chapple <i>et al.</i> (2007) ⁹	RCT	Adults with OAB (men included)	4 arms: fesoterodine 8 mg, fesoterodine 4 mg, tolterodine ER 4 mg, placebo	Fesoterodine improved storage LUTS, greater improvement in symptoms with 8 mg with higher risk of dry mouth; fesoterodine overall well tolerated.

Abbreviations: BOO, bladder outlet obstruction; ER, extended release; LUTS, lower urinary tract symptoms; OAB, overactive bladder; RCT, randomized controlled trial.

Combination with α -blockers

The combination of antimuscarinics with α -blockers is well supported for men experiencing persistent storage symptoms despite α -blockade. As previously described in this chapter, α -blockers relieve BOO and improve both storage and voiding LUTS. When combined with an antimuscarinic, a synergistic effect on both voiding and storage symptoms is achieved.⁴ Clinical trials such as TIMES (tolterodine and tamsulosin) and SATURN (solifenacin and tamsulosin) have shown significantly greater improvements in symptom scores and quality of life with combination therapy than with either agent alone.^{6,10} Similar outcomes were reported with combination treatment with other tolterodine studies, propiverine and oxybutynin ER,⁵ but not with fesoterodine.¹¹

A summary of key findings of relevant studies regarding combination therapy with antimuscarinics and α -blockers is presented in **TABLE 2**.

TABLE 2 Summary of Key Findings: Combination Antimuscarinic and α -Blocker Therapy

Study	Study type	Patient population	Drugs studied	Key findings
TIMES trial: Kaplan <i>et al.</i> (2006) ⁶	RCT	Men with LUTS and OAB symptoms	Tolterodine ER, tamsulosin, or both	Combination superior to monotherapy for symptom reduction; low risk of retention in tolterodine arms.
SATURN trial: Van Kerrebroeck <i>et al.</i> (2013) ¹⁰	RCT	Men with voiding + storage LUTS	Solifenacin, tamsulosin, combination, or placebo	Combination superior to monotherapy for quality of life improvement and efficacy; good tolerability.
Kaplan <i>et al.</i> (2011) ⁵	Systematic review	Men with storage LUTS, with and without BPO	Multiple antimuscarinics with or without α -blocker/5-ARI	Decreased storage LUTS without increased risk of retention in men without significant BPO and low PVR.
Kaplan <i>et al.</i> (2012) ¹¹	RCT	Men with persistent storage LUTS on α -blockers	Fesoterodine add-on (4 mg with optional increase to 8 mg after 4 weeks)	Fesoterodine did not provide significant benefit over α -blocker monotherapy; side effect rates comparable; low retention rates.

Abbreviations: 5-ARI, 5 α -reductase inhibitor; BPO, benign prostatic obstruction; ER, extended release; LUTS, lower urinary tract symptoms; OAB, overactive bladder; PVR, post-void residual; RCT, randomized controlled trial.

Side effects and long-term risks

Xerostomia, constipation, and blurred vision are the most frequently reported adverse effects, often contributing to discontinuation of antimuscarinics.⁹ Of increasing concern is the long-term risk associated with cumulative anticholinergic exposure. Epidemiologic studies have shown an association of long-term use of antimuscarinics to increased risk of cognitive impairment and dementia, particularly in older adults.^{12,13} This has led to growing emphasis on limiting the use of anticholinergics in men over 65 years, especially those with existing cognitive impairment¹⁴ or high anticholinergic burden from other medications.

Patient and drug selection, dose escalation

When selecting an antimuscarinic agent, clinicians should consider factors such as central nervous system (CNS) penetration, receptor selectivity, and overall tolerability. Oxybutynin, due to its high CNS penetration, is generally less favored in older adults. Newer, more selective agents, such as fesoterodine, which demonstrate improved receptor selectivity and lower CNS penetration, may offer better long-term safety profiles and are more suitable for older patients or those with polypharmacy concerns. There is evidence of CNS safety for other long-acting antimuscarinics in short-term studies.^{14,15} Dose escalation strategies and the use of extended-release formulations may reduce the incidence of side effects and improve drug adherence while preserving therapeutic efficacy.⁷

A practical approach involves initiating treatment at a lower dose, followed by re-assessment within 6 to 12 weeks to evaluate symptom control, side effects, and PVR. Dose escalation should be considered only if the initial

regimen is well tolerated and further symptom improvement is clinically warranted. All dose adjustments should be accompanied by close monitoring to ensure safety, especially in men with evidence of BOO or elevated PVR. The clinician should always prescribe the lowest clinically effective dose for their patients, even in the absence of risk factors, and regularly reassess the efficacy and tolerability of these agents.¹⁶

Beta-3 adrenoceptor agonists

Monotherapy

Beta-3 agonists provide symptom relief by stimulating β_3 -adrenergic receptors in the detrusor muscle, resulting in relaxation during the bladder filling phase. This mechanism increases bladder capacity and reduces urgency without impairing detrusor contraction, which is theoretically useful in men with BOO or elevated PVR.^{1,17}

Clinical trials such as SCORPIO, ARIES, and CAPRICORN have demonstrated that mirabegron significantly improves urgency, frequency, and incontinence episodes in patients with OAB compared with placebo.^{18–21} In male populations, mirabegron is particularly useful due to its lack of impact on detrusor contractility and its favorable safety profile.

A summary of key findings of relevant studies regarding mirabegron monotherapy is presented in **TABLE 3**.

A second β_3 agonist, vibegron, has been studied extensively in various populations and has been approved for use in many countries.²²

TABLE 3 Summary of Key Findings: Mirabegron Monotherapy

Study	Study type	Patient population	Drugs studied	Key findings
SCORPIO: Khullar <i>et al.</i> (2013) ¹⁸	RCT	Adults with OAB	Mirabegron 50 mg and 100 mg daily; tolterodine ER 4 mg (active control); placebo	Both mirabegron doses significantly reduced storage LUTS vs. placebo; efficacy similar to tolterodine for some endpoints. Mirabegron had fewer side effects than tolterodine.
CAPRICORN: Herschorn <i>et al.</i> (2013) ¹⁹	RCT	Adults with OAB	Mirabegron 25 mg and 50 mg vs. placebo	Mirabegron showed significant reduction in LUTS vs. placebo; 50 mg dose showed greater improvement in voided volume and incontinence episodes.
ARIES: Nitti <i>et al.</i> (2013) ²¹	RCT	Adults with OAB	Mirabegron 50 mg and 100 mg daily vs. placebo	Both mirabegron doses produced significantly greater reductions in frequency and incontinence vs. placebo; favorable safety profile.

Abbreviations: ER, extended release; LUTS, lower urinary tract symptoms; OAB, overactive bladder; RCT, randomized controlled trial.

Combination with α-blockers

Mirabegron can be safely combined with α-blockers to improve persistent storage LUTS in men already optimized on α-blockade. The MATCH and PLUS studies support this strategy, showing greater efficacy in symptom reduction with the combination of mirabegron and tamsulosin, without increased risk of catheter-dependent urinary retention.^{23,24} This combination may be particularly advantageous in patients with storage LUTS and decreased detrusor contractility or higher baseline PVR.

A summary of key findings of relevant studies regarding mirabegron and α-blocker combination therapy is presented in **TABLE 4**.

TABLE 4 Summary of Key Findings: Mirabegron and α-Blocker Combination Therapy

Study	Study type	Patient population	Drugs studied	Key findings
MATCH: Kakizaki <i>et al.</i> (2020) ²³	RCT	Men with OAB symptoms already on tamsulosin	Tamsulosin + mirabegron vs. tamsulosin + placebo	Combination improved storage symptoms and overall LUTS more than tamsulosin alone.
PLUS: Kaplan <i>et al.</i> (2020) ²⁴	RCT	Men with persistent OAB symptoms despite tamsulosin	Tamsulosin + mirabegron vs. tamsulosin + placebo	Combination showed greater reductions in storage LUTS; urinary retention rates higher in the combination group but overall low.

Abbreviations: LUTS, lower urinary tract symptoms; OAB, overactive bladder; RCT, randomized controlled trial.

Similarly, vibegron, versus placebo, has been shown to be safe and efficacious in reducing persistent OAB symptoms in men treated with α-blockers with/without 5ARIs.²⁵

Side effects

Mirabegron is generally well tolerated, with the most common side effects being hypertension, nasopharyngitis, and urinary tract infection.²⁶ It is not associated with cognitive side effects like antimuscarinics, making it a favorable choice for older adults and those with polypharmacy concerns.²⁷ However, blood pressure monitoring is recommended, especially in patients with hypertension, and is essential in patients with poorly controlled hypertension.

Vibegron is also well tolerated. The most common adverse events in clinical trials were headache and nasopharyngitis.²⁸ Unlike mirabegron, vibegron has not been shown to increase blood pressure. With indirect comparison of vibegron and mirabegron in systematic reviews and network meta-analyses^{29,30} and direct comparison,³¹ the incidence of hypertension of both drugs was equivalent and similar to that of placebo.

Patient and drug selection, dose escalation

Mirabegron is an appropriate option for patients who are intolerant of antimuscarinics, have a high anticholinergic burden, or are at increased risk of cognitive decline. It should be used with caution in patients with poorly controlled hypertension, as elevations in blood pressure have been reported. Moreover, individuals with high cardiovascular risk have generally been excluded from pivotal clinical trials; therefore, mirabegron should be prescribed cautiously in this population.

In the UK, European Union, Brazil, Japan, and other Asian countries and regions (including Hong Kong, China, and South Korea), the recommended dose is 50 mg/day, while a dose of 25 mg/day is available for special populations (e.g., patients with severe renal impairment or moderate hepatic impairment). In North America, Australia, and some Asian countries (e.g., Singapore and Malaysia), the recommended starting dose is 25 mg/day, with an optional increase to 50 mg/day.³²

Pivotal studies reported no significant change in PVR and low risk of urinary retention with mirabegron;^{18,19,23,24} however, monitoring PVR at baseline and regularly during clinical follow-up is recommended, especially in high-risk patients with significant BOO.

Vibegron, another β -3-adrenergic receptor agonist with a similar mechanism of action, is emerging as a promising alternative and may offer comparable efficacy, with similar evidence of safety in men in randomized studies.^{25,33}

Combination therapy: Antimuscarinics and β -3 agonists

Combining an antimuscarinic with a β -3 agonist targets detrusor overactivity through dual pathways—reduction of cholinergic stimulation and enhancement of adrenergic relaxation. This combination provides an option for patients with persistent symptoms despite monotherapy and is supported initially by evidence from the phase 2, multi-dose trial (SYMPHONY)³⁴ and studied further in the add-on trial (BESIDE)³⁵ and combination starting trial (SYNERGY),³⁶ which combined mirabegron with solifenacin. No cases of urinary retention were observed in these trials.

A summary of key findings of relevant studies regarding mirabegron and anticholinergic combination therapy is presented in **TABLE 5**.

In men, this combination is typically reserved for refractory cases, and where careful monitoring of PVR and cognitive risk is feasible. While the risk of urinary retention is low, caution is warranted in patients with significantly impaired bladder emptying and BOO. In older or frail patients, preference may be given to antimuscarinics that have more favorable CNS impact if used in combination with a β -3 agonist.¹⁴

TABLE 5 Summary of Key Findings: Mirabegron and Anticholinergic Combination Therapy

Study	Study type	Patient population	Drugs studies	Key findings
SYMPHONY: Abrams <i>et al.</i> (2017) ³⁴	RCT	Adults with OAB	Mirabegron + solifenacin (various doses) vs. monotherapy vs. placebo	Combination improved symptoms more than monotherapy.
BESIDE: Drake <i>et al.</i> (2016) ³⁵	RCT	OAB patients with incontinence despite solifenacin 5 mg	Solifenacin 5 mg + mirabegron vs. solifenacin 5 mg or 10 mg	Combination superior to both doses of solifenacin monotherapy.
SYNERGY: Herschorn <i>et al.</i> (2017) ³⁶	RCT	Adults with OAB	Mirabegron + solifenacin vs. monotherapy vs. placebo	Combination produced greater reductions in storage LUTS; slightly higher side effects in combination group.

Abbreviations: LUTS, lower urinary tract symptoms; OAB, overactive bladder; RCT, randomized controlled trial.

Special considerations: Subpopulations and real-world challenges

Adherence: Persistence with therapy remains low across all classes of antimuscarinics, driven largely by side effects (dry mouth, constipation) and lack of perceived benefit. Extended-release formulations, choice of newer and more selective agents, and better counseling may improve outcomes. Beta-3 agonists have slightly better short-term persistence.^{37,38}

Cognitive risk: The cumulative anticholinergic burden in older patients is an increasing concern. Anticholinergic burden refers to the cumulative risk of taking multiple medications with anticholinergic properties, including the risk of increased side effects and the development of dementia.³⁹ Patients with dementia risk or on CNS-acting medications (e.g., selective serotonin reuptake inhibitors [SSRIs], antipsychotics) should generally try to avoid antimuscarinics.⁴⁰ However, there are instances, such as in patients who are unresponsive to β -3 agonists, when it may be appropriate to prescribe an antimuscarinic. Changes in cognition have not been reported in short-term studies with fesoterodine,⁴¹ trospium,⁴² and solifenacin.^{15,43} Similarly, darifenacin has evidence of CNS safety,⁴⁴ except for one study.⁴⁵ Oxybutynin has been shown to have adverse cognitive effects,⁴⁶ and there are case reports of tolterodine and cognitive dysfunction.⁴⁷ Although short-term studies have shown safety, long-term use may increase the dementia risk.^{13,48} Elderly patients who are prescribed antimuscarinics should be carefully monitored for benefit versus adverse events.¹⁴ Before prescribing an antimuscarinic medication, the patient's medication list should be reviewed to identify other medications with anticholinergic properties. Non-pharmaceutical recommendations, such as lifestyle changes, can also be reinforced to reduce the need for medication or increased dosage.

Storage LUTS with an elevated PVR and BOO: Men with elevated PVR (> 150–200 mL) or significant voiding symptoms are best managed with an α -blocker combined with a β -3 agonist. Antimuscarinics should be avoided or used cautiously in these settings.¹⁶

Cost and access: Across healthcare systems, cost considerations and different reimbursement policies may limit access, particularly to β -3 agonists, which are often more expensive than generically available antimuscarinics.

Topic	Recommendation	LoE	GoR
Muscarinic Receptor Antagonists	Offer muscarinic receptor antagonists alone to men with predominant storage LUTS.	II	B
	Offer muscarinic receptor antagonists in combination with an α -blocker to men with persistent storage LUTS despite therapy with α -blockers.	II	B
	Avoid the use of antimuscarinics in men with elevated PVR (> 150 mL) or cognitive impairment.	II	B
Beta-3 Agonists	Offer β -3 agonists to men with predominant storage LUTS.	II	B
	Offer β -3 agonists in combination with an α -blocker to men with or persistent storage LUTS despite therapy with α -blockers.	II	B

Abbreviations: GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms, PVR, post-void residual.

Challenges in Medical Treatment of LUTS

In our daily clinical practice, many challenges arise in the medical treatment of men with LUTS. This section discusses the impact of intravesical prostatic protrusion, treatment adherence, and nocturia. Finally, considerations for medication selection and patient follow-up are presented.

The challenge of intravesical prostatic protrusion (IPP)

IPP is an anatomical variant of BPE present in about 10% of men with BPE/LUTS. IPP is classified as grade I (< 5 mm), grade II (5–10 mm), and grade III IPP (> 10 mm), with the latter representing severe IPP.¹

IPP has a strong impact on BPO and the degree of BPO increases with the severity of IPP.² Among patients with grade I or II IPP, only 21% demonstrate obstruction, while this percentage rises to 96% in patients with grade III IPP.^{2,3} Furthermore, the severity of prostatic protrusion has also been shown to exert an independent effect on the risk of urinary tract infection, acute urinary retention, likelihood of requiring surgery and, more generally, on the clinical progression of BPE/LUTS.⁴

From a therapeutical viewpoint, the detection of an intraprostatic protrusion of the prostate in patients with BPE is of great clinical importance, as it can affect the efficacy of pharmacologic treatment.⁵ In patients with LUTS, an IPP > 10 mm appears to predict poor response to α -adrenoceptor antagonists (α -blockers) in terms of subjective or objective outcomes.^{6–8}

Patients with IPP also demonstrate a poor response to 5-ARIs, either as monotherapy or in combination with α -blockers. Data shows that the presence of IPP is significantly associated with a higher risk of treatment failure, acute urinary retention, and surgical intervention in patients with BPE/LUTS assuming dutasteride.^{9,10} Failure of 5-ARI therapy in preventing clinical progression has also been reported when dutasteride is used as add-on treatment in patients with IPP who are resistant to α -blocker monotherapy.¹¹ Similar to α -blockers, lack of response to 5-ARIs has been observed mainly in men with “significant” IPP, typically exceeding a threshold of 10 mm to 13 mm in different studies.

Currently, there are insufficient published data to evaluate the efficacy of other pharmacologic options—such as PDE5Is or herbal therapies—in patients with significant IPP.

Overall, available evidence suggests that patients with BPE/LUTS presenting with severe IPP (> 10 mm, grade III) often exhibit resistance to common pharmacologic treatments. This should be taken into consideration in the treatment selection process to avoid long, ineffective trials of pharmacologic therapy. Patients with grade III IPP should be informed that currently available drugs are unlikely to offer significant and durable symptom relief, and in the case of severe LUTS, more invasive treatment options may be considered as first-line therapy, avoiding a predictable therapeutic delay. Therefore, the degree of IPP should be assessed routinely before counseling patients with LUTS about potential therapeutic solutions.

The challenge of treatment adherence

Treatment adherence to medication for LUTS is generally low, with only 30% of men remaining compliant with treatment after 12 months.¹² A systematic review and a network meta-analysis on the medical management of OAB found that the overall persistence and adherence rates of anticholinergics and mirabegron at 12 months were 21.8% and 58.9%, respectively.¹³ Persistence and adherence rates were associated with age, gender, anticholinergic exposure history, type of medication, study type, and study year.¹³

The reasons for lower adherence are numerous and only partially understood. A major factor appears to be the discrepancy between patient expectations and the perceived improvement in quality of life. Adverse events may also lead to treatment discontinuation. In addition, adherence is consistently lower with combination therapy compared with monotherapy and tends to be lower in real-world studies compared with clinical trials.¹² Low adherence has also been associated with higher hospitalization rates, emphasizing the need to improve treatment adherence to BPE/LUTS drugs.¹²

Furthermore, patients with easier and more frequent access to follow-up visits may remain on therapy longer, as they feel “followed and cared,” and this may explain the consistently reported higher adherence in clinical trials. These observations underline the importance of adequate counseling at two key stages: a) during the initial visit, to explore the individual’s values and preferences and to set realistic treatment expectations; and b) during follow-up visits, to identify and appropriately address reasons for complete or partial dissatisfaction.

The challenge of nocturia and nocturnal polyuria

The International Continence Society (ICS) defines nocturia in two ways;¹⁴

- **Symptom:** The number of times urine is passed during the main sleep period. After waking to void for the first time, each subsequent urination must be followed by sleep or the intention to sleep. The number of nocturnal voids should be quantified using a bladder diary.
- **Sign:** The number of times an individual passes urine during the main sleep period, from the time they have fallen asleep up to the intention to rise from that period. This measure is derived from the bladder diary.

Nocturia is very common in patients with LUTS, often due to the increased prevalence of comorbid conditions in the age groups affected by BPE. Establishing a causal link between nocturia and BPE is challenging, and without such evidence, it is not appropriate to suggest that nocturia will improve with BPE treatment with any degree of certainty. Voiding and storage symptoms should be regarded as potentially independent variables. Overall, available evidence suggests that nocturia is unlikely to improve with either medical or interventional treatment of BPE.

Crucially, nocturia often results from multiple contributory mechanisms other than BPE, mandating a detailed and comprehensive clinical evaluation. A properly completed 3-day bladder diary is particularly valuable in this context.¹⁵ Factors related to urine production are:¹⁴

1. **24-hour polyuria**—Excessive excretion of urine resulting in profuse and frequent micturition. Defined as > 40 mL per kg body weight per 24 hours.
2. **Nocturnal polyuria**
 - **Symptom:** The passage of large volumes of urine during the main sleep period. This should be quantified using a bladder diary.
 - **Sign:** Excessive production of urine during the individual’s main sleep period. This should be quantified using a bladder diary.

Sleep disturbance is another key factor, as any sleep disorder increases the risk of waking at night and voiding. In many cases, it may be difficult for patients to determine whether they awaken due to the need to void or they voided because they were already awake.

Lower urinary tract dysfunction (LUTD) may also contribute, particularly in cases of overactive bladder syndrome,¹⁶ underactive bladder syndrome,¹⁷ and chronic pelvic pain/bladder pain syndrome.¹⁸

An assessment algorithm was developed in the PLanning Appropriate Nocturia Evaluation and Treatment (PLANET) study, which performed systematic reviews of nocturia due to cardiovascular,¹⁹ nephrologic,²⁰ endocrine,²¹ neurological,²² and sleep medicine²³ causes. Together with prior systematic reviews of urologic causes of nocturia, these findings were integrated into an overarching consensus statement.²⁴ Key relevant conditions from past medical history need to be identified, notably:

1. Sleep medicine: Insomnia, restless legs syndrome, and periodic limb movements of sleep, parasomnias, and obstructive sleep apnea.
2. Cardiovascular: Hypertension (which may be nocturnal hypertension with normotensive daytime blood pressure) and congestive heart failure.
3. Renal: Chronic kidney disease.
4. Endocrine: Diabetes mellitus or insipidus, overactive thyroid or profoundly underactive thyroid, pregnancy/menopause, and testosterone deficiency.
5. Neurology: Most neurological diseases are potentially relevant. The possibility that one of these conditions may be present without previous diagnosis should always be considered. Numerous medications are potentially relevant—most notably diuretics, but also some antihypertensives, medicines that cause glucose to be excreted in the urine, lithium (which can induce nephrogenic diabetes insipidus), and steroids (glucocorticoid or mineralocorticoid). Adjusting the drug regimens for medicines of this type is rarely straightforward.

Conservative management recommendations include fluid management,²⁵ and evening elevation of the legs. Fluid advice is reasonable if there is a clear behavioral contribution to nocturia. If fluid intake is secondary to fluid loss, i.e., catching up to compensate for fluid depletion (indicated by severe thirst), fluid restriction is not recommended. Evening leg elevation is commonly recommended, and in some cases compression stockings may help reduce nocturia episodes but generally provide marginal benefit at best.

Medications for LUTD can be trialed if there is a primary indication and no major contraindication—for example, a trial of OAB medications if urgency is present, particularly for nocturnal urgency. Medications for treating voiding dysfunction may also be considered, but patients should be counseled that improvement in nocturia is uncertain. The advantage of pharmacologic therapy is that treatment can be discontinued if it fails to improve symptoms.

Currently, the only medication indicated for nocturia specifically is desmopressin.^{26,27} Desmopressin acetate, a synthetic analog of arginine vasopressin (AVP), is a selective agonist of vasopressin receptor 2 that induces antidiuresis and has been shown to be effective and well tolerated in adults with nocturia associated with nocturnal polyuria (NP), reducing urine production and improving nocturia in NP patients.¹⁵ Most clinical trials evaluating desmopressin have been characterized by short follow-up durations, study limitations, and imprecision. The efficacy of desmopressin is dose dependent, and dose titration is fundamental to achieving

a therapeutic effect. Desmopressin is available in oral tablet, sublingual tablet, and nasal spray formulations, although not all formulations are available in every single country.

In men < 65 years with NP, desmopressin treatment should be initiated at a low dose of one 0.1-mg tablet per day, taken before bedtime. The dose can be titrated over a 4-week period up to a maximum of 0.4 mg per day. Sublingual tablets and nasal spray formulations are much more powerful than common tablets, and dose titration should therefore be adjusted accordingly.

There are important cautions for prescribing this treatment to reduce risk of hyponatremia, particularly in the elderly, those on multiple medications, and those with low sodium at baseline. In men > 65 years, the suggested dose usually corresponds to the lowest dose available for a given formulation and cannot be increased in the case of lack of therapeutic response. However, even a low dose should be prescribed with particular caution in patients of over age of 75 years, a group that is strongly underrepresented and under-investigated in the available trials.

If a contributory medical mechanism is likely, discussion with medical specialists in relevant therapeutic areas may be initiated. However, nocturia is not commonly evaluated or managed in specialties such as cardiovascular or endocrine medicine. Obstructive sleep apnea is a common (underdiagnosed) condition, which can be a major driver of NP, for which continuous positive airway pressure (CPAP) therapy can yield reduction in nocturia.²⁸ Some patients, however, do not tolerate the CPAP mask well, and will ultimately decide for themselves whether to continue treatment with CPAP.

Strategy in treatment selection

Several drugs are available for the treatment of LUTS, which may be used as monotherapy or in combination.

Physicians worldwide consider α -blockers the “usual” first-line monotherapy, and switch after 6 to 8 weeks to different drugs or to a combination treatment with 5-ARIs, antimuscarinics, or β -3 agonists in the case of symptom persistence. In particular, the persistence of storage symptoms may justify add-on treatment with antimuscarinics or β -3 agonists, or a switch to antimuscarinic or β -3 agonist monotherapy. In cases of larger prostate (e.g., > 40 mL), which indicates a higher risk for disease progression and better response to 5-ARIs, there is a strong rationale for prescribing either combination therapy with an α -blocker and 5-ARI, or 5-ARI monotherapy. Patients with LUTS and erectile dysfunction can be successfully treated with tadalafil 5 mg once daily, following the “two birds with one stone” principle. Tadalafil can also be safely used in combination with α -blockers or 5-ARIs without any significant tolerability issues. These general principles are well reflected in therapeutic algorithms and continue to inform real-life prescribing patterns globally.^{29,30}

Individual patient characteristics—such as symptom severity and type, prostate volume, $Q_{\max}$, PVR, and presence of middle lobe—should guide the selection of appropriate treatment. Predictive models have been developed to better inform both clinicians and patients and enrich their discussion. The available predictive models and their applications are presented in [Chapter 6](#) of this Consultation.

From a therapeutic strategy perspective, the balance between success and failure should also be dependent on the tolerability profile. Comorbidities and patient preferences are key factors to consider for achieving an individualized approach. Less selective α -blockers (doxazosin, terazosin) have clear antihypertensive activity, which can increase the risk of orthostatic hypotension and falls, particularly in hypotensive patients or patients taking other antihypertensive drugs, due to possible synergic effects. On the other hand, more selective agents (alfuzosin, and especially tamsulosin and silodosin) exhibit a more favorable cardiovascular safety profile but are associated with an increased risk of dry ejaculation.

The 5-ARIs are the only drugs for BPE/LUTS that can undoubtedly modify the natural history of the disease and reduce the risk of progression, in terms of AUR and need for surgery. However, their sexual side effects, the reported (although questionable) persistence of side effects after discontinuation in a few cases (the so-called “post-finasteride syndrome”), and concerns about possible psychological adverse events may make urologists hesitant to prescribe these drugs from the beginning or for patients who are interested in preserving their sexual function. On the other hand, phytotherapeutics (*Hexanic Serenoa repens*) have a low incidence of adverse events, especially those related to sexual and ejaculatory function but with a modest efficacy.

Antimuscarinics may cause xerostomia and constipation, and have a higher risk of cognitive impairment and dementia, therefore limiting their use in men with constipation, or men over 65 years, with existing cognitive impairment or high anticholinergic burden from other medications. Beta-3 agonists may be a better options for these patients, though they should be avoided in those with poorly controlled hypertension.

Given the big differences among LUTS drugs in terms of mechanism of action, clinical outcomes, and tolerability profile, an optimal treatment strategy should be guided by thorough patient assessment and shared discussion. This approach allows clinicals to tailor therapy from the outset, avoid ineffective trials, prevent adverse events where possible, and select the most appropriate medical therapy for each individual patient.

Follow-up

Patients receiving α -blockers, muscarinic receptor antagonists, β -3 agonists, or PDE5Is, either as monotherapy or in combination with 5-ARIs, should be initially reviewed after 4 to 6 weeks to assess symptomatic benefit and adverse events. If a favorable balance between efficacy and tolerability is achieved, treatment may be continued with regular follow-up visits. For patients receiving 5-ARIs, the first follow-up should be after 3 to 6 months and again at 12 months.

Thereafter, annual review is suggested for all patients. However, patients should be informed that BPE/LUTS are progressive conditions and advised to seek medical attention in the case of symptom deterioration, regardless of the scheduled follow-up timeframe. Follow-up visits should always include a detailed history, symptoms questionnaires, uroflowmetry, and PVR volume measurement. In patients presenting with predominantly storage-phase symptoms or nocturnal polyuria, a frequency-volume chart should be completed before any follow-up visit.²⁹

In patients taking 5-ARIs and adhering to a PSA screening protocol, it is important to set a new PSA baseline level after 6 months of treatment.

In patients taking desmopressin, serum sodium concentration should be measured frequently during the first month of treatment, and thereafter every 3 months. However, patients taking desmopressin who are older than 65 years or present a higher risk of hyponatremia, a stricter monitoring schedule should be proposed for the duration of treatment.

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Watchful Waiting and Lifestyle Interventions

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Phosphodiesterase Type 5 Inhibitors (Monotherapy and in Combination)

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Phytotherapy for Male LUTS

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COMMITTEE

04

**INVASIVE SURGICAL
TREATMENTS**

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Table of Contents

Introduction by Prof. Peter Gilling, CNZM, MD, FRACS	155
Principles of Electrosurgery by Lori Lerner, MD	155
Physics	156
Mechanisms of delivery: electrosurgery and tissue effect	158
Types of electrodes	161
Applications in BPH	162
Complications	163
Conclusion	165
Transurethral Incision of the Prostate (TUIP) by Lori Lerner, MD	165
Transurethral Resection of the Prostate (TURP) by Akhil Das, MD, FACS	168
Equipment	169
Technique	169
Open Simple Prostatectomy by Tevita Aho, FRACS(Urol), FRCS(Eng)	170
Reducing the morbidity of OSP	171
Level 1 evidence comparing endoscopic BPO therapies to OSP	172
Studies comparing OSP to less invasive nonendoscopic forms of AEP (LSP and RASP)	172
Conclusion	173
Anatomical Endoscopic Enucleation of the Prostate by Naeem Bhojani, MD	178
Introduction	178
Energy sources used for AEEP	179
Holmium laser enucleation of the prostate (HoLEP)	179
Thulium:YAG laser enucleation of the prostate	179
LBO:YAG enucleation of the prostate (PVP-EP)	179
Thulium fiber laser enucleation of the prostate	180
Bipolar enucleation of the prostate (Bipolar)	180
Surgical techniques: <i>en bloc</i> vs. lobe-based approaches	180
Early apical release	180
Safe morcellation: key principles	181
Advantages of AEEP	181

Table of Contents

Disadvantages of AEEP	181
Patient selection and preoperative considerations	181
Preoperative evaluation	181
Future perspectives in AEEP	182
Conclusion	182
Vaporization of the Prostate <i>by Luca Cindolo, MD, PhD, FEBU</i>	182
Robotic Simple Prostatectomy <i>by Juliet Han, MD</i>	185
Benefits and comparison with other techniques	185
Surgical technique	187
Transperitoneal: transvesical approach	187
Transperitoneal: transcapsular approach (Millin technique)	188
Intrafascial simple prostatectomy	189
Comparing enucleation techniques	190
Mucosal reconstruction: trigonization or circular anastomosis	190
Single-port robotic simple prostatectomy	190
Conclusion	190
Aquablation <i>by Christopher Kelly, MD</i>	191
Conclusion <i>by Prof. Henry Woo, MBBS, DMedSc, FRACS(Urol), FACS</i>	196
Procedural Video	197
References	198

Introduction

In 2012, Committee 5 of the ICUD BPH Consultation reported on “Surgical Therapies and New Treatments.” The resulting Chapter had a significant focus on the various types of Laser Prostatectomy and the different wavelengths involved, which were topical at the time. TURP and Open Prostatectomy were covered and a relatively small section was devoted to Minimally Invasive Treatments, with a range of “legacy” procedures, which are no longer recommended for a variety of reasons.

The 2025 BPH Consultation reflects the changing emphasis in benign prostatic hyperplasia (BPH) surgical treatments with a separate Committee and Chapter now for minimally invasive therapies (MISTs) and an expanded repertoire of invasive surgical treatments with a couple of notable additions and consolidation of existing techniques. Robotic assisted simple prostatectomy and Aquablation have quite quickly become standard treatments with a sound scientific backing and are recommended in the American Urologic Association (AUA) and European Association of Urology (EAU) guidelines. Robotic assistance for both techniques is a notable signal for the future of surgical techniques. The various laser wavelengths have consolidated behind two main techniques—enucleation and vaporization. Anatomical Endoscopic Enucleation of the Prostate has become an overarching term for a family of techniques and wavelengths and is steadily gaining ground on TURP. Laser Vaporization centers now on the 180 W 532 nm “GreenLight” laser rather than the spread of wavelengths and different power levels from 2012.

This chapter is a good representation of the “Invasive” BPH treatments currently on offer and includes those available in developing countries as well as the latest offerings with cutting-edge technology.

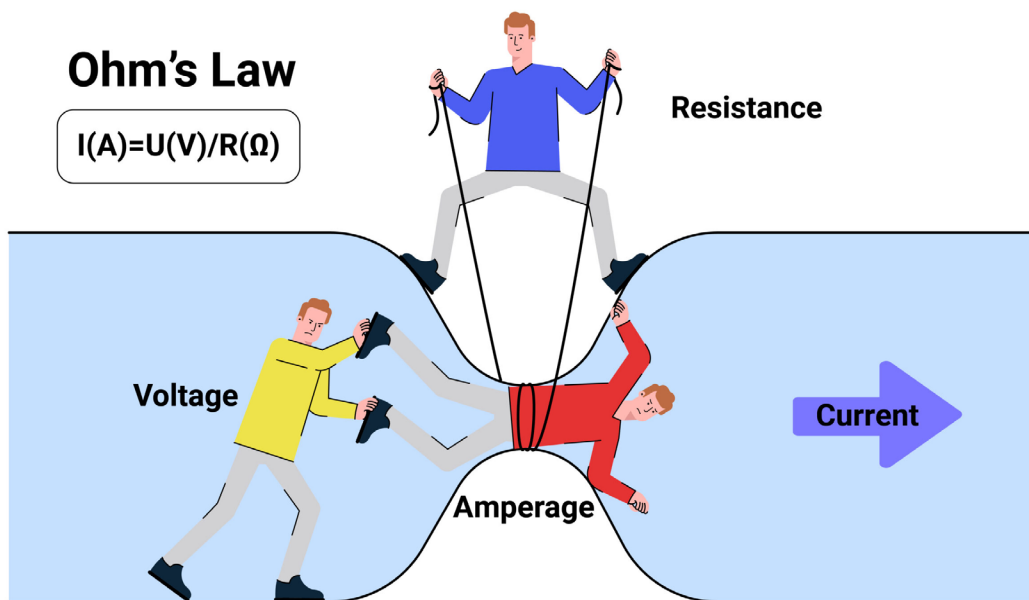
Principles of Electrosurgery

While reports exist of even earlier utilization, the clearest use electricity for medical purposes dates to the 18th century. The following 100 years saw continued evolution, and in 1897, Franz Nagelschmidt coined the term diathermy, launching widespread acceptance among surgeons.^{1,2} Today, electrosurgery is defined as the application of a high-frequency electric current to biological tissue as a means to cut, coagulate, desiccate, or fulgurate. Unlike electrocautery, which utilizes a heated instrument to directly treat tissue, electrosurgery includes the patient in the circuit and current enters the patient’s body. In Urology, both monopolar and bipolar electrosurgery are frequently utilized in open and endoscopic surgery—the main difference between the two being the pathway of the current. When applying electrosurgery for the surgical treatment of benign prostatic hyperplasia, the added requirement of use in a fluid environment is essential.

Physics

To understand electrosurgery, one must first understand electrical circuits. As the electrical current is delivered, it travels through and heats tissue. Electrical current (I) is defined as the amount of electricity (flow of electrons) moving through a conductor over a specific amount of time. Voltage (V) is the force that causes this flow (current) against Resistance (R). Resistance, which is present in all human tissues (termed impedance with high-frequency AC), is measured in Ohms. Electrosurgery requires the presence of a circuit for current to flow—described by Ohm's Law (**FIGURE 1**).

FIGURE 1 Ohm's Law.



Source: Elementary notions of electrosurgery. Accessed June 21, 2025.

<https://arce.ro/elementary-notions-of-electrosurgery>³

When voltage is applied to tissue, a simple electrical circuit forms between the voltage source and the tissue. The generated electrical current passes through the tissue, which acts as a resistor within this circuit. The higher the inherent tissue resistance is, the greater the voltage that is needed to push the current through. Water content in tissue impacts resistance, with the higher the water, the less resistance there is and the lower the voltage that is required. When tissues are cauterized during surgery, they become less electrically conductive, increasing their resistance, and requiring higher amounts of voltage for current to penetrate to the tissues beneath.²

Heat is produced when the electrical energy of the voltage source is converted into thermal energy. In other words, heat is created as a result of time, resistance, and current per cross-sectional area. The smaller the electrode, the

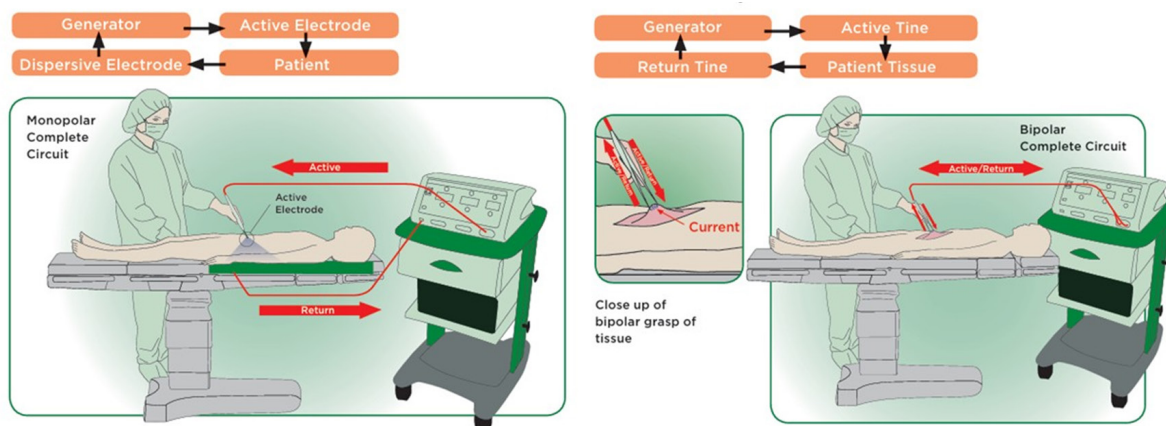
more localized the heat delivery. In contrast, large electrodes require a longer duration of current application to achieve the same heat production.³

There are two types of electrical current—Direct Current (DC) and Alternating Current (AC). With DC, the electrons flow in only one direction (e.g., simple battery). With AC, the electrons constantly change direction, moving between positive and negative poles as the current flows along a circuit (e.g., electrical wall outlet). The frequency at which AC oscillates between the positive and negative poles is measured in Hertz (Hz), or cycles per second (1 Hz = 1 cycle/sec).

Standard electrical current alternates at a frequency of 60 cycles per second (Hz). While electrosurgical systems used in the operating room could function at this frequency, electrical current transmitted through body tissue at 60 cycles would cause excessive neuromuscular stimulation, which could lead to electrocution. In 1881, Morton found that an oscillating current at a frequency of 100,000 Hz could pass through the human body without inducing pain, spasm, or burn. As nerve stimulation requires a certain physiological time, rapidly changing direction of the current prevents depolarization and, therefore, neuromuscular activity ceases. Modern-day electrosurgical units (ESU) use frequency ranges of 200,000 Hz to 5,000,000 Hz.^{2,4,5}

Although electrosurgery is traditionally described as either in bipolar or monopolar mode, in fact, all electrosurgery is bipolar. A closed circuit is necessary so that electrical current can flow through tissue from an entry (active electrode) through tissue to an exit (the return or dispersive electrode). If only the entry electrode is active and the return electrode is inactive, the application is called monopolar electrosurgery. If both the entry and return electrodes are active, the application is bipolar (**FIGURE 2**).

FIGURE 2 Monopolar and bipolar modes of electrosurgery.



Source: Principles of Electrosurgery. Accessed June 21, 2025.

<http://embiolab.ifac.cnr.it/SitesP2/biblio/dainserire/Electrosurgery/Electrosurgery1.pdf>⁶

In monopolar electrosurgery, the narrow “active electrode” concentrates the current (and therefore the power) at the intended site of action, elevating the intracellular temperature. The “dispersive electrode” acts as the other pole, “processing” the same amount of current but dispersing it over a much larger surface area (the grounding pad). This dispersion of current prevents the temperature from rising enough to injure underlying skin, thereby preventing tissue injury.

Monopolar energy has a more superficial and narrower field of effect, while bipolar has a greater depth and diameter effect. With bipolar energy, the tissue between the jaws is treated and desiccated, which increases resistance. Therefore, as continued energy is applied, the current flows toward the path of least resistance, which is neighboring tissue. As a result, bipolar energy can lead to a greater degree of thermal effect with more tissue ischemia as compared to monopolar energy.^{3,4} The presence of charring, which increases tissue resistance, can alert the user that spread of thermal injury will occur. At times this could be the desired effect but when this is not the case, application of energy should be stopped. Modern generators can measure resistance and alter delivery of energy.

Mechanisms of delivery: electrosurgery and tissue effect

The temperature rise of the tissue from electrosurgery leads to tissue effects such as cutting (vaporization), fulguration (coagulation), and desiccation (dehydration). Depending on how the energy is applied and the tools utilized, any of these effects can be realized. In fact, any surgical tool that increases tissue temperature can achieve these same effects. The transformation of electrical energy to heat follows Joule’s Law, which is expressed by the following equation:

$$\text{Energy} = (\text{current}/\text{cross-sectional area}) \times \text{Resistance} \times \text{Time}$$

Variables that impact the tissue effect produced during electrosurgery include the current, the size of the active electrode, the water content of the tissue being treated, and time.⁵

a) Current:

The higher the electrical current, the more heat is produced at the tip of the active electrode. Modern ESUs have the option to alter current settings and intensity, which will impact tissue effects.

b) Size of the active electrode:

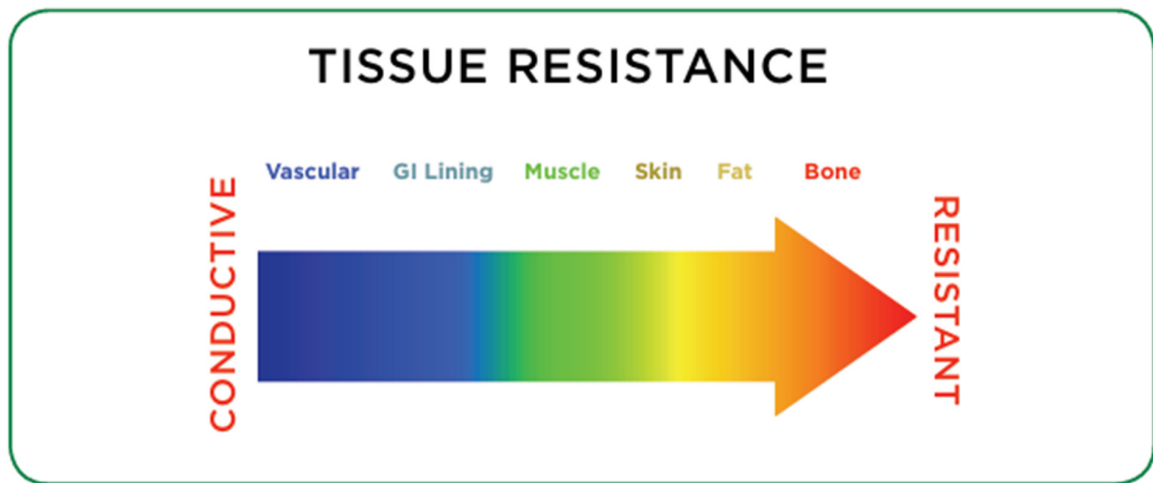
Generated heat is inversely proportional to the surface area of the electrode; thus, the smaller the electrode, the more localized and intense the heat energy produced. A 50% reduction in the circular radius of the electrode leads to a 16-fold increase in thermal change.

c) Type of tissue:

Tissues vary widely in resistance, a factor largely dependent on the water content of the cells and the vascularity of the tissue, which is another source of water to the target area. For example, bone and fat have

higher electrical resistance than skin and muscle (**FIGURE 3**). Compounding this, when electrosurgery is applied, progressive tissue desiccation increases tissue resistance, which reduces current intensity. Eschar has a relatively high resistance to electrical current, both in tissue and on the electrode. As such, keeping electrodes clean and free of charred material will enhance performance by maintaining a lower resistance within the surgical circuit.

FIGURE 3 Tissue resistance.



Source: *Principles of Electrosurgery*. Accessed June 21, 2025.

<http://embiolab.ifac.cnr.it/SitesP2/biblio/dainserire/Electrosurgery/Electrosurgery1.pdf>⁶

d) Time:

Regardless of the energy setting on the ESU, the longer the generator is activated, the more heat is produced. If resistance to the current is high, it will follow the path of least resistance and travel to adjacent tissue causing thermal spread. Recognizing this effect can both enhance the desired result or reduce risk if this is not the intent.

Electrosurgical waveforms: cut, blend, and coagulation:

Electrosurgical generators are able to produce a variety of electrical waveforms. As waveforms change, so will the corresponding tissue effects. The ESUs used in modern electrosurgery provide two outputs labeled cut (Yellow) and coagulation (Blue).

- **Cutting mode (Yellow):**

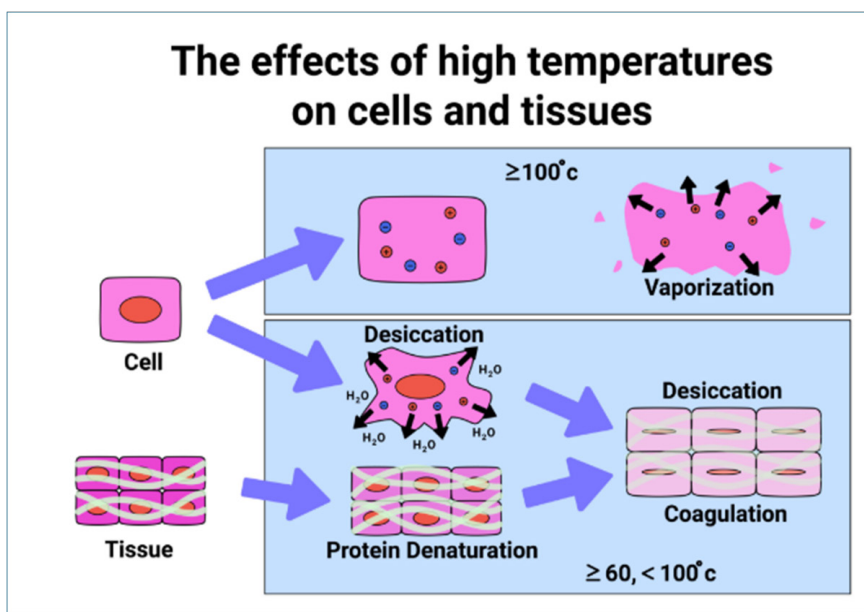
In this mode, the unit generates a high-frequency current with a low voltage and a 100% work cycle. For as long as the pedal/button is depressed, the unit is active with the current crossing the patient's body the

entire time. This leads to rapid temperature rise and resulting vaporization, producing a “cut” with minimal adjacent tissue injury.

- **Coagulation mode (Blue):**

In this mode, the unit generates a high-frequency AND high-voltage current with a limited work cycle (about 6%) given the limited time it is activated. This interrupted, dampened cycle produces less heat and, as such, creates a coagulum (hydrothermal bridges between proteins are broken and those proteins reconfigure and bind new structures). This occurs at temperatures between 60–100 °C (**FIGURE 4**). Coagulation can be accomplished via contact coagulation (desiccation/dehydration of the cells)—usually confined to larger vessels, or spray coagulation (fulguration) for broad area coagulation.

FIGURE 4 Effects of high temperatures on cells and tissues.



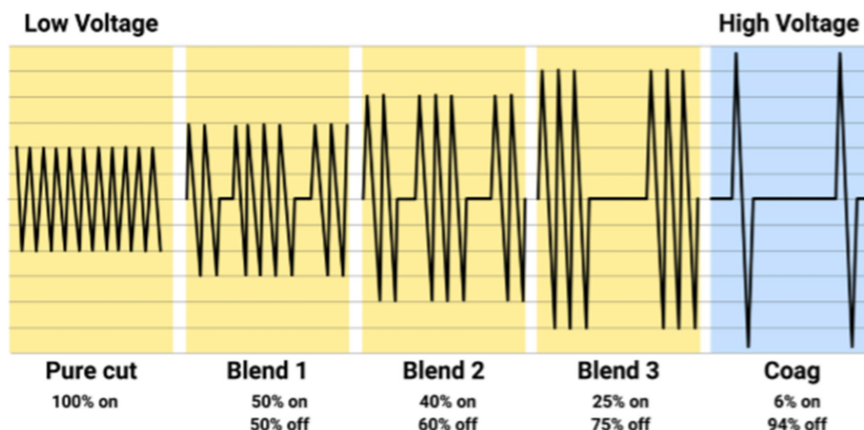
Source: *Elementary notions of electrosurgery*. Accessed June 21, 2025.

<https://arce.ro/elementary-notions-of-electrosurgery>³

- **Blend:**

A “blended current” is not a mixture of both cutting and coagulation current but rather a modification of the duty cycle, or a current with intermediate characteristics. A lower duty cycle as compared to a pure cut setting will produce less heat. Blend settings can be adjusted to deliver the heat in desired areas. In **FIGURE 5**, Blend 1 is used to vaporize tissue with minimal hemostasis, whereas Blend 3 has maximum hemostasis but less cutting.

FIGURE 5 Waveforms.



Source: Elementary notions of electrosurgery. Accessed August 25, 2025.

<https://arce.ro/elementary-notions-of-electrosurgery>³

Safety considerations when using electrosurgical devices:

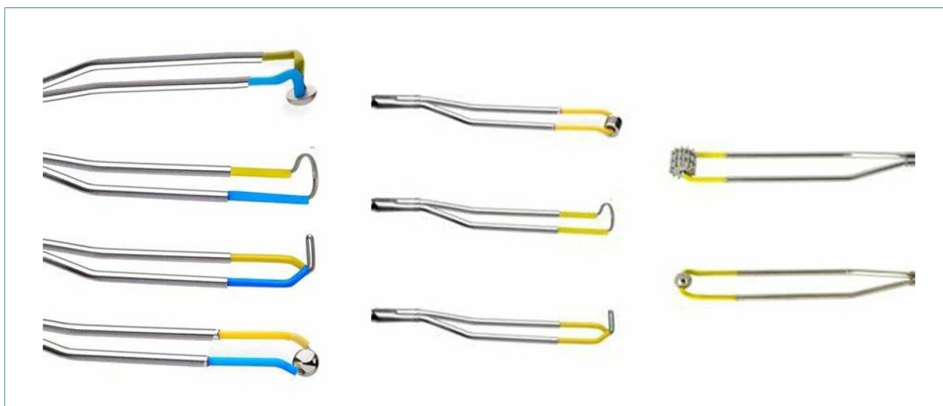
- As the thermal effect of prolonged activation can lead to non–target tissue injury, it is advisable to use brief intermittent activation, or the shortest duration of continual activation as is needed.
- Start with the lowest possible power setting and low-voltage waveform and increase if needed.
- The dispersive pad for monopolar electrosurgery should be applied to well-perfused, dry skin over a large muscle away from bony prominences and conductive prostheses, the latter of which should be kept out of the direct path of the electrical current.
- If needed, prepare the skin site of the dispersive pad by shaving excess hair and avoiding alcohol/flammable cleansing products. The chosen site should be clear of any potential fluid that could leak under the dispersive pad. The larger the surface area of contact between the dispersive pad and the patient, the lower the current density, heat generated, and risk of thermal burns.
- For patients with an implantable cardiac device, the use of bipolar over monopolar electrosurgery is preferred. When necessary, the implantable cardiac device can be temporarily deactivated to prevent accidental discharge intraoperatively.

Types of electrodes

The active electrodes used for BPH surgery can have many designs (**FIGURE 6**) and are activated by a foot pedal. In general, electrodes with a point, hook, narrow tip, or bladed edge are generally used to concentrate current and power, for the purpose of tissue vaporization and cutting, such as with a transurethral incision of the prostate (TUIP) or incision of a bladder neck. Loop electrodes can be used for both resection and coagulation, and those with a ball or button attachment can be used to vaporize and coagulate. In BPH surgery, the morphology of the prostate and patient characteristics often dictate which electrodes are employed. For example, a patient

on a blood thinner with a small prostate may push the urologist toward bipolar button vaporization, whereas a large prostate in a patient without anticoagulation could be approached with either a monopolar or bipolar loop, depending on the anticipated duration of the case based on surgeon experience.

FIGURE 6 Various monopolar and bipolar endoscopic electrodes used in BPH.



Source: Combined images from Electronics Services Centre (ESC Medicams). Accessed June 24, 2025.

<https://www.escmedicams.com/online-store/Urology-Instruments-Storz-Type-Electrodes-Bipolar-Loops-Plasma-Button-p551375011>⁶

Applications in BPH

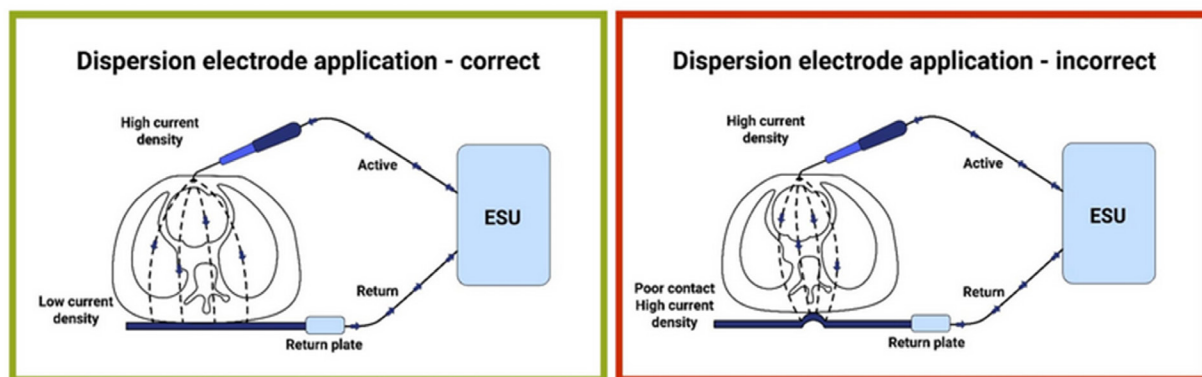
- Open procedures:
 - The most used energy source in open surgery, including open prostatectomy, is monopolar electrosurgical energy.
- Endoscopic procedures:
 - Transurethral resection procedures (TUR) can use either monopolar or bipolar energy. Monopolar energy has the added requirement of hypotonic fluid use during surgery, as saline is a conductive media and will ground the active monopolar electrode, rendering it ineffective. The use of hypotonic irrigation fluid can lead to hyponatremia and TUR syndrome. In some comorbid patients, this risk can be significant. As a result, most urologists have transitioned to bipolar energy for prostate resection, as saline can be used without any loss of current or efficacy. All that said, and as already mentioned, bipolar electrosurgery can lead to a wider thermal effect, which can result in greater tissue slough post-TUR. Additionally, monopolar energy is better able to control bleeding and better concentrate energy.
 - Hemostatic fulguration using bugbee electrode.
- Laparoscopic/Robotic procedures:
 - The most used energy source in laparoscopic/robotic BPH surgery is monopolar electrosurgical energy.

Complications

The most common complication from electrosurgery is related to thermal injury at an unintended site—either locally around the target area (thermal spread), or from inadvertent delivery of energy from one of the following mechanisms:

1. Unintended or prolonged activation of the active electrode causing extension of heat beyond the intended site, or injury to a distant site if the active electrode is in contact with a non-target area when accidentally activated.
2. When the electrosurgical unit is activated without the active electrode in contact with the tissue (i.e., open circuit activation), a high-voltage level emerges at the active instrument and may cause stray currents.
3. Inadequate contact between the dispersive pad and the patient's skin affects the return of the current to the generator. If the dispersive pad is partially detached through bony prominences, adipose tissue, excessive hair, scar tissue, presence of fluid or lotions, or dryness of the pad, the current exiting the body will have excessively high density at the attached site. This non-dispersed heat can lead to unintended burns at the site of the dispersive pad (**FIGURE 7**). ESUs with a return electrode monitoring system can mitigate the risk by inactivating the ESU if the resistance between the patient's body and the dispersive pad is too high.

FIGURE 7 Relationship between current density and area of ground contact.



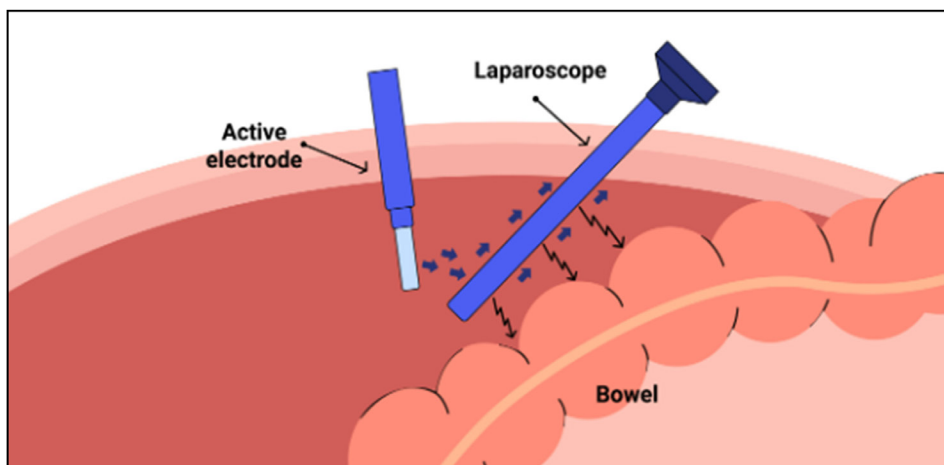
Source: *Elementary notions of electrosurgery*. Accessed August 25, 2025.

<https://arce.ro/elementary-notions-of-electrosurgery>³

4. Implantable devices that use electric current may be affected by electrosurgery and could have life-threatening consequences, such as with cardiac implants. Adverse effects include damage to the device, inability to deliver pacing or shocks, lead tissue interface damage, and electrical reset. The risk of interference is low in procedures where the path between the active electrode and dispersive pad does not cross the implant or its leads; therefore, location of the dispersive pad is vital. That said, some diffusion of current can occur and when feasible, it is safer to use bipolar electrosurgery or another energy source (i.e., laser or ultrasound).

5. Conductive prosthetics are another risk, as the material in the prosthetic can become heated if the electrical current passes through it. As such, the prosthetic should not be included in the direct path of the circuit.
6. Insulation breakdown may allow current to escape along the shaft of the active electrode and harm tissue it comes into contact with, or heat an instrument it is touching, such as with laparoscopic trocars. These injuries can occur outside the field of view and may go unnoticed, presenting themselves later as delayed injury.
7. Direct coupling describes what occurs when the active electrosurgical instrument makes contact with another instrument (**FIGURE 8**). Surgeons may employ this technique purposefully to direct a strong current to a very focal spot (i.e., using the Bovie to touch a right angle that is securing a vessel or pointing to a vessel and utilizing “arcing” to cauterize). However, unintended contact that leads to direct coupling can lead to injury, generally outside the field of view, such as described above.

FIGURE 8 Effect of conductive instrument contact.

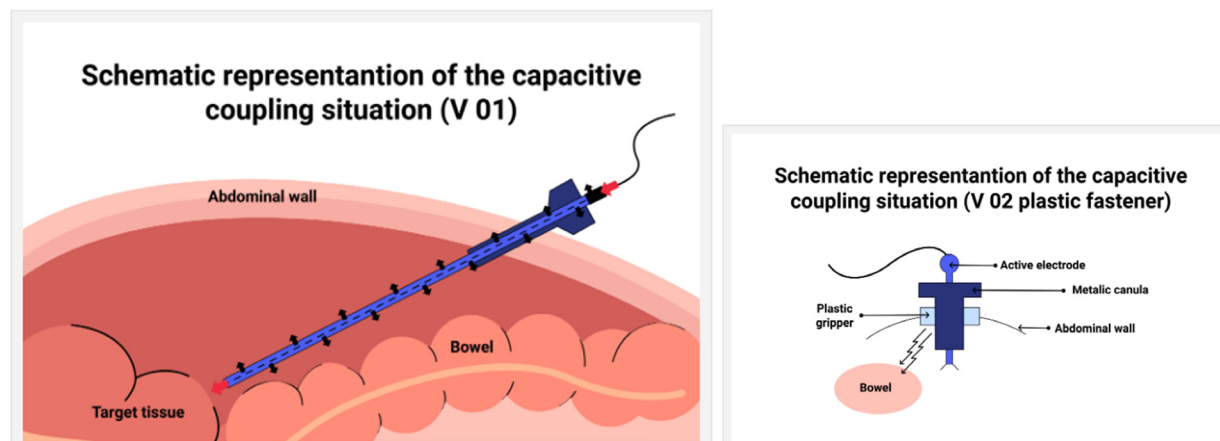


Source: *Elementary notions of electrosurgery*. Accessed August 25, 2025.

<https://arce.ro/elementary-notions-of-electrosurgery>³

8. In the monopolar mode, capacitive coupling injury occurs when the surrounding charge is not allowed to conduct back to and disperse as intended. In laparoscopic surgery, this can develop when a metal cannula is anchored to the skin with a nonconductive plastic grip. In this scenario, the electrical field builds up around the activated electrosurgical instrument and cannot be conducted to the abdominal wall because the plastic retainer acts as an insulator. Consequently, bowel or any other nearby conductor can become the target of a relatively high-power density discharge (**FIGURE 9**).⁷

FIGURE 9 Capacitive coupling injury mechanism.



Source: *Elementary notions of electrosurgery*. Accessed August 25, 2025.

<https://arce.ro/elementary-notions-of-electrosurgery>³

Conclusion

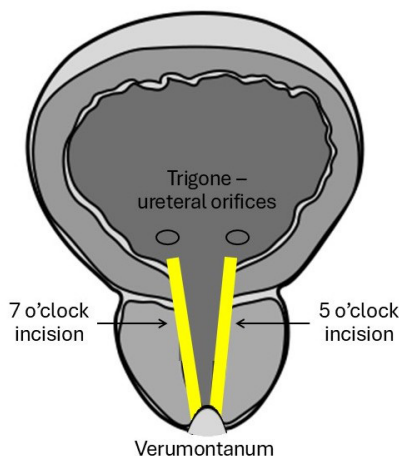
Electrosurgery is vital in urologic surgery, particularly endoscopic surgery including BPH. Understanding the principles of both monopolar and bipolar surgery allows for safe application, particularly when tailoring a surgical approach based on the patient's clinical condition and unique factors. Despite the myriad energy sources used to treat BPH, electrosurgery remains an essential tool in the large armamentarium available.

Transurethral Incision of the Prostate (TUIP)

Direct vision transurethral incision of the prostate (TUIP) was first reported by Ahmad Orandi in 1973, specifically for use in small prostates where more aggressive resection was not necessary.¹ In his original report, Orandi described using a knife electrode to create deep incisions from the ureteral orifice to the lateral edge of the verumontanum, all through a perineal urethrostomy. These days, extension of the incision more typically runs from the bladder neck to the veru and does not involve the trigone as it was originally described. In fact, Orandi himself modified his approach to reduce the risk for retrograde ejaculation that he encountered with incisions that included the trigone and bladder neck (**FIGURE 1**). In fact, in younger patients he would avoid incising the bladder neck completely and focus on only the prostate, using a "short and shallow" approach.² He found his greatest success with prostates smaller than 20 grams and believed those over 40 grams to be "large" and less appropriate. Nowadays, the small prostate suitable for TUIP is usually defined as ≤ 30 grams.³

FIGURE 1 Transurethral incision of the prostate.

Incisions can be carried from the trigone through the bladder neck to the side of the veru; from the bladder neck to the side of the veru; or from distal to the bladder neck only through the prostate to the side of the veru. How extensive the incision is (both in width and length) depends on factors such as shape of the prostate (bilobar vs. trilobar), elevation of the bladder neck, and how the channel appears. In general, it is wise to start more minimal and extend as indicated based on what it takes to "open" the prostatic fossa.



Source: Image courtesy of Dr. Lori Lerner.

Given the over 50-year history of TUIP in the urologic armamentarium, the efficacy of this procedure has been proven. Prospective trials dating back to the 1980s, if not earlier, have shown improvements in symptoms and $Q_{\max}$, with evidence of International Prostate Symptom Score (IPSS) reduction. Over the years, modifications have been reported that include various depths, locations and extent of the incisions, and tools used to make them (including cold knife, bipolar and monopolar knife/loop electrodes, and laser technologies, such as holmium and thulium). In 2002, Ruzić *et al.* set out to evaluate whether modifications impacted outcomes, comparing the “long and deep” approach organically described by Orandi against the “short and shallow” approach he later utilized. The group achieved excellent results, with no significant differences between the two groups in reduction in IPSS (-17 and -15 points, respectively) and $Q_{\max}$ change (mean improvement of approximately 10 mL/sec), supporting either approach.⁴

In 2016, Cakiroglu *et al.* compared TUIP and silodosin 8 mg. At 1 year, the decrease in mean IPSS and post-void residual (PVR), and the improvement of mean maximal $Q_{\max}$, were significant in both groups ($P = .000$). No significant change occurred in International Index of Erectile Function (IIEF) scores of either group. The TUIP group had significantly greater improvement in IPSS (4.7 ± 2.0 vs. 5.7 ± 2.6 ; $P = .005$) and $Q_{\max}$ (20.8 ± 23.2 vs. 26.5 ± 26.8 ; $P = .000$) as compared to the silodosin group.⁵

A meta-analysis published in 2010 reported on randomized controlled trials (RCTs) comparing TUIP with TURP.⁶ A total of 795 participants across 10 RCTs were included. There was no difference in the degree of symptomatic improvement between the two procedures; however, improvement in $Q_{\max}$ was lower for TUIP compared to TURP. That said, blood transfusion and TUR syndrome rates were higher after TURP. Urinary retention, urinary tract infection, strictures, and incontinence did not differ between the two approaches. TUIP was associated with a shorter duration of operation and length of hospital stay but a higher reoperation rate.

A randomized controlled trial published in 2012 included 86 subjects with small prostates (≤ 30 g) who were followed for 4 years after being randomized to receive TUIP or TURP.⁷ The mean age of the participants was 65 years, with a baseline IPSS of 19 and prostate size of 28 g. In these men, long-term mean change from baseline in IPSS was similar between the TUIP and TURP groups (weighted mean difference [WMD], 0.5; 95% CI, -0.2 to 1.2), as was the need for reoperation and blood transfusion. In terms of sexual side effects, erectile dysfunction was reported for 8% of TUIP group compared to 20% for TURP group, though this difference was not significant (relative risk [RR], 0.4; 95% CI, 0.1–1.3). In contrast, there was a significant difference in reports of retrograde ejaculation (RE), with a total of 30 participants experiencing RE (9 in the TUIP arm and 21 in the TURP arm).

Retrograde ejaculation is a frequent concern with TUIP. In Ruzić *et al.*'s study, only one patient complained of retrograde ejaculation whether they had the “long and deep” or “short and shallow” approach.⁴ However, this has not been the findings of many others. While modifications have been described, it remains a risk irrespective of technique and energy source, with up to 27% incidence reported when using the holmium laser.^{8,9} Porreca *et al.* used the holmium laser to make incisions at 3 o'clock and 9 o'clock, as opposed to 5 o'clock and 7 o'clock, and were able to reduce the incidence to 19% without affecting voiding outcomes.¹⁰ Carilli *et al.* investigated use of the thulium laser to make incisions while preserving paracollicular and supramontanal tissue near the verumontanum, yielding a retrograde ejaculation rate of 11.7%.¹¹ The range of occurrence is large between surgeons and studies, making it difficult to definitively report a reliable rate. As a result, it is vital to counsel patients that this risk exists independent of how the procedure is performed or the energy source used to perform the procedure.

In conclusion, TUIP for small prostates is an efficacious procedure that can lead to significant improvements in urine flow rates, symptoms, and quality of life, with a low risk for urinary incontinence. Anejaculation can occur and merits appropriate counseling.

TABLE 1 Transurethral Incision of the Prostate Recommendation

Topic	Recommendation	LoE	GoR
Transurethral incision of the prostate	Offer transurethral incision of the prostate to men with LUTS needing surgical treatment and prostate size < 30 mL without a middle lobe.	II	A

Abbreviations: GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms.

Transurethral Resection of the Prostate (TURP)

Transurethral resection of the prostate (TURP) was one of the most important urologic surgical procedures of the 20th century, as its development and adoption gave patients an endoscopic and less morbid BPH surgical treatment option, compared to open simple prostatectomy. Over the years, medical therapy, office-based therapies, and the adoption of endoscopic enucleation of the prostate have resulted in less use of TURP treatment for BPH. However, TURP remains the gold standard for treating bladder outlet obstruction caused by BPH, serving as the benchmark against which newer treatments—such as prostate artery embolization, endoscopic enucleation of the prostate (EEP), and robotic simple prostatectomy—are compared to in studies.

TURP has long been the gold standard for BPH treatment due to its proven long-term efficacy and durability, with follow-up data extending up to 25 years—unmatched by other surgical options. It effectively improves urinary symptoms, as evidenced by comprehensive urodynamic studies and systematic reviews.^{1–12} Meta-analyses demonstrate a 72% reduction in IPSS, a 3.3-point improvement in quality of life (QoL) scores, a 120% increase in maximum flow rate after 12 months, and reduction in PVR by 70%.^{2,6} Multiple studies demonstrate a relatively low retreatment rate, with secondary procedures such as re-TURP, urethrotomy, or bladder neck incision (BNI) occurring in 5.8%, 12.3%, and 14.7% of cases at 1, 5, and 8 years, respectively.^{3,5,6,9,10,12,13} While EEP has demonstrated much lower retreatment rates at 0–1.4% at 7–10 years, the adoption of EEP in the United States has lagged compared to TURP, with EEP accounting for only 3.2% of all BPH procedures in the United States between 2000–2019 compared to TURP accounting for 45.1%.^{14,15} This can be partially explained by EEP's steep learning curve and reimbursement concerns. TURP remains the most common BPH endoscopic treatment taught and performed in the United States.¹⁴

TURP can be completed using monopolar or bipolar energy. Unlike monopolar TURP, bipolar TURP confines energy between the active resection loop and a passive pole located on the resectoscope tip, avoiding the need for the energy to travel through the body to a skin pad. While monopolar TURP requires iso-osmolar non-electrolyte solutions such as sorbitol, mannitol, or glycine, bipolar TURP is performed using 0.9% NaCl solution. This significantly reduces the risk of acute dilutional hyponatremia during prolonged resection, thereby minimizing the likelihood of TUR syndrome. Regarding the comparative efficacy, effectiveness, and safety of monopolar versus bipolar TURP, there are five systematic reviews and meta-analyses published between 2009 and 2015 that compared bipolar TURP to monopolar TURP.^{16–20} No significant differences were found between monopolar and bipolar TURP in improving IPSS and peak urinary flow rates at 12 months. However, safety outcomes favored bipolar TURP, including shorter catheterization time, reduced length of stay, lower risk of dilutional hyponatremia, and a decreased incidence of TUR syndrome. Bipolar TURP also showed benefits in reducing clot retention, bleeding, hemoglobin drops, and the need for blood transfusion, though some outcomes exhibited high heterogeneity or lacked statistical significance in certain analyses.^{16–20}

Equipment

Equipment for TURP includes a resectoscope and a working element with a resecting device. A variety of devices are available for removing prostatic tissue, including traditional cutting loops, rollers, roller balls, and buttons. Cutting loops are designed for monopolar or bipolar electrosurgical cutting and coagulation and are further categorized into “thin loops” and “thick loops.” Thin loops, made of firm wires, offer higher current density for cleaner cuts but are less effective at coagulating blood vessels compared to thick loops. Thick loops, which are several times the diameter of thin loops, may experience more tissue drag, but this can be offset by increasing the electrosurgical generator’s power output.

Rollers, roller balls, and buttons remove prostatic tissue through desiccation, achieved by lightly passing the device over tissue with increased power settings. This process desiccates and carbonizes the tissue, leaving minimal residual material. Although these devices require longer treatment times for larger glands, they generally provide superior coagulation compared to loop resection. The choice of device usually comes down to surgeon preference.

Technique

TURP resection is usually started at the bladder neck and median lobe. Typically, the median lobe is resected down until circular bladder neck fibers are encountered. This should be continued until the bladder, bladder neck, and prostatic fossa are flush at the same level. This resection is to be completed distally to just proximal to the verumontanum. The verumontanum is the key landmark during TURP; careful attention is needed to avoid resecting tissue distal to the verumontanum in order to avoid injury to the external urethral sphincter complex. Once the median lobe is resected, one can begin resecting the lateral lobes. This should be completed from “bottom-to-top” from 7 o’clock to 11 o’clock on the right and 5 o’clock to 1 o’clock on the left side. Resection from bottom to top allows for more superior tissue to fall into the working space as the lower tissue is resected and facilitates more efficient resection. Again, careful attention must be paid to avoid resecting distal to the verumontanum. Lastly, attention can be turned to the anterior prostate. Most patients only have a small amount of anterior prostatic tissue. Resection begins just inside the bladder neck and should end proximal to the verumontanum. This concludes the resection phase of the surgery. Hemostasis is obtained with the resecting device’s coagulation setting. Bleeding vessels are often encountered at the bladder neck and anterior prostate, so special attention should be paid to fulgurating these areas.

To empty the bladder of the resected prostate tissue, the bladder is then irrigated using an Ellik evacuator, which creates a Venturi effect to collect prostate tissue chips at the bottom of the bulb. Plastic or glass versions of an Ellik evacuator or a Toomey syringe can be used instead. After evacuating chips and clots, the prostate and bladder are reexamined, and any remaining chips can be individually removed using the resectoscope loop. This evacuation process can sometimes cause mild bleeding, which is controlled by further hemostasis with coagulation. This concludes the surgical procedure. Typically, a 22 or 24 French 3-way Foley catheter is placed at the conclusion of the case and continuous bladder irrigation is initiated.

TABLE 1 Transurethral Resection of the Prostate Recommendations

Topic	Recommendations	LoE	GoR
Transurethral resection of the prostate	Offer transurethral resection of the prostate (monopolar or bipolar) to men with LUTS needing surgical treatment and prostate size between 30 mL and 80 mL.	I	A
	Clinicians may use TURP as a treatment option for larger prostates, depending on their expertise and the availability of alternative methods.	III	C

Abbreviations: GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms, TURP, transurethral resection of the prostate.

Open Simple Prostatectomy

Open simple prostatectomy (OSP) is the oldest prostate disobstructing procedure for benign prostatic obstruction (BPO) and is still considered the gold standard for the surgical management of men with prostate > 80–100 g in parts of the world where less invasive forms of anatomical enucleation of the prostate (AEP) are not yet available.

The first experiences of open removal of the prostate were via the perineum. It seems likely that the first open partial “prostatectomy” occurred unintentionally as collateral damage sustained while “cutting for the stone” in the 17th or 18th century. Theodor Billroth performed the first intentional partial prostatectomy blindly via a perineal approach in Vienna in 1867. Hugh Hampton Young and William Stewart Halsted performed the first perineal prostatectomy under direct vision in Baltimore in 1904.¹

Perhaps the earliest description of the suprapubic or transvesical approach to the prostate was documented by Jean Amussat in 1827. While performing a suprapubic cystotomy to remove a bladder stone, Amussat saw a rounded tumor projecting into the bladder from the bladder neck (almost certainly the median lobe of the prostate) and cut it off using scissors. The patient survived and had a durable outcome.² A deliberate transvesical approach to disobstruct the prostate by partially removing the median lobe was described by Leopold van Dittel from Austria in 1885, although sadly the first patient to undergo this procedure succumbed to sepsis soon after. Total transvesical AEP was first undertaken on both sides of the Atlantic in the 1880s, by William Belfield in October 1886 in Chicago, United States, and Edward Atkinson in December 1887 in Leeds, United Kingdom.¹ Sir Peter Freyer from the United Kingdom helped to popularize transvesical AEP by repeatedly publishing his eventually very large experience as it progressed (1,674 cases completed by 1920), although it remained a significantly morbid procedure with hospital stays often measured in months.³ The transvesical approach to OSP was subsequently improved by others including John Thomson Walker (United Kingdom) and Harry Harris (Australia).¹

Terence Millen developed and popularized the retropubic approach for AEP, approaching the obstructive adenoma through the anterior prostatic capsule, without the need for traversing the bladder or the perineum. He published his initial series of retropubic prostatectomies in 1945.⁴ Millen's technique, along with improvements in anesthesia, sterilization and postoperative care, reduced the morbidity of and improved patient outcomes for OSP. Both the transvesical and retropubic approaches to OSP remain in use to this day.

Transurethral resection of the prostate (TURP) was introduced in the 1930s following the development of the use of electrocautery endoscopically under cystoscopic guidance, which had been pioneered in the treatment of bladder tumors.⁵ As the use of TURP increased, that of OSP began to decline, particularly for men with prostates < 100 g.

The introduction of less invasive endoscopic, laparoscopic and robot-assisted approaches for AEP has led to a further significant decline in the use of OSP for men with prostates > 80 cc in countries with access to the newer, often more expensive technologies required.

Reducing the morbidity of OSP

The most common complications of OSP relate to bleeding during or after surgery. Contemporary series report blood transfusion rates of up to 26% **TABLE 1.**^{6–8} Reducing OSP-related blood loss remains a priority for investigation.

Perioperative tranexamic acid (TXA) reduced intraoperative blood loss and blood transfusion rates by up to 50% in a randomized trial.⁹ Another trial reports reduced blood loss, operation time, and length of stay when TXA is given.¹⁰

Although transvesical OSP is the most common approach used in Africa,¹¹ and probably worldwide **TABLE 1**, a modified retropubic approach described by Srouji *et al.* caused less blood loss, fewer episodes of postoperative clot retention, and had a lower blood transfusion rate compared to transvesical OSP in a randomized trial.^{12,13}

The inflation of a rectal balloon adjacent to the prostate for 15 minutes after transvesical OSP was investigated in another randomized trial.¹⁴ There was significantly less hemoglobin reduction, postoperative irrigation volume, shorter catheter and hospital time, and fewer blood transfusions in the balloon group. No rectal complications were experienced.

A retrospective study also suggests a 6-week course of dutasteride prior to OSP might significantly reduce perioperative blood loss.¹⁵

With regard to major nonurological complications, a large national Austrian study in the 1990s (23,123 cases) showed no significant differences in myocardial infarction and mortality between TURP and OSP.¹⁶

Level 1 evidence comparing endoscopic BPO therapies to OSP

Anatomic endoscopic enucleation of the prostate (AEEP) has the strongest evidence-based claim to be a replacement for OSP with randomized trials and meta-analyses reporting equivalent efficacy, urodynamic relief of bladder outlet obstruction, and durability, but less blood loss, lower blood transfusion rates, and shorter catheter time and length of hospital stay compared to OSP (**TABLES 2–4**).^{17–29}

One randomized trial and one nonrandomized study from Italy both found the global cost of holmium laser enucleation of prostate (HoLEP) to be significantly cheaper than OSP.^{30,31}

OSP has also been compared to surgical resection and vaporization techniques, and prostate artery embolization (PAE) in randomized studies. These procedures remove less of the transition zone than AEP and are, consequently, less effective and durable than OSP, although they offer less blood loss with shorter catheter time and length of stay (**TABLES 5–7**).^{32–35}

Interestingly, urethral stricture and bladder neck contracture are seen not only after transurethral procedures for BPO but also after OSP (**TABLES 2, 4–6**).

Studies comparing OSP to less invasive nonendoscopic forms of AEP (LSP and RASP)

There is a relative paucity of Level 1 evidence for less invasive nonendoscopic forms of AEP.

Several nonrandomized comparisons of OSP and laparoscopic simple prostatectomy (LSP) report similar functional outcomes but different shorter term results. Baumert reported longer operating time, but less blood loss, and shorter catheter time and hospital stay for LSP.³⁶ Porpiglia *et al.* reported that LSP offers less blood loss but no significant differences in operating time, blood transfusion, catheter time, and hospital stay.³⁷ Sfredo *et al.* reported no differences in blood loss or postoperative complications.³⁸

The main disadvantage of LSP is its long learning curve.^{26,36,39} It has largely been superseded by robotic-assisted simple prostatectomy (RASP), which is widely accepted to be easier and faster to learn.

Studies comparing RASP to OSP consistently report equivalent functional outcomes, with less blood loss, and shorter catheter times and hospital stays favoring RASP. While some studies also report fewer blood transfusions and perioperative complications for RASP,^{40,41} others do not.⁴²

Single-port transvesical RASP is the most recent form of AEP. A nonrandomized study comparing it to OSP reports less blood loss, fewer blood transfusions, and shorter catheter and hospital times for RASP. It also reports the unique advantage of not routinely requiring any postoperative continuous bladder irrigation.⁴³

Conclusion

OSP is the original form of AEP. Advances in surgical technique and patient care since its initial development in the 1880s have significantly reduced its morbidity and mortality. However, the relatively recent introductions of less invasive forms of AEP (AEEP, LSP, and RASP), which are as efficacious and durable as OSP, but with reduced blood loss, fewer blood transfusions, and shorter catheter and hospital times, have rendered OSP virtually obsolete in some parts of the world.

Nevertheless, OSP continues to play an important role in the management of men with large-volume BPO who live in areas where less invasive forms of AEP are not available.

TABLE 1 Contemporary OSP Series

Study	Country	No	Dates	Approach	Op time (min)	Enucleated weight (g)	Catheter time (days)	Hospital stay (days)	Blood transfusion number (%)	Mortality (%)
Obi <i>et al.</i> ⁶	Nigeria	148	Jan 2011–Dec 2020	Transvesical, 91.9% Retropubic, 8.1%	99.6	86.1	6.8	7.9	26.1	0.7
Kyei <i>et al.</i> ⁷	Ghana	200	Jan 2010–Sep 2013	Transvesical, 90% Retropubic, 10%	101.3	110.8			23.5	
Elshal <i>et al.</i> ⁸	Egypt	163	Apr 2002–Dec 2012	Transvesical, 100%			7.9	8.1	25.2	1.2

Abbreviations: op, operative; OSP, open simple prostatectomy.

TABLE 2 Randomized Trials of HoLEP Versus OSP

Study	No	Prostate Volume (mL)	PSA (ng/mL) Pre Post	IPSS Pre Post	Q _{max} (mL/s) Pre Post	PVR (mL) Pre Post	Op time (min)	Catheter time (days)	Hospital Stay (days)	Blood transfusion number (%)	Reoperation (%)
Kuntz <i>et al.</i> ¹⁷ 5-year follow-up ¹⁸											
HoLEP	60	114.6	Not reported	22.1 3.0	3.8 24.3	280 10.6	136	1.3	2.9	0	Bladder neck contracture, 1 (1.7%) Urethral stricture, 2 (3.3%)
Open (Transvesical)	60	113.0	Not reported	21.0 3.0	3.6 24.4	292 5.3	91	8.1	10.5	8 (13.3%)	Bladder neck contracture, 3 (5.0%) Urethral stricture, 1 (1.7%)
Naspro <i>et al.</i> 2-year follow-up ¹⁹											
HoLEP	41	113.27	Postop PSA not reported	20.1 7.9	7.83 19.19	Not reported	72.1	1.5	2.7	2 (4.9%)	Bladder neck contracture & urethral stricture, 3 (7.3%)
Open (Transvesical)	39	124.21	Postop PSA not reported	21.6 8.1	8.32 20.11	Not reported	58.3	4.1	5.4	7 (17.9%)	Bladder neck contracture & urethral stricture, 3 (7.7%)

Abbreviations: HoLEP, holmium laser enucleation of the prostate; op, operative; OSP, open simple prostatectomy; PSA, prostate-specific antigen.

TABLE 3 Randomized HoLEP Versus OSP Urodynamic Data

Study	PdetQmax (cmH ₂ O)		Schafer grad		<i>P</i> value
	Pre	Post	Pre	Post	
Naspro <i>et al.</i> 1-year urodynamic follow-up ¹⁹					
HoLEP	80.6	30.6	3.8	0.7	< .001
Open	83.1	34.8	3.1	0.8	< .001
<i>P</i> value	0.94	0.66	0.33	0.18	

Abbreviations: HoLEP, holmium laser enucleation of the prostate; OSP, open simple prostatectomy.

Source: Data from European Urology, Vol. 50, Naspro R, Suardi N, Salonia A, et al., Holmium laser enucleation of the prostate versus open prostatectomy for prostates > 70 g: 24-month follow-up, pp. 563–568, Copyright Elsevier (2006).¹⁹

TABLE 4 Randomized Bipolar AEEP Versus OSP Trials

Study	No	Prostate Volume (mL)	PSA (ng/mL) Pre Post	IPSS Pre Post	Q _{max} (mL/s) Pre Post	PVR (mL) Pre Post	Op time (min)	Catheter time (days)	Hospital Stay (days)	Blood transfusion number (%)	Reoperation (%)
Tagreda <i>et al.</i> 6-month follow-up ²⁰											
Bipolar enucleation & resection	45	110	4	25 3	9.4 19.3	195 15	77	2	All 3 days or less	0	Bladder neck contracture, 0 Urethral stricture, 1 (2.2%)
Open (Retropubic)	45	112	3.8	24 3	8.9 17.7	190 0	99	7	7	2 (4.4%)	Bladder neck contracture, 1 (2.2%) Urethral stricture, 0
Chen <i>et al.</i> 6-year follow-up ²¹											
Bipolar Enucleation	80	110	2.9 1.8	25.6 3.5	4 25.2	240 20	121.2	1.7	3	0	Bladder neck contracture & urethral stricture, 4 (5%)
Open (Transvesical)	80	114.5	3.0 1.8	25.7 3.0	4 25.7	249 16.5	101.7	6.2	8	4 (5%)	Bladder neck contracture & urethral stricture, 5 (6.25%)
Rao <i>et al.</i> 1-year follow-up ²²											
Bipolar Enucleation	43	116.2	4.8 0.6	24.8 3.4	5.8 26.6	83.4 5.1	111.2	3.3	5.4	0	Bladder neck contracture, 0 Urethral stricture, 1 (2.5%)
Open (Transvesical)	40	110.2	4.5 0.6	24.5 3.5	5.9 25.6	81.4 5.5	109.6	6.2	9.3	4 (10%)	Bladder neck contracture, 2 (5.3%) Urethral stricture, 3 (7.9%)

Abbreviations: AEEP, anatomical endoscopic enucleation of the prostate; HoLEP, holmium laser enucleation of the prostate; IPSS, International Prostate Symptom Score; op, operative; OSP, open simple prostatectomy; PVR, post-void residual.

TABLE 4 Randomized Bipolar AEEP Versus OSP Trials (*continued*)

Study	No	Prostate Volume (mL)	PSA (ng/mL) Pre Post	IPSS Pre Post	Q _{max} (mL/s) Pre Post	PVR (mL) Pre Post	Op time (min)	Catheter time (days)	Hospital Stay (days)	Blood transfu- sion number (%)	Reoperation (%)
Geavlete <i>et al.</i> 1-year follow-up ²³											
Bipolar enucleation	70	132.6	8.5 0.8	25.3 4.1	5.9 25.4	164 21.4	91.4	1.5	2.1	1 (1.4%)	Bladder neck contracture, 1/64 (1.6%) Urethral stricture, 2/64 (3.1%)
Open (Transvesical)	70	129.7	8.4 0.8	25.6 4.3	5.7 25.1	168 20.9	87.5	5.8	6.9	6 (8.6%)	Bladder neck contracture, 1/63 (1.6%) Urethral stricture, 2/63 (3.1%)
Ou <i>et al.</i> 1-year follow-up ²⁴											
Bipolar enucleation & resection	47	132.2	5.9 1.6	23.2 5.6	5.9 15.5	89.6 28.3	100.4	4.3	5.8	3 (6.4%)	Urethral stricture, 1 (2.1%)
Open (Transvesical)	45	139.5	5.6 1.2	25.1 5.8	5.1 16.9	81.3 25.1	105.6	7.6	9.3	3 (6.7%)	0
Geavlete <i>et al.</i> 1-year follow-up ²⁵											
Bipolar vaporization	80	126.7	8.0 3.1	24.4 4.5	6.9 22.8	158 25.2	118.1	1.3	2.1	0	Not reported
Bipolar resection	80	121.8	7.6 2.0	25.2 4.4	6.4 24.9	152 27.6	99.5	2.2	3.2	1 (1.25%)	Not reported
Bipolar enucleation	80	122.6	8.1 0.7	24.7 4.2	6.6 25.6	134 19.7	87.4	1.6	2.5	1 (1.25%)	Not reported
Open (Transvesical)	80	128.7	7.8 0.7	24.9 3.9	6.5 25.2	142 24.3	79.4	5.4	6.7	6 (7.5%)	Not reported

Abbreviations: AEEP, anatomical endoscopic enucleation of the prostate; HoLEP, holmium laser enucleation of the prostate; IPSS, International Prostate Symptom Score; op, operative; OSP, open simple prostatectomy; PVR, post-void residual.

TABLE 5 Randomized Bipolar Resection Versus OSP Trial

Study	No	Prostate Volume (mL)	PSA (ng/mL) Pre Post	IPSS Pre Post	Q _{max} (mL/s) Pre Post	PVR (mL) Pre Post	Op time (min)	Catheter time (days)	Hospital Stay (days)	Blood transfusion number (%)	Reoperation for urethral stricture, bladder neck contracture, BPO number (%)
Giulianelli <i>et al.</i> 3-year follow-up ³²											
Bipolar resection	70	83.3	2.2	31.6 2.0	4.1 23.0	87.8 10	71	48	72	0	Bladder neck contracture, 4 (3%)
Open (Transvesical)	70	84.3	2.8	31.6 4.0	4.2 20.0	84.7 10	63	120	144	9 (12.9%)	Bladder neck contracture, 11 (8%)

Abbreviations: BPO, benign prostatic obstruction; IPSS, International Prostate Symptom Score; op, operative; OSP, open simple prostatectomy; PSA, prostate-specific antigen; PVR, post-void residual.

Source: Modified from Giulianelli R, Brunori S, Gentile BC, et al. Comparative randomized study on the efficaciousness of treatment of BOO due to BPH in patients with prostate up to 100 gr by endoscopic gyrus prostate resection versus open prostatectomy. Preliminary data. Arch Ital Urol Androl. 2011;83(2):88–94.³²

TABLE 6 Randomized GreenLight Vaporization Versus OSP Trial

Study	No	Prostate Volume (mL)	PSA (ng/mL) Pre Post	IPSS Pre Post	Q _{max} (mL/s) Pre Post	PVR (mL) Pre Post	Op time (min)	Catheter time (days)	Hospital stay (days)	Blood transfusion number (%)	Reoperation for urethral stricture, bladder neck contracture, BPO number (%)
Skolarikos <i>et al.</i> 18-month follow-up ^{33,34}											
GreenLight vaporization	65	93	6.2 2.4	21 8.5	8.6 16	97 15	80	1	2	0	3 (5)
Open	60	96	6.3 2	20 10	8 15	89 12	50	5	6	8 (13%)	3 (5)

Abbreviations: BPO, benign prostatic obstruction; IPSS, International Prostate Symptom Score; op, operative; OSP, open simple prostatectomy; PSA, prostate-specific antigen; PVR, post-void residual.

Source: Modified with permission from Skolarikos A, Papachristou C, Athanasiadis G, Chalikopoulos D, Deliveliotis C, Alivizatos G. Eighteen-month results of a randomized prospective study comparing transurethral photoselective vaporization with transvesical open enucleation for prostatic adenomas greater than 80 cc. J Endourol. 2008;22(10):2333–2340. doi:10.1089/end.2008.9709.³⁴

TABLE 7 Randomized Prostate Artery Embolization Versus OSP Trial

Study	No	Prostate volume (mL)		PSA (ng/mL)		IPSS		PdetQmax (cmH ₂ O)		BOOI		PVR (mL)	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Lebani <i>et al.</i> 6-month follow-up ³⁵													
Prostate artery embolization	23	107	84.9	5.89	5.8	27.4	10.1	104	98.6	93.7	83.8	158	75.7
Open	25	123	37.5	7.95	1.6	30	6.5	125	46.6	116	20.3	140	49.6

Abbreviations: BOOI, Bladder Outlet Obstruction Index; IPSS, International Prostate Symptom Score; OSP, open simple prostatectomy; PSA, prostate-specific antigen; PVR, post-void residual.

Source: Data from Urology, Vol. 189, Lebani BR, Porto DDS, da Silva ABD, et al. Randomized controlled trial comparing open simple prostatectomy or prostate artery embolization in large prostates: clinical and urodynamic assessment - PoPAE study, pp. 94–100, Copyright Elsevier (2024).³⁵

TABLE 8 Open Simple Prostatectomy Recommendation

Topic	Recommendation	LoE	GoR
Open simple prostatectomy	Open prostatectomy should be offered to men with LUTS needing surgical treatment and prostate size larger than 80 mL in the absence of alternative enucleation methods.	I	A

Abbreviations: GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms.

Anatomical Endoscopic Enucleation of the Prostate

Introduction

Anatomical endoscopic enucleation of the prostate (AEEP) is a highly effective surgical technique used to treat BPH, a condition characterized by the progressive enlargement of the prostate gland leading to LUTS.¹ AEEP is performed as a transurethral procedure using different energy sources (lasers and bipolar energy), and allows for the removal of the entire transition zone of the prostate for complete de-obstruction of the bladder. The evolution of the surgical management for BPH has transitioned from open simple prostatectomy and TURP to modern, minimally invasive techniques. These advancements have significantly improved patient outcomes, particularly for men with large prostate glands, by reducing morbidity, improving efficacy, and minimizing complications.²

The concept of AEEP emerged as an alternative to open simple prostatectomy, aiming to replicate its efficacy while minimizing invasiveness. Since its development by Gilling and Fraundorfer using the holmium:yttrium aluminum garnet (Ho:YAG) laser, different lasers have been used to perform AEEP including the GreenLight, diode, thulium:YAG, and more recently the thulium fiber. Furthermore, AEEP can also be performed using monopolar or bipolar energy. The efficacy and safety of AEEP, regardless of energy source used, have been widely demonstrated.³

Energy sources used for AEEP

Various energy sources have been employed in AEEP, each with distinct advantages and limitations. Understanding these energy sources is crucial for optimizing surgical outcomes and ensuring patient safety.

Holmium laser enucleation of the prostate (HoLEP)

The Ho:YAG laser produces energy at a wavelength of 2140 nm and is a pulsed laser with a penetration depth of 0.4 mm into prostatic tissue. It results in vaporization without deep coagulation; however, dissipating heat causes coagulation of small and medium vessels 2 to 3 mm deep, leading to excellent hemostasis. The Ho:YAG laser has a high peak power that helps to separate tissue, namely prostate tissue, away from the prostatic capsule, which is the significant advantage of this laser. The Ho:YAG laser is excellent for vaporization and precise incision and enucleation. There have been recent advances in holmium laser technology with the introduction of holmium laser pulse modulation including Moses pulse modulation, virtual basket, and vapor tunnel. In the case of Moses technology and virtual basket, this involves a double “bubble” or pulse emission, allowing better laser energy delivery to the target tissue. Several studies have demonstrated the benefit of holmium pulse modulation in improving hemostasis, decreasing operative time, and allowing same-day discharge in a significant number of cases.

Thulium:YAG laser enucleation of the prostate

The thulium:yttrium aluminum garnet (Thulium:YAG) laser produces energy at a wavelength of 2013 nm and has a penetration depth of 0.2 mm into prostatic tissue. Unlike the Holmium:YAG laser, the Thulium:YAG laser is a continuous laser that results in more charring of tissue than the Holmium:YAG laser. There are 120 W and 200 W Thulium:YAG lasers, which have equivalent surgical outcomes and safety. The thulium:YAG laser results in vaporization with excellent coagulation, and it has demonstrated excellent outcomes for AEEP.

LBO:YAG enucleation of the prostate (PVP-EP)

The lithium triborate YAG (LBO:YAG) laser is derived from the Nd:YAG laser. The Nd:YAG laser (wavelength 1064) is passed through a lithium-triborate (LBO) crystal, resulting in half of its wavelength (532 nm) and doubling of its frequency. The LBO:YAG laser is absorbed by hemoglobin, and its penetration depth is 0.8 mm. This laser is best used for vaporization of tissue, although there are reports of it being used for AEEP.

Thulium fiber laser enucleation of the prostate

The thulium fiber laser (TFL) produces energy at a wavelength of 1940 nm and has a penetration depth of 0.15 mm into prostatic tissue. It results from the activation of thulium ions by a diode laser. This laser uses a silica fiber instead of YAG crystals and therefore has less energy consumption and heat production. TFL has a lower peak power than the Ho:YAG laser and therefore does not separate tissue as well. This laser has excellent hemostasis but can result in charring if it is put in direct contact with tissue. TFL is excellent for precise incision and AEEP.

Bipolar enucleation of the prostate (Bipolar)

This cost-effective technique utilizes standard bipolar equipment and eliminates the need for specialized lasers. However, it carries a higher bleeding risk and may cause increased postoperative irritative symptoms.⁴

Surgical techniques: *en bloc* vs. lobe-based approaches

Different surgical techniques are employed in AEEP, each with specific advantages and challenges.

A two-lobe, three-lobe, or *en bloc* technique can be utilized depending on patient anatomy and surgeon preference. The two-lobe technique in most cases is a modification of the three-lobe technique in which a single 5 o'clock or 7 o'clock incision is made from the bladder neck to the verumontanum. The lateral lobe is enucleated as described, and the small median lobe is then enucleated along with the remaining lateral lobe. The main advantage is one less incision, which shortens the operative time and increases the efficiency of AEEP. Some surgeons may elect to perform a 3-lobe technique if a large median lobe is present and often perform it during the initial learning curve for AEEP and when tackling very large (> 200 g) glands. The *en bloc* technique for AEEP, which involves enucleating the entire transition zone adenoma as one tissue block, is increasingly being utilized for AEEP due to its improved enucleation efficiency and some reports of better early continence.

Early apical release

In order to reduce early temporary incontinence after AEEP, early dissection of the sphincter from the adenoma has been advocated. Data supporting this technique to reduce early temporary incontinence is scarce. For this technique, as enucleation of the lateral lobe begins and as the lateral lobe is lifted, the mucosa between the sphincter and the adenoma is incised progressively up to 1 o'clock (left lobe) and 11 o'clock (right lobe). The most critical part of this technique is the anterior incision between 1 o'clock and 11 o'clock, as the sphincter is difficult to identify and is often more proximal to and fused with the adenoma. Once this incision is made, the enucleation is completed as previously described. Typically, when early apical release is utilized, there is no mucosal strip to divide, as these mucosal attachments are divided as part of the sphincter adenoma separation.

Safe morcellation: key principles

Morcellation is a critical step for extracting enucleated prostate tissue from the bladder. To ensure safety and efficacy, several principles should be adhered to, including adequate bladder distension to create a stable working space, controlled suction for efficient tissue removal without excessive movement, proper blade positioning to prevent bladder wall injury, bladder pressure regulation to minimize mucosal trauma, and continuous endoscopic visualization to ensure real-time safety monitoring.^{5,6}

Advantages of AEEP

AEEP offers several advantages compared to traditional BPH treatment options. It provides superior long-term outcomes with lower retreatment rates than TURP.⁷ The minimally invasive approach reduces blood loss and shortens hospital stays.⁸ The technique is effective for all prostate sizes, preserves erectile function, and reduces the risk of bleeding, minimizing complications.^{8–10}

Disadvantages of AEEP

Despite its many benefits, AEEP has some drawbacks. The steep learning curve requires specialized training and experience.^{11,12} The operative time may be longer, especially during the initial learning phase. Retrograde ejaculation is expected. Postoperative temporary incontinence can be common; however, it can be reduced with an early sphincter release technique.^{8,13} Additionally, the initial cost is higher due to the need for a morcellator with or without specialized laser equipment.¹²

Patient selection and preoperative considerations

Selecting the appropriate patients for AEEP is critical for optimizing surgical outcomes. Ideal candidates include those with moderate-to-severe LUTS refractory to medical therapy, prostate sizes exceeding 80 grams to 100 grams, and patients seeking a durable, minimally invasive solution.¹

Preoperative evaluation

A comprehensive history and physical examination are essential to assess LUTS severity, previous treatments, and comorbid conditions. Prostate imaging, such as transrectal ultrasound or magnetic resonance imaging (MRI), helps evaluate prostate size and morphology. Uroflowmetry and post-void residual measurements determine the extent of obstruction. Laboratory tests, including prostate-specific antigen (PSA) levels, renal function tests, and coagulation profiles, are done as necessary. Additionally, patient counseling is crucial to discuss benefits, risks, and postoperative expectations.¹⁴

Future perspectives in AEEP

As technology continues to advance, several innovations are expected to improve the efficacy and accessibility of AEEP. Robot-assisted prostate enucleation aims to enhance precision and reduce operator fatigue.¹⁵ Advanced laser technologies are being developed to refine energy delivery for more efficient tissue removal and hemostasis. Artificial intelligence (AI) and machine learning may assist in surgical planning and training. Improved morcellation devices are also being designed to increase safety and efficiency in tissue extraction.⁵

Conclusion

AEEP represents a paradigm shift in the surgical management of BPH. By offering durable outcomes with reduced morbidity, AEEP is a superior alternative to traditional techniques, particularly for large prostate glands. Advances in energy sources and surgical methodologies continue to refine the procedure, making it more accessible and effective with a lower complication rate. Future innovations in technology including new robotic platforms and modular training will further enhance the adoption of AEEP, optimizing patient care in the years to come.

TABLE 1 Anatomical Endoscopic Enucleation of the Prostate Recommendation

Topic	Recommendation	LoE*	GoR
Anatomical endoscopic enucleation of the prostate	Offer enucleation of the prostate to men with LUTS needing surgical treatment and prostate size larger than 80 mL.	*The LoE varies for the different energy sources: Ho:YAG laser, LoE I Tm:YAG laser, LoE II Diode laser, LoE II Plasmakinetic energy, LoE II LSP/RASP, LoE III	A
	Enucleation techniques can be offered to men with LUTS needing surgical treatment and prostate size 30-80 mL as an alternative to TURP.	*The LoE varies for the different energy sources: Ho:YAG laser, LoE I Tm:YAG laser, LoE II Diode laser, LoE II Plasmakinetic energy, LoE II	A

Abbreviations: GoR, Grade of Recommendation; LoE, Level of Evidence; LSP, laparoscopic simple prostatectomy; Ho:YAG, holmium:yttrium aluminum garnet; LUTS, lower urinary tract symptoms; RASP, robotic-assisted simple prostatectomy; Tm:YAG, thulium:yttrium aluminum garnet; TURP, transurethral resection of the prostate.

Vaporization of the Prostate

Several strategies and energy sources for the vaporization of hyperplastic tissue have been tested and implemented in clinical practice. Lasers, as an energy source, offer an inherent advantage over standard monopolar or bipolar

electrocautery, being relatively bloodless and posing a lower risk of hyponatremia. Consequently, they are becoming increasingly available.

Although various laser wavelengths ([potassium titanyl phosphate (KTP), holmium:yttrium aluminum garnet (Ho:YAG), Thulium]) and delivery systems ([end-firing, side-firing, interstitial]) remain available for photoselective vaporization of the prostate (PVP), each with distinct characteristics and potential advantages, current clinical practice recognizes the 532 nm 180 W GreenLight Laser as the optimal tool for PVP. This preference is primarily due to the significantly reduced operative times and shorter hospital stays of GreenLight Laser.

The GreenLight Laser source consists of either kalium-titanyl-phosphate (KTP) or lithium triborate (LBO), operating at a wavelength of 532 nm with a penetration depth of 0.8 mm to 3 mm. It is primarily absorbed by hemoglobin, explaining its excellent hemostatic properties and its predominant use in patients on anticoagulants or antiplatelets. Historically, the first 80 W generator (KTP) was developed, followed by a 120 W generator in 2006 and, ultimately, a 180 W generator in 2010.¹

In 2006, the 120 W LBO laser was introduced, utilizing diode-pumped Nd:YAG laser light emitted through an LBO crystal instead of a KTP crystal. This modification resulted in a higher-powered 532 nm wavelength while retaining the same 70-degree deflecting, side-firing, silica fiber delivery system. The 120 W system improved focus and power density, thereby reducing operative times and increasing ablation efficiency.^{2,3} While the 120 W laser PVP procedure was widely adopted, some studies reported high surgical retreatment rates (9%–16%) in patients with larger prostates (volumes > 80 mL). These findings highlighted the need for an improved energy delivery system.^{4,5}

To enhance the efficiency, efficacy, and durability of PVP treatments, the 180 W XPS system was introduced specifically for prostate procedures.⁶ This new system, featuring increased power, improved fiber optics, and a water-cooled laser fiber (Moxy fiber), enhanced tissue ablation efficiency and ensured more uniform and rapid energy distribution.⁷ It has been safely and effectively adopted in various clinical scenarios.^{8,9}

The 180 W PVP GreenLight laser vaporization has emerged as a viable alternative to TURP, reducing postoperative catheterization time, shortening hospitalization duration, and minimizing complications, particularly in patients with coagulation disorders.⁹

Two-year data from the GOLIATH trial demonstrated that the 180 W system ensures durable symptom improvement, proving to be noninferior to standard TURP.¹⁰

During a standard PVP procedure, the surgeon ablates prostatic tissue by treating the bulging adenoma from the prostatic urethra outward toward the prostatic capsule (inside-out). Several groups have worked to standardize the procedural steps as follows:

1. The laser is set at 180 W for vaporization and 40 W for coagulation, using a Moxy Fiber.
2. A preliminary cystoscopy is performed, and a working space is created.
3. The lateral lobes are progressively treated until the capsule is reached, and the paracollicular tissue is vaporized.
4. The median lobe and the bladder neck are treated.

To overcome some limitations of standard PVP (e.g., difficulty identifying cleavage planes, vaporization of high-volume glands), alternative techniques have been developed and proposed.^{11–13}

Despite the introduction of the novel XPS system, several groups have assessed the clinical differences between the 180 W and 120 W systems.¹⁴ However, a comprehensive and systematic comparison of long-term outcomes and patient recovery has been lacking.^{15,16} Recently, some studies have reported comparative analyses of the clinical efficacy and safety of GreenLight 120 W HPS versus 180 W XPS vaporization for BPH treatment.¹⁷

Regarding surgical outcomes, the 180 W system demonstrated significant advantages over the 120 W system in terms of operative time (mean difference [MD], 12.70; 95% CI, 5.29–20.11; $P = .0008$), lasing time (MD, 10.09; 95% CI, 0.85–19.33; $P = .03$), and postoperative catheterization duration (MD, 0.43; 95% CI, 0.12–0.74; $P = .007$). However, no significant differences were observed in hospital length of stay (MD, 0.57; 95% CI, –0.33 to 1.46; $P = .21$).

In terms of functional outcomes, no significant differences were found in IPSS ($P = .10$), $Q_{\max}$ ($P = .81$), or PVR ($P = .88$), except for QoL ($P = .02$) and PSA ($P = .003$). The improvement in QoL scores and PSA reduction observed with the 180 W XPS system likely reflects better patient satisfaction and a greater reduction in prostate volume, potentially enhancing the long-term effectiveness of the treatment.

A lower overall complication rate (odds ratio [OR], 1.52; 95% CI, 1.14–2.04; $P = .005$), as well as reduced minor complications (OR, 1.84; 95% CI, 1.27–2.66; $P = .001$) and urinary retention rates (OR, 1.80; 95% CI, 1.02–3.16; $P = .04$), were associated with the 180 W XPS system. However, no significant differences were observed in major complications ($P = .64$), capsular perforation ($P = .18$), dysuria ($P = .59$), retreatment rates ($P = .17$), bladder neck contracture ($P = .60$), or urethral stricture ($P = .93$).

In conclusion, PVP is a safe and effective surgical method for the treatment of symptomatic benign prostatic obstruction. From a literature overview, the results achieved by PVP, particularly those obtained using the high power system (180 W), largely overlap the results historically obtained with TURP. Several PVP multicentric and worldwide experiences showed a dramatic improvement in hospital stay, limited bleeding risks (in patients under active anticoagulants/antiplatelets), and a comparable operative time, maintaining a stable low complication rate.

TABLE 1 Vaporization of the Prostate Recommendations

Topic	Recommendation	LoE	GoR
Vaporization of the prostate	Offer LBO laser vaporization of the prostate to men with LUTS needing surgical treatment and prostate size 30–80 mL as an alternative to TURP.	I	A
	Offer laser vaporization of the prostate to men with increased bleeding diathesis with a prostate volume < 80 mL.	III	C

Abbreviations: GoR, Grade of Recommendation; LBO, lithium triborate; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; TURP, transurethral resection of the prostate.

Robotic Simple Prostatectomy

Robotic simple prostatectomy (RSP) has emerged as an effective surgical intervention for managing BPH, particularly in patients with significantly enlarged prostates unresponsive to medical therapy. The first laparoscopic simple prostatectomy was performed in 2002. However, due to the technical challenges and a steep learning curve associated with the laparoscopic approach, the adoption of the robotic platform has made RSP a widely used method for surgically treating large prostate glands.¹ Robotic simple prostatectomy is currently integrated into the recent updated BPH guidelines and is generally recommended as treatment for prostates larger than 80 grams.^{2,3}

Benefits and comparison with other techniques

Open simple prostatectomy and robotic simple prostatectomy are both effective surgical options for treating BPH in patients with large prostate glands. Historically, open simple prostatectomy (OSP) was considered the gold standard for prostate glands larger than 80 mL. However, the morbidity of the operation—including increased estimated blood loss (EBL), length of stay, and transfusion rate approaching 25%—has led to a shift toward minimally invasive techniques. These include robotic and endoscopic approaches, such as HoLEP, which have evolved to become an important part of the armamentarium for managing large prostate glands.

A systematic review and meta-analysis was performed to assess outcomes of RSP to OSP in the treatment of BPH. This included 764 patients across 27 observational studies with a mean prostate volume of 113.5 cc. In patients who underwent RSP, the mean operative duration was 141 minutes with mean intraoperative EBL of 284 mL. The mean increase in Q_{max} was 14.3 mL/s and mean improvement in IPSS was 17.2. Compared to OSP, the RSP group experienced significantly shorter hospital stays, reduced catheter duration, and lower EBL, although surgical duration was longer. However, no differences in perioperative complications, improvements in Q_{max} , or IPSS scores were identified between the two procedures.⁷

More recent systematic reviews and meta-analyses comparing RSP to OSP again showed no differences between IPSS and $Q_{\max}$. However, the RSP group had lesser EBL (weighted median difference [WMD], 292–563 mL), shorter catheter duration (WMD, ~2 days), length of stay (WMD, 2.52–2.85 days), and lower rate of complications (OR, 0.49). Consistently, the operative time was longer with RSP (WMD, ~43 minutes).^{8,9} There is robust evidence showing the similar efficacy of RSP to OP, while improving intraoperative and perioperative parameters.

Multiple studies have shown the technical feasibility and reproducibility of RSP for the treatment of enlarged prostates, particularly with the exponential use of the robotic platform in urologic surgery.^{4,5} We have seen a significant increase in adoption of the RSP over the years, with an estimated learning curve of about 10 to 12 cases for experienced robotic surgeons.⁶

Compared to the learning curve for RSP, the learning curve for HoLEP appears to be steeper, with an approximate 50-case learning curve reported throughout multiple studies.^{10–12} A systematic review and meta-analysis comparing the efficacy, efficiency, and safety of HoLEP with RSP was published in 2025. HoLEP and RSP had equal efficacy in terms of PVR and maximum urinary flow rate. However, HoLEP had reduced operative time by 49.48 minutes, length of stay by 1.5 days, and catheter duration by 3.8 days. Additionally, RSP patients had 1.87 times higher risk for grade 2 complications, 3.41 times higher risk for grade 3 complications, and HoLEP decreased risk of blood transfusions by 75%.¹³

To date, there is one multicenter RCT published in 2021 comparing LSP, RSP, and HoLEP for prostates larger than 120 mL. In this study, LSP was associated with significantly prolonged catheter durations relative to RSP and HoLEP. Additionally, both LSP and RSP were linked to extended hospital stays but demonstrated lower incidences of *de novo* bladder storage symptoms. A median follow-up of 26 months did not demonstrate any significantly different functional or perioperative results between LSP, RSP, and HoLEP.¹⁴

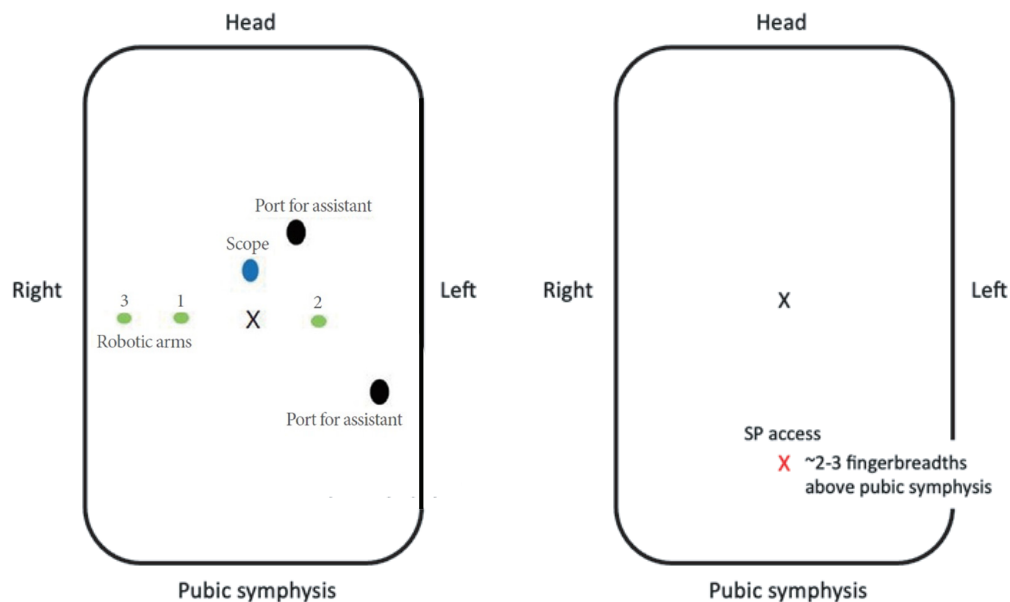
Lee *et al.* performed a retrospective analysis of patients who underwent HoLEP, OSP, and RSP for prostates larger than 80 mL. HoLEP had the shortest operative time (1.4 vs. 2.7 vs. 3.8 hours), length of stay (0.65 vs. 4.2 vs. 2.6 days), and catheter duration (0.38 vs. 9.9 vs. 11.2 days), compared to OSP and RSP, respectively. The lowest EBL was also identified with HoLEP (66 vs. 795 vs. 326 mL).¹⁵

A single institution comparative analysis was performed for patients with extremely large prostates larger than 200 grams undergoing HoLEP versus RSP, where 31 patients underwent RSP and 22 underwent HoLEP. There was improvement in maximum flow rate (+10.60 mL/s vs. +10.70 mL/s; $P = .724$), reduction in IPSS (-12.50 vs. -9; $P = .246$), and improvement in quality of life (-3 vs. -3; $P = .880$), although there were no differences between the two groups. The median operative time was similar (150 vs. 132.5 minutes; $P = .665$), with lower amount of tissue resected in the RSP group (134.5 vs. 180 g; $P = .029$). The complication rates were similar, with similar catheter duration, and lower hospitalization time in the HoLEP group.¹⁶

Surgical technique

In general, robotic simple prostatectomy may be performed via a transperitoneal or extraperitoneal approach, and the adenomectomy can be performed via a transvesical approach or transcapsular (Millin) approach. Port placement and patient positioning are similar to the conventional robotic radical prostatectomy setup (**FIGURE 1**). However, newer robotic platforms, such as the da Vinci Single Port platform, have allowed the surgery to be carried out through a single infraumbilical incision via the transvesical approach.

FIGURE 1 Robotic simple prostatectomy port configuration (left, multi-port; right, single-port).



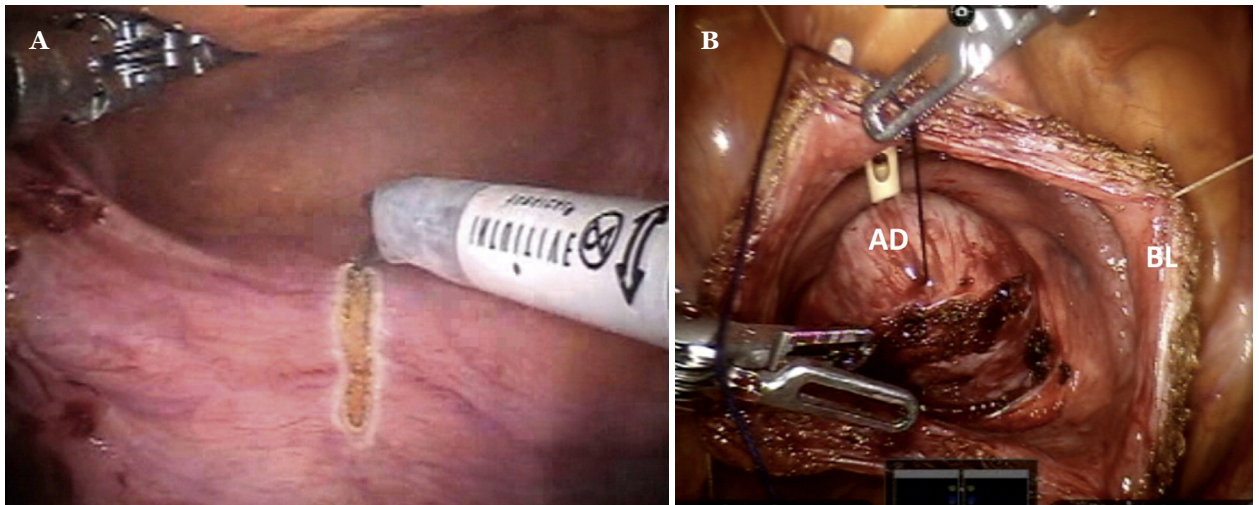
Source: Reproduced from Cho JM, Moon KT, Yoo TK. Robotic simple prostatectomy: why and how?. Int Neurourol J. 2020;24(1):12–20. doi:10.5213/inj.2040018.009¹⁷

Transperitoneal: transvesical approach

In the transperitoneal transvesical approach, the bladder is filled with saline until adequately distended. A vertical cystotomy is performed at the bladder dome to gain access to the prostate adenoma (**FIGURE 2**). Then the bladder wall may be fixated to the anterior and lateral abdominal walls with stay sutures for adequate retraction and maximum visibility. The mucosa is incised at the prostate-bladder interface, ensuring adequate distance from the ureteral orifices. The prostate adenoma is then enucleated after accessing the plane between the adenoma and the prostate capsule. The plane is then developed circumferentially using a combination of blunt dissection and electrocautery to ensure adequate hemostasis throughout. Use of retraction suture, bedside assistant, or use of the fourth arm can assist with adequate adenoma retraction.

Once the adenoma is enucleated, additional hemostasis is obtained using electrocautery and/or suture ligation. Mucosal advancement or bladder neck reconstruction may be performed, as discussed later in this chapter. The cystotomy is closed with absorbable sutures and tested to ensure adequate closure.^{17,18}

FIGURE 2 A) Vertical cystotomy made at the bladder dome. B) The adenoma (AD) is incised at the bladder-prostate junction posteriorly, and the bladder (BL) wall is shown retracted with stay sutures to the abdominal wall.

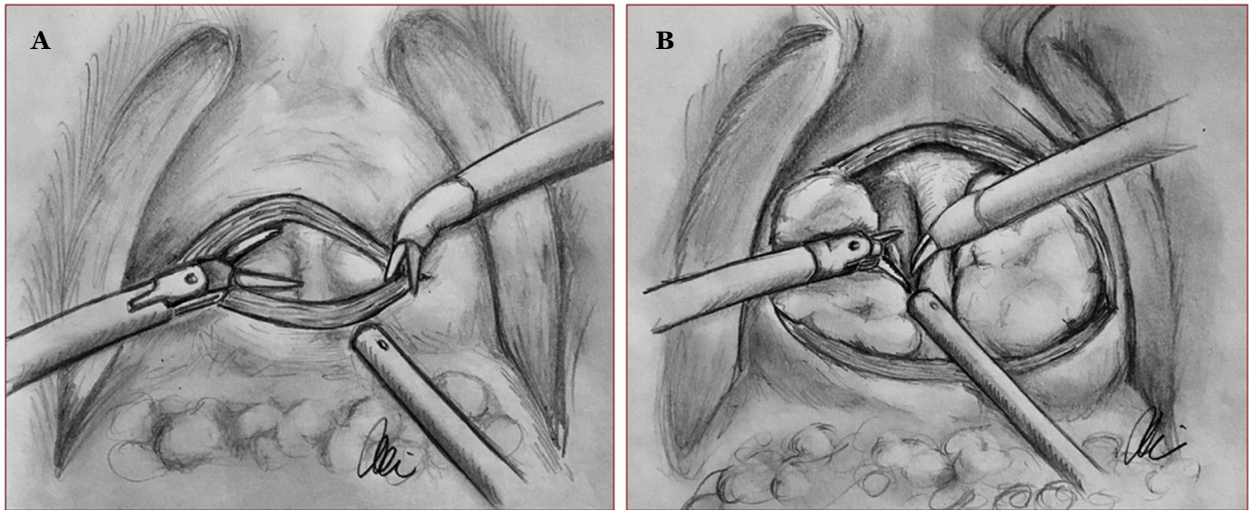


Source: Reprinted from *European Urology*, Vol. 66/No. 2, Leslie S, Abreu AL, Chopra S, et al., *Transvesical robotic simple prostatectomy: initial clinical experience*, pp. 321–329, Copyright (2014), with permission from Elsevier.¹⁸

Transperitoneal: transcapsular approach (Millin technique)

In the transperitoneal transcapsular approach, the bladder is dropped from the anterior abdominal wall, and the prostate is accessed anteriorly. The anterior prostatic capsule is incised transversely until the adenoma plane is reached, and the adenoma is enucleated circumferentially. Once the adenoma is fully enucleated, hemostasis is obtained, and mucosal reconstruction may be performed. Then closure of the capsulotomy concludes the procedure. This approach may be preferred for patients with long apical to bladder neck distances.¹⁷

FIGURE 3 A) Transverse prostate capsulotomy to identify the adenoma plane of dissection. B) Adenoma dissection away from urethra.



Source: Reprinted from *European Urology*, Vol. 80/No. 2, Porpiglia F, Checcucci E, Amparore D, et al., *Urethral-sparing robot-assisted simple prostatectomy: an innovative technique to preserve ejaculatory function overcoming the limitation of the standard Millin approach*, pp. 222–233, Copyright (2021), with permission from Elsevier.¹⁹

Intrafascial simple prostatectomy

In 2013, the intrafascial technique was described by Clavijo *et al.* where the plane for enucleation lies between the prostatic fascia and prostatic capsule, similar to a radical prostatectomy. However, this approach preserves the neurovascular bundles, seminal vesicles, and periprostatic fascia and spares the puboprostatic ligaments. Additionally, the intrafascial technique aims to reduce intraoperative blood loss, postoperative hematuria, and therefore reduce the need for postoperative bladder irrigation.²⁰

Extraperitoneal

The extraperitoneal space is opened with balloon insufflation and finger dissection. Once the robotic trocars are inserted, a transvesical or transcapsular approach for adenoma enucleation may be performed. This technique is now preferred via the single-port (SP) platform and may be beneficial in patients with hostile abdomens or inability to tolerate the Trendelenberg position.^{17,21}

Comparing enucleation techniques

A retrospective analysis performed by Martín Garzón *et al.* analyzed 236 minimally invasive simple prostatectomies, with 82 laparoscopic, 79 RSP Millin approach, and 75 RSP intrafascial approach. Intraoperative and postoperative outcomes were similar among the three procedures, with similar transfusion and complication rates, and postoperative functional outcomes such as IPSS, Sexual Health Inventory for Men (SHIM), continence, and $Q_{\max}$. The intrafascial technique did not require post-operative irrigation.²²

Mucosal reconstruction: trigonization or circular anastomosis

The two major techniques for mucosal reconstruction after adenoma enucleation in RSP include trigonization or a circular vesicourethral anastomosis. Trigonization involves advancing the posterior bladder neck mucosa to the distal urethral mucosa to reapproximate the mucosa, recreate the prostatic fossa, promote hemostasis, and also aid in smooth catheter entry. The circumferential vesicourethral anastomosis, where the bladder neck is circumferentially sutured to the urethra, was first described in 2012 by Coelho *et al.* as a modification to the standard trigonization. This aims to even further decrease perioperative blood loss and decrease the need for postoperative continuous bladder irrigation.^{23,24}

Single-port robotic simple prostatectomy

The introduction of the SP robot has prompted some to use this technology for simple prostatectomy as well. A study by Ramos *et al.* described the surgical technique, which generally consists of a 3-cm suprapubic incision and transvesical access to the adenoma, adenoma enucleation, and mucosal reconstruction. The outcomes of 117 cases showed median robotic console time of 107 minutes and EBL of 100 mL. Most patients were discharged within 24 hours with a tolerable pain score. Postoperative IPSS and flow rate remained improved at 1 year.²⁵ Postoperative narcotic use was also reduced for patients undergoing SP RSP compared to multi-port RSP, while maintaining efficacy in BPH treatment.²⁶

Conclusion

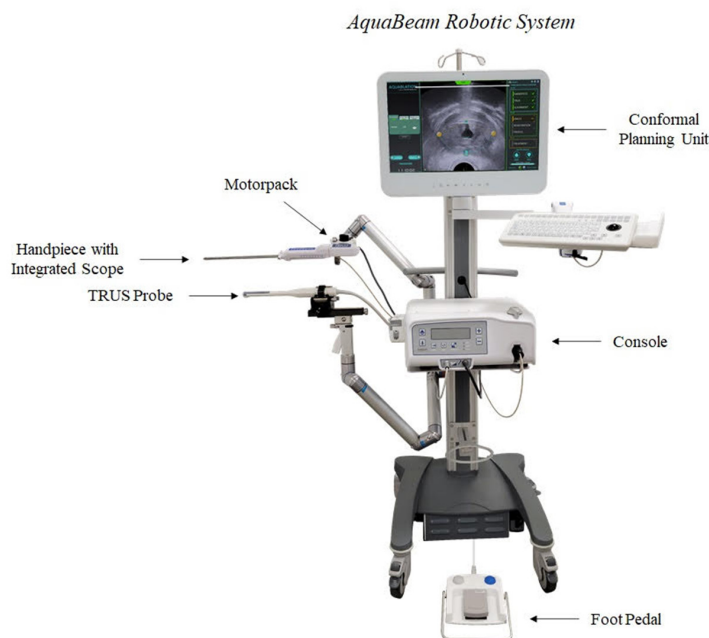
Robotic simple prostatectomy represents a significant advancement in the surgical treatment of BPH, offering patients a minimally invasive option with reduced perioperative morbidity and allowing for faster recovery.

Aquablation

Aquablation has become an integral treatment option for surgeons to effectively manage BPH while minimizing possible side effects. Not only has the literature proved the success of Aquablation, but Aquablation has also been endorsed by all major society guidelines. As recommended by the AUA, Canadian Urological Association (CUA), and EAU guidelines, the Aquablation procedure may be offered to patients suffering from LUTS/BPH with a prostate volume between 30 mL and 80 mL, though it has been shown to be effective in larger prostate volumes as well.¹ This technique utilizes an ultrasound-guided robot-assisted waterjet that can precisely target and ablate prostatic tissue. It was first described by Faber *et al.* (2015)² and continues to be used with both the Aquabeam and the HYDROS systems (PROCEPT BioRobotics Corporation, Redwood City, California, United States).^{3,4}

The first-generation Aquablation device, the Aquabeam robotic system, consists of three main components: the robotic armpiece, console, and conformal planning unit (CPU). Other components include the motorpack, stepper, foot pedal, handpiece articulating arm, transrectal ultrasound articulating arm, handpiece, and scope (**FIGURE 1**). The second-generation HYDROS system consists of three main components: the HYDROS Robotic System, the HYDROS TRUS Probe, and the HYDROS Handpiece (**FIGURE 2**). The HYDROS Robotic System itself comprises further components beyond the scope of this chapter.

FIGURE 1 PROCEPT's first-generation Aquablation device: the Aquabeam Robotic System.



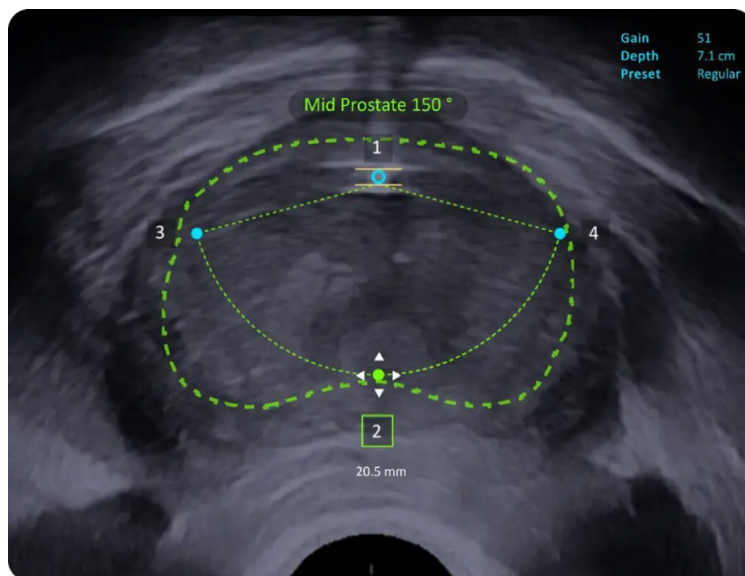
Source: Image courtesy of PROCEPT BioRobotics Corporation.

FIGURE 2 PROCEPT's second-generation Aquablation device, the HYDROS System features AI-powered treatment planning with FirstAssist AI™, advanced image guidance, and a more streamlined workflow than the previous Aquabeam system.



Source: Image courtesy of PROCEPT BioRobotics Corporation.

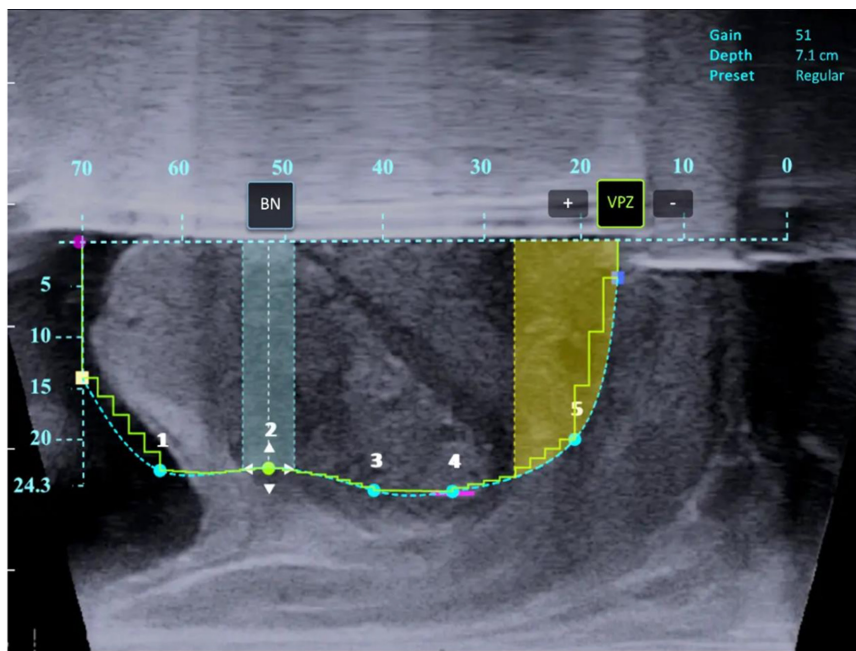
FIGURE 3 Transverse ultrasound view of the widest cross-section of the prostate during the angle-planning step. This step can also be performed for planning removal of an intravesical median lobe.



Source: Image courtesy of PROCEPT BioRobotics Corporation.

The procedure sequence is the same with both generations of the device: once the transrectal ultrasound (TRUS) is positioned, and the handpiece inserted into the bladder, the scope lens is retracted just proximal to the external sphincter. The user then aligns the jet to the ultrasound image to ensure congruency in treatment planning. The system's mapping software then aids the surgeon in registering the jet to the ultrasound image, measuring the appropriate water jet angles, and defining the jet depth throughout the treatment zone (**FIGURE 3**). Two built-in customizable safety zones are automatically provided in the final plan: one to set the bladder neck water jet angle at 120-degrees maximum and the other at a verumontanum protection zone (VPZ) aimed to not treat a 30-degree wedge of prostatic urethral floor proximal to and at the verumontanum (**FIGURE 4**). A high velocity jet then ablates the prostate tissue according to the desired plan under direct ultrasound guidance. After the ablation is complete, the handpiece is removed, the bladder is evacuated of clots, and the resectoscope is inserted to perform focal bladder neck cauterization (FBNC), further resection of treated tissue, and any required hemostasis. Once hemostasis is achieved, a 3-way catheter is inserted into the bladder and placed on traction and continuous bladder irrigation (CBI). Patients may be discharged the same day with a catheter or stay overnight if CBI is required. Catheter duration varies typically from 1 to 4 days depending on the surgeon's preferences.⁵

FIGURE 4 Sagittal ultrasound view of the prostate. This step allows the surgeon to outline the treatment plan as well as to define and protect critical anatomy. The bladder neck protection zone is labeled in blue, and the verumontanum protection zone (VPZ) is colored in yellow.



Source: Image courtesy of PROCEPT BioRobotics Corporation.

Initial results of Aquablation were reported by Gilling *et al.* in a small prospective, multicenter trial at three Australian centers including 21 men with prostate sizes 30 mL to 120 mL.⁶ The study demonstrated a drop in IPSS from 23 to 6.8 and an increased urinary flow rate from 8.7 mL per second to 18.3 mL per second at 1 year follow-up. Prostate volumes also decreased from a mean 57 mL at baseline to 35 mL, which represented an average decrease of 39%. The study did not show any peri- or postoperative adverse events such as urinary incontinence or sexual dysfunction (as measured by the Male Sexual Health Questionnaire-Ejaculatory Dysfunction Domain, [MSHQ-EjD]).⁶

Further studies have since compared Aquablation to other established bladder outlet procedures. The Waterjet Ablation Therapy for Endoscopic Resection of Prostate Tissue (WATER) trial, a double-blind randomized trial across 17 centers, directly compared TURP (monopolar and bipolar) and Aquablation in terms of safety and efficacy and has served as the basis for many of the evidence-based guidelines in BPH management.⁷ The study found no significant difference seen in overall mean operative time between the groups, though resection time was significantly less with Aquablation. Aquablation was found to be noninferior to TURP in terms of meeting its standard safety profile. The safety profile included patients with Clavien-Dindo grade 2 or higher complications, as well as those with any grade 1 events that resulted in a persistent disability—lasting at least 3 months before treatment—such as ejaculatory or erectile dysfunction, or incontinence. Efficacy data demonstrated Aquablation was noninferior to TURP in terms of average IPSS score postoperatively (mean score of 6.0 and 6.7, respectively, at 6 months). PVR scores were similar in both groups at 180 days, and urinary flow rate ($Q_{\max}$) at 180 days was relatively higher in the Aquablation group. The study also found that among sexually active men, the rate of anejaculation was significantly lower in those treated with Aquablation than with TURP (10% vs. 36%; $P < .001$).⁷ Five-year data of this trial demonstrated minimal change in MSHQ-EjD for those patients treated with Aquablation, which was superior to the results in the TURP arm, and no change in the IIEF score within the Aquablation cohort.⁸

The WATER II trial then expanded on this data by investigating Aquablation's safety and feasibility in larger prostates (80–150 mL).¹ This trial did not compare Aquablation to TURP but rather compared it to an objective performance criterion (OPC) to assess noninferiority to other modalities. This Water II study was a prospective trial utilizing the same safety and efficacy endpoints as the first trial and found that Aquablation was noninferior in terms of safety and IPSS score improvement. At 3 months, postoperative prostate volumes were reduced by an average of 44%. Of note, bleeding complications were recorded in 9.9% of the cohort prior to discharge, with 5.9% (6 patients) requiring perioperative blood transfusions. However, this study was prior to the addition of focal bladder neck cauterization, which eventually significantly decreased postoperative bleeding complications.⁹

When patients were stratified by prostate volumes between 30 mL and 80 mL and those with prostate volumes 80 mL to 150 mL, the 12-month outcomes of the WATER and WATER II trials showed no significant difference in postoperative IPSS scores or $Q_{\max}$, indicating the effectiveness and safety of Aquablation with various prostate sizes.¹⁰ The overall outcome trends of the WATER trials were corroborated by a literature review by Hwang *et al.* (2019), which revealed noninferior symptom relief of Aquablation as compared to TURP, with lower risk of sexual dysfunction with Aquablation (as measured by MSHQ-EjD and IIEF).¹¹ In this study, larger prostates (50–80 mL) demonstrated a more pronounced superior safety and efficacy benefit.¹¹ When comparing the long-

term outcomes of the WATER and WATER II trials at 5 years, both patient cohorts treated with Aquablation experienced significant improvement in IPSS scores and increases in $Q_{\max}$.¹² These patients also remained free of BPH medications and surgical retreatment at 5 years. Recent prospective trials have continued to reinforce the findings that Aquablation has a significant impact on IPSS score improvement, increased urinary flow, with relatively low rates of adverse outcomes such as incontinence, erectile dysfunction, or ejaculatory dysfunction.^{13,14}

When comparing the WATER and WATER II trials, there were more bleeding complications noted in the WATER II trial, which can be expected given the larger prostate sizes studied.¹⁰ The most common Clavien-Dindo grade III or greater adverse event was gross hematuria. These studies did not incorporate a standard intraoperative hemostasis regimen. PROCEPT eventually developed a structured postablation hemostasis protocol (known as “Focal Bladder Neck Cauterization”) to minimize hematuria. Selective bladder neck cautery and resection with standard traction techniques applied postoperatively have been found to substantially reduce the risk of transfusion, regardless of prostate size.¹⁵ In April 2021, a publication of > 2000 patients undergoing this technique yielded a transfusion rate of 0.8% for treated prostates with volumes of 20 mL to 363 mL.⁹

Oumedjbeur *et al.* showed greater durability of Aquablation over TURP at 5 years in a subset analysis from a large, double-blind, multicenter (the WATER study), prospective RCT of 96 men with prostate volumes of 50 mL to 80 mL.¹⁶ As compared to TURP, Aquablation had significantly greater reduction in IPSS scores, achieved a significantly lower rate of Clavien-Dindo grade 1P and 2+ events at 3 months follow-up, and was associated with significantly lower postoperative ejaculatory dysfunction. Aquablation was also associated with a significantly lower rate of surgical retreatment at 6 months. The risk of bleeding remained similar after 6 months for the two groups. Besides Aquablation’s noninferiority and, in some cases superiority, to TURP in terms of safety and efficacy, operating time is typically shorter than with other procedures and does not increase significantly with larger glands compared to other BPH modalities.¹⁷

In comparison to other surgical options for BPH, Aquablation has shown similar efficacy and safety outcomes. When compared to Rezūm and UroLift for prostates up to 80 mL, Aquablation was superior in QoL, $Q_{\max}$, and PVR. Although UroLift showed greater improvement in MSHQ-EjD scores, the patients in this cohort had the greatest rates of retreatment out of the three options. Postoperative urinary retention rates were highest in those treated with Aquablation.¹⁸ However, Aquablation has also been found to be safe and effective in select patients who had failed previous BPH treatments.¹⁹

A recent network meta-analysis compared outcomes of Aquablation and HoLEP.²⁰ At 12 months, the HoLEP procedure was associated with better outcomes in terms of IPSS, QoL, PVR, and $Q_{\max}$ improvements, though it was associated with higher rates of incontinence. There was a higher risk of hemoglobin loss and risk of blood transfusion with Aquablation as well as higher rates of retreatment. Despite the difference in functional outcomes, Aquablation operative time and hospital stays were significantly lower, presenting a compelling alternative in the outpatient setting.²⁰

Most recently, Justo Quintas *et al.* further investigated the comparison of Aquablation versus HoLEP. In a prospective, comparative, nonrandomized, multicenter study of 150 patients, the authors compared the short-

term efficacy of the two BPH procedures.²¹ The study found no significant differences between the two treatment groups in IPSS, IPSS-QoL, peak urinary flow rate, and PVR at 6 months. Ejaculatory dysfunction rates were significantly lower in Aquablation than HoLEP (6.6% vs. 89.3%; $P < .0001$). HoLEP was associated with smaller prostate volumes after treatment (18.1 ± 6.5 vs. 46.5 ± 25.02 mL; $P < .001$). Intraoperatively, Aquablation demonstrated significantly shorter tissue removal time (5.5 vs. 9.8 min; $P < .0001$) but no difference in total operative time (49.1 ± 15 vs. 43.9 ± 26.8 min, $P = .052$). Postoperative hemoglobin drops were higher in the Aquablation groups; however, there was no statistically significant difference in transfusion rates (1.3 vs. 1.3%; $P = .31$).²¹ Ultimately, this study demonstrated a similar efficacy between Aquablation and HoLEP, with HoLEP associated more strongly with ejaculatory dysfunction and postoperative stress urinary incontinence.

Overall, the current literature supports Aquablation as an efficacious and safe option in the surgical management of BPH, with profound long-term outcomes as well as low rates of complications and adverse outcomes. Further research involving larger study populations, long-term follow-up, and well-designed RCTs will be crucial to validate the observed trends and to generalize our conclusions about Aquablation in comparison to other BPH procedures. Nonetheless, initial data indicate a promising role for Aquablation as a primary treatment modality for BPH.

TABLE 1 Aquablation Recommendation

Topic	Recommendation	LoE	GoR
Aquablation	Offer Aquablation to men with LUTS needing surgical treatment and prostate size 30–80 mL as an alternative to TURP.	II	B
	Aquablation may be used for larger prostates in select cases depending on the expertise of the surgeons.	III	C

Abbreviation: GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; TURP, transurethral resection of the prostate.

Conclusion

Despite intense interest in the development of MISTs, the traditional approach of removing tissue to effect de-obstruction continues to be the mainstay of our armamentarium for the surgical management of benign prostatic obstruction. Constant incremental tweaks in the way such surgery is performed create a higher bar against which other treatments must be compared. We have newer ways to remove tissue and other methods are likely to appear, but TURP continues to be the mainstay procedure in urological practice. It is worth being reminded that the TURP technique and technology we have today as well as the outcomes bear little resemblance to those of 50 years ago. Furthermore, while TURP was thought to have replaced its predecessor gold standard of simple prostatectomy, the latter has never really gone away and continues to be an essential part of our treatment offering.

Procedural Video



Aquablation® Procedural Video

Source: SIU Academy®.

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05

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Table of Contents

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Introduction and Overview	220
Water Vapor Thermal Therapy—Rezūm	220
Prostate volume: optimal range and efficacy	220
Anatomical features: median lobe and complex variants	221
Symptom severity: IPSS and patient selection	221
Prior treatment history: medical and surgical	221
Comorbidities and contraindications	221
Durability of symptom relief and retreatment rates	222
Sexual function: erectile and ejaculatory outcomes	222
Patient-reported outcomes and satisfaction	223
Patient preferences, goals, and quality-of-life considerations	223
Effectiveness and safety in special populations	223
Limitations and gaps in the evidence	224
Conclusion	224
Prostatic Urethral Lift—UroLift	225
Prostate size and UroLift eligibility	225
Anatomical features: median lobe, prostate shape, and variants	225
Median lobe and intravesical prostatic protrusion	225
Prostate shape and imaging	225
Rare anatomical variants	226
Symptom severity and types	226

Table of Contents

Prior treatment history	226
Comorbidities and contraindications	226
Comorbidity burden	226
Bleeding risk and anticoagulation	227
Infection risk	227
Absolute and relative contraindications	227
Long-term durability and retreatment	228
Sexual function outcomes	228
Patient preferences and quality-of-life considerations	228
Special populations and complex histories	228
Management of retreatment after UroLift failure	229
Safety and efficacy in large prostates and complex anatomy	229
Emerging contraindications and patient factors	229
Conclusion	230
Temporary Intraprostatic Devices—iTIND	231
Prostate volume and iTIND outcomes	231
Anatomical features: median lobe and intravesical prostatic protrusion	231
Symptom severity and quality of life	232
Prior BPH treatments and iTIND candidacy	232
Comorbidities and contraindications to other therapies	232
Long-term efficacy, safety, and retreatment	233
Patient subgroups: age, symptom severity, ethnicity	234
Clinical decision tools and patient selection algorithms	234
Rare or emerging contraindications	234
Real-world retreatment rate and patient satisfaction beyond 3 years	234
Conclusion	235
Intraprostatic Balloon Treatment—Optilume BPH	236
Efficacy and safety outcomes of Optilume across patient subgroups	236
Prostate size, anatomy, and symptom severity	236

Table of Contents

Anatomical variants: median lobe and complex anatomy	236
Patients with prior failed BPH interventions	236
Patients with significant comorbidities	237
Long-term efficacy and retreatment rates	237
Guideline and expert consensus on patient selection	238
Contraindications and less effective scenarios	238
Comparative effectiveness and ongoing research	239
Real-world and registry data	239
Off-label or investigational use	239
Summary: the optimal BPH patient for Optilume	240
Conclusion	240
Prostate Artery Embolization	241
Patient selection criteria for PAE	241
Efficacy and safety across patient subgroups	241
Prostate volume	241
Symptom severity	242
Comorbidities and age	242
Urinary retention and high-risk populations	242
Sexual function and quality of life	242
Prior failed therapies	242
Small prostate volumes and atypical anatomy	243
Comparative effectiveness: PAE vs. TURP and other therapies	243
Long-term efficacy and durability	243
Technical and anatomical predictors of success	243
Cost-effectiveness	244
Emerging and investigational indications	244
Contraindications and populations with reduced efficacy	245
Conclusion	245
Emerging Therapies—Transperineal Laser Ablation	246

Table of Contents

Patient selection: prostate size and anatomy	246
Impact of prior BPH treatments	246
Comorbidities and contraindications	246
Functional outcomes: symptom relief, sexual function, and durability	247
Procedural safety and complication rates	248
Long-term outcomes and retreatment	248
Special populations: large prostates, anatomical variants, and prior radiation	248
Technical and operator-dependent factors	249
Patient-reported outcomes, preferences, and satisfaction	249
Cost-effectiveness	249
Predictors of outcomes and complications	250
Conclusion	250
Ultrasound Ablation	251
Guideline-based indications and patient selection criteria	251
Prostate size ranges: optimal and limiting factors	251
Symptom severity and prior treatment history	252
Comorbidities and contraindications	252
Efficacy, safety, and patient-reported outcomes	253
Long-term efficacy, safety, and retreatment	253
Cost-effectiveness and resource utilization	254
Real-world adoption and accessibility	254
Ongoing clinical trials and recent evidence	255
Patient perspectives and preferences	255
Guideline updates	255
Conclusion	256
Temporary Intraprostatic Devices/Stents	257
Temporary prostatic stents: devices and clinical context	257
Published indications and ideal patient selection criteria	257
Contraindications and patient factors limiting suitability	257
Device-specific differences in patient selection	258

Table of Contents

Clinical outcomes and complication rates compared to other BPH management options	258
Long-term clinical outcomes and durability	259
Patient-reported outcomes and quality of life	259
Cost-effectiveness and healthcare resource implications	259
Real-world adherence and satisfaction	260
Patient subgroups: who derives the greatest benefit or risk?	260
Device-specific features influencing selection and outcomes	261
Conclusion	261
Permanent Intraprostatic Devices/Stents	262
Patient selection criteria for permanent prostatic stents or implants	262
Guideline-based indications and quantitative selection parameters	262
Contraindications and special considerations	262
Influence of comorbidities	263
Comparative outcomes, risks, and long-term data	263
Functional outcomes and complication rates	263
Comparative efficacy with other BPH therapies	264
Long-term durability and patient-reported outcomes	264
Device-specific technical considerations and selection	265
Technical attributes and customization	265
Device-specific selection criteria and advantages	266
Real-world effectiveness, cost-effectiveness, and health economic outcomes	267
Real-world registry and post-marketing data	267
Cost-effectiveness and health economic outcomes	267
Implementation, monitoring, and future directions	268
Stepwise implementation and monitoring	268
Future research and ongoing trials	268
Conclusion and actionable recommendations	268
Procedural Videos	270
References	271

Introduction and Overview

The landscape of benign prostatic hyperplasia (BPH) management has evolved dramatically in recent years, with a growing number of minimally invasive surgical therapies (MISTs) emerging as alternatives to traditional medical therapy and surgical procedures. This chapter aims to provide a comprehensive overview of these MIST options, each discussed in its own section by experienced contributors. Our focus is to offer insight into the characteristics, outcomes, and patient selection criteria associated with each modality.

Importantly, this chapter emphasizes the identification of patient-specific anatomical and clinical factors that contribute to successful outcomes. By matching the right procedure to the right prostate in the right patient, clinicians can optimize care and minimize complications, enhancing both functional outcomes and quality of life. With detailed discussion of procedural nuances, efficacy data, complication profiles, and evolving evidence, this resource is intended to help guide current clinical practice and inform future directions in BPH treatment.

Water Vapor Thermal Therapy—Rezūm

Prostate volume: optimal range and efficacy

The initial pivotal randomized controlled trials (RCTs) of Rezūm enrolled men with prostate volumes between 30 cc and 80 cc, demonstrating significant and durable improvements in International Prostate Symptom Score (IPSS), quality of life (QoL), and maximum urinary flow rate ($Q_{\max}$) over 5 years, with a low surgical retreatment rate (4.4%) and preservation of sexual function.^{1,2} These data established Rezūm as an effective and safe option for prostates in the 30 cc to 80 cc range.

Subsequent real-world studies and systematic reviews have expanded the evidence base to include prostates as small as 20 cc and as large as 120 cc. In a large retrospective study, outcomes at 12 months were similar across all volume groups (< 30 cc, 30–80 cc, > 80 cc), with no significant differences in efficacy endpoints.³ A systematic review and meta-analysis of 471 men with prostates $\geq$ 80 cc found significant improvements in IPSS, $Q_{\max}$, and post-void residual (PVR), with low rates of serious complications and surgical retreatment at a median follow-up of 6 months.⁴ These findings are corroborated by large multicenter registries and cohort studies, which report similar improvements in symptom scores and flow rates in men with large prostates, with no increase in serious adverse events or loss of sexual function.^{5–9}

While the strongest and most durable evidence supports Rezūm in the 30 cc to 80 cc range, the therapy is now considered effective and safe for prostates from 20 cc up to at least 120 cc, with appropriate patient counseling regarding minor adverse events such as hematuria, which may be more common in larger glands.^{3–6,9}

Anatomical features: median lobe and complex variants

The presence of a median lobe has historically complicated BPH management, but Rezūm's mechanism allows for targeted ablation of obstructive tissue, including the median lobe. The pivotal trial and subsequent studies found that patients with median lobe involvement experienced similar improvements in IPSS, $Q_{\max}$, and QoL as those without, with no increase in adverse events or sexual dysfunction.^{1,10–13} Real-world data confirm that median lobe involvement does not negatively impact efficacy or safety, and Rezūm is suitable for this anatomical subgroup.^{5,11–13}

For other complex anatomical variants, such as prior pelvic surgery, treated urethral strictures, or bladder diverticula, Rezūm remains a viable option provided the prostatic urethra is accessible and there is sufficient obstructive tissue.^{14–16} However, untreated or severe urethral strictures are a relative contraindication until adequately managed, as they may impede access and increase procedural risk.^{14,15} The presence of bladder diverticula does not preclude Rezūm treatment, but comprehensive preoperative evaluation is necessary to ensure that prostatic obstruction is the primary driver of symptoms.^{14,15}

Symptom severity: IPSS and patient selection

Rezūm is most effective in men with moderate-to-severe lower urinary tract symptoms (LUTS), defined as a baseline IPSS of 8 or greater. In these patients, Rezūm provides rapid, clinically meaningful, and durable improvements in symptom scores, quality of life, and urinary flow, with a low risk of retreatment and preservation of sexual function.^{1,3,5,6,13,14,17–20} The benefit in men with mild LUTS (IPSS ≤ 7) is limited; while some may experience improvements in quality of life or nocturia, the overall magnitude of symptom improvement is minimal, and transient worsening of symptoms may occur.¹⁸ Therefore, Rezūm should be reserved for those with moderate-to-severe symptoms or specific quality-of-life goals, such as bothersome nocturia or a strong desire to discontinue medications.¹⁸

Prior treatment history: medical and surgical

Rezūm is effective and safe in patients with prior medical or surgical BPH treatments, including those with failed transurethral resection of the prostate (TURP), UroLift, or prior Rezūm.^{3,21} Studies demonstrate significant improvements in IPSS, $Q_{\max}$, and QoL in these populations, with retreatment rates and adverse event profiles comparable to those in treatment-naïve patients.²¹ The mechanism of action—targeted thermal ablation—remains effective in prostates previously altered by other interventions, provided there is residual obstructive tissue.²¹

Comorbidities and contraindications

Rezūm is particularly suitable for patients with significant comorbidities, including those on anticoagulation, with urinary retention, or at high surgical risk due to advanced age or multimorbidity. The procedure can be performed under local anesthesia, with a low risk of significant bleeding, making it safe for patients who cannot

discontinue anticoagulation.^{16,23} Multiple studies have demonstrated that Rezūm is effective in relieving catheter dependency in patients with urinary retention, with success rates for achieving catheter independence ranging from 70% to over 90%.^{12,22–25} The safety profile remains favorable in these high-risk populations, with most adverse events being mild and transient.^{23–26}

Absolute contraindications include active urinary tract infection, uncorrected coagulopathy, and inability to access the prostatic urethra. Relative contraindications include very large prostate volumes (well above 100–120 cc), severely scarred or fibrotic prostates, and untreated or severe urethral strictures.^{14,23} The presence of a penile prosthesis or artificial urinary sphincter may require special consideration but is not an absolute contraindication.¹⁴

Criterion	Details	References
Prostate volume	30–80 cc (RCTs); 20–120 cc (real-world, registry)	1–4
LUTS severity	Moderate-to-severe LUTS (IPSS ≥ 8–13); mild LUTS only if bothersome nocturia	1,3,5
Median lobe	Included; median lobe can be treated	1–3
Prior BPH therapy	Prior medical/surgical therapy not exclusionary	2,3,6
Comorbidities	Suitable for elderly, multimorbid, anticoagulated patients	2,6,7
Contraindications	Active UTI, uncorrected coagulopathy, inaccessible prostatic urethra	3,6,7

Abbreviations: BPH, benign prostatic hyperplasia; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms; RCTs, randomized controlled trials; UTI, urinary tract infection.

Durability of symptom relief and retreatment rates

Long-term data from RCTs demonstrate that Rezūm provides durable symptom relief, with sustained improvements in IPSS, QoL, and Q_{max} out to 5 years, and a surgical retreatment rate of approximately 4–5%.^{1,17,27} Real-world studies corroborate these findings, with similar durability and low retreatment rates across a range of prostate sizes, anatomical features, and prior treatment histories.^{3,5,14,17,27} In large prostates (≥ 80 cc), short- to medium-term data support durable outcomes, but longer-term follow-up is needed.^{4,6,9} Predictors of retreatment include smaller prostate volume, greater number of injections, and early suboptimal symptom response.²⁸

Follow-up duration	Retreatment rate (%)	Predictors of retreatment	References
1 year	2–5	Smaller prostate, more injections	1–3
3–5 years	4.4–5.7	Early suboptimal symptom response	3–6

Sexual function: erectile and ejaculatory outcomes

Preservation of sexual function is a key advantage of Rezūm. Multiple studies, including RCTs and long-term real-world cohorts, demonstrate that Rezūm does not cause clinically significant deterioration in erectile or ejaculatory function.^{1,5,29–32} In fact, some men with baseline erectile dysfunction experience improvement after

Rezūm, likely due to relief of LUTS and discontinuation of medications with sexual side effects.³⁰ Compared to TURP and other surgical options, Rezūm is associated with a much lower risk of retrograde ejaculation and erectile dysfunction.^{29,31–37} Among minimally invasive treatments (MISTs), Rezūm is comparable to UroLift and Aquablation in terms of sexual function preservation.³⁸

Patient-reported outcomes and satisfaction

Patient-reported outcomes and satisfaction rates with Rezūm are high. The pivotal trial and real-world registries report substantial and durable improvements in IPSS, quality of life, and BPH Impact Index, with most patients able to discontinue BPH medications and return to normal activities rapidly.^{1,5,18,22} The preservation of sexual function, low retreatment rate, and minimal perioperative morbidity are consistently cited as drivers of patient satisfaction.^{5,14,18,22} Comparative studies and network meta-analyses indicate that Rezūm offers similar patient-reported outcomes and satisfaction as other MISTs, with a more favorable profile for sexual function preservation compared to TURP.^{14,38–43}

Timepoint	IPSS reduction (%)	QoL improvement (%)	Q _{max} increase (%)	References
3 months	48–53	45–50	44–60	1–5
12 months	59	67	74	2,3,6
3–5 years	47–65	43–67	44–67	1,5–7

Abbreviations: IPSS, International Prostate Symptom Score; Q_{max}, maximum urinary flow rate; QoL, quality of life.

Patient preferences, goals, and quality-of-life considerations

Rezūm is particularly preferable for BPH patients who prioritize preservation of sexual function, wish to avoid long-term medication, seek a minimally invasive and office-based procedure with rapid recovery, and desire durable symptom relief without the risks of major surgery or anesthesia.^{1,3,14,18,22,38,42,46} These preferences are especially relevant for sexually active men, those intolerant of or unwilling to continue pharmacotherapy, individuals with significant comorbidities, and patients who value a quick return to normal activities. Shared decision-making is essential to align treatment selection with individual patient goals and expectations.^{14,38,46}

Effectiveness and safety in special populations

Rezūm is safe and effective in very elderly, frail, and multimorbid patients, including those with catheter dependency due to urinary retention secondary to BPH.^{24–26,47} The rates of symptom improvement, catheter independence, and adverse events are comparable to those seen in younger and less comorbid populations, with most complications being mild and transient.^{24–26,47} High baseline PVR is a risk factor for prolonged catheterization and urinary tract infection, but does not preclude eventual symptom relief.⁴⁸ There is insufficient evidence to support the use of Rezūm in patients with neurogenic bladder or significant detrusor underactivity, and such cases should be approached with caution and individualized assessment.^{14,24–26}

Limitations and gaps in the evidence

Despite the robust evidence base, important limitations remain. Long-term data in large prostates and special populations are limited, and the durability of outcomes beyond 12 months to 24 months in these groups is not fully established.^{4,6,9} There is a lack of high-quality, head-to-head comparative studies between Rezūm and other MISTs or standard surgical options, and the optimal dosing for large prostates is not yet standardized.^{4,6,37} Predictors of success and failure are incompletely defined, and more research is needed to clarify the role of Rezūm in men with mild LUTS or specific patient-reported outcomes.^{13,18,47,49} Ongoing and recent prospective studies and registries are expected to address many of these gaps, which will help refine future patient selection criteria.^{5,6,14,47,49}

Conclusion

Rezūm water vapor thermal therapy is best suited for men with moderate-to-severe LUTS due to BPH who desire durable symptom relief, preservation of sexual function, and a minimally invasive, office-based procedure with rapid recovery. The therapy is effective and safe across a broad range of prostate sizes (20–120 cc), including those with median lobe involvement, prior medical or surgical treatments, and significant comorbidities. It is particularly advantageous for patients who are poor candidates for traditional surgery, those on anticoagulation, and those with catheter dependency due to urinary retention. The safety profile is favorable, with most adverse events being mild and transient, and the risk of retreatment is low. Shared decision-making, individualized patient selection, and thorough preoperative evaluation are essential to optimize outcomes. Ongoing research will further refine the role of Rezūm in the BPH treatment algorithm and expand its applicability to broader patient populations.^{1,3–6,14,18,22,38,44–46,50}

Topic	Recommendation	LoE	GoR
Water Vapor Thermal Therapy (WVTT)	Offer water vapor thermal therapy to men with LUTS due to BPO interested in preserving ejaculatory function and/or avoiding anesthesia, who accept less de-obstruction with a greater need for retreatment (compared to TURP), in prostates between 30–80 mL (or larger in select cases) without bladder neck obstruction.	II	B

Abbreviations: BPO, benign prostatic obstruction; GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; TURP, transurethral resection of the prostate.

Prostatic Urethral Lift—UroLift

Prostate size and UroLift eligibility

The most authoritative guidance on prostate size for UroLift candidacy comes from the American Urological Association (AUA) guideline, which recommends UroLift for patients with prostate volumes between 25 cc and 75 cc and in the absence of an obstructive median lobe.¹ This recommendation is grounded in the inclusion criteria of pivotal RCTs such as the L.I.F.T. study, which enrolled men with prostates between 30 mL and 80 mL, with a mean volume of approximately 42 mL.² Systematic reviews and meta-analyses confirm that the evidence base for UroLift is strongest in this size range.^{2,3}

Real-world studies from Japan and Germany have reported safe and effective outcomes for UroLift in patients with prostates up to 100 mL, with no significant difference in postoperative urinary status among groups stratified by prostate size (< 30 mL, 30 to < 50 mL, and ≥ 50 mL).^{4,5} However, these studies did not include patients with prostates > 100 mL, and the evidence for efficacy and safety in this population remains limited. Larger prostates require longer operative times and more implants, and outcomes may be less predictable.^{4–6} For prostates > 100 mL, alternative surgical options such as endoscopic enucleation are generally preferred.⁷

Anatomical features: median lobe, prostate shape, and variants

Median lobe and intravesical prostatic protrusion

Historically, the presence of a prominent or obstructive median lobe (OML) was considered a contraindication to UroLift, as early trials excluded these patients.^{1–3} The concern was that UroLift’s mechanical retraction would not adequately address the “ballvalve” obstruction caused by a median lobe protruding into the bladder neck.⁸ However, recent evidence, including the MedLift study and real-world analyses, demonstrates that UroLift can be safely and effectively performed in selected patients with OML, provided that the procedural technique is adapted to address the unique anatomical challenges.^{9–11} Outcomes in OML patients are comparable to those with only lateral lobe enlargement, though more implants may be required.^{9–11} The AUA guideline has not yet fully incorporated these findings, but the presence of OML is now considered a relative rather than an absolute contraindication, with candidacy determined by detailed anatomical assessment and surgeon expertise.^{9–11}

Prostate shape and imaging

The overall shape and configuration of the prostate, particularly the degree of intravesical prostatic protrusion (IPP), are important in both the pathophysiology of obstruction and the technical feasibility of UroLift.⁸ IPP is a strong predictor of bladder outlet obstruction and failure of medical therapy.⁸ Magnetic resonance imaging

(MRI) and transrectal ultrasound can provide valuable information about prostate morphology and guide patient selection and implant placement, especially in complex anatomies.^{12,13} UroLift is most effective when the obstructing tissue is amenable to lateral retraction; significant IPP or a large, mobile median lobe may require modified techniques or alternative therapies.^{9–11,14}

Rare anatomical variants

Patients with high bladder neck or unusual lobe configurations may still be candidates for UroLift, but technical modifications are often necessary. For example, combining UroLift with a limited transurethral incision or resection of the bladder neck can improve outcomes in patients with high bladder neck or unfavorable anatomy while preserving sexual function.¹⁴ Careful intraoperative cystoscopic assessment and individualized implant placement are essential to optimize results and minimize complications.^{5,9,11,14,15}

Symptom severity and types

UroLift is indicated for men with moderate-to-severe LUTS attributed to BPH, typically defined as an IPSS of at least 13.^{1,2,10,16} The pivotal trials and systematic reviews consistently required this threshold for enrollment, and patients with this level of symptom burden experienced clinically meaningful improvements in IPSS, QoL, and urinary flow rates.^{2,10,16} UroLift provides improvement across the spectrum of LUTS, with the most pronounced effects on voiding (obstructive) symptoms such as weak stream, intermittency, and incomplete emptying, but also benefits storage (irritative) symptoms.^{2,10,16} There is no robust evidence supporting the use of UroLift in men with mild symptoms (IPSS < 8), as these patients are generally managed conservatively.^{1,2}

Prior treatment history

UroLift is best suited for men who have failed or are intolerant of medical therapy for BPH, such as α -blockers or 5 α -reductase inhibitors, and who have not previously undergone surgical intervention for BPH.^{2,5,17–19} Most pivotal trials and real-world studies excluded patients with prior prostate surgery due to concerns about altered anatomy and suboptimal outcomes.^{2,5,17–19} There is emerging literature on the management of patients who have undergone UroLift and subsequently require further surgical intervention, such as TURP or holmium laser enucleation of the prostate (HoLEP), but UroLift is not typically performed after other surgical procedures.²⁰ Patients with a history of urinary retention may still be considered for UroLift, provided the retention is due to obstructive BPH and not detrusor failure.^{4,5}

Comorbidities and contraindications

Comorbidity burden

UroLift can be performed under local anesthesia, making it attractive for patients with significant comorbidities or high anesthesia risk.^{3,17,19} However, recent real-world studies indicate that patients with a high comorbidity

burden (American Society of Anesthesiologists [ASA] score ≥ 3) experience less durable improvements in symptom scores and a higher rate of treatment failure, with 36% requiring additional intervention for recurrent LUTS.²¹ Comorbidity is not an absolute contraindication, but it is associated with a higher likelihood of suboptimal outcomes and should be discussed during preoperative counseling.²¹

Bleeding risk and anticoagulation

Post-marketing surveillance has revealed a higher-than-expected rate of significant bleeding complications with UroLift in real-world practice, particularly in patients on chronic anticoagulation or with underlying coagulopathies.^{22,23} The risk of major bleeding is higher than previously reported in clinical trials, and anticoagulation status should be carefully evaluated. Patients with unmodifiable bleeding risk may not be ideal candidates for UroLift, and alternative therapies may be preferable.^{22,23}

Infection risk

UroLift is associated with a low incidence of infectious complications, but active urinary tract infection (UTI) is a temporary contraindication until adequately treated.²⁴ Chronic immunosuppression or diabetes mellitus does not appear to significantly increase the risk of infectious complications following UroLift.²⁴

Absolute and relative contraindications

Absolute contraindications to UroLift include active UTI, urethral stricture, or bladder pathology that would preclude safe device placement.^{1,3} The presence of an obstructive median lobe is now considered a relative contraindication, with candidacy determined by anatomical assessment and surgeon expertise.^{9–11} Prostate volume > 100 mL is a relative contraindication due to limited evidence for efficacy and safety.⁴

Patient factor/Contraindication	Impact on UroLift candidacy	References
Bleeding risk/anticoagulation	Higher real-world rates of major bleeding; caution in unmodifiable bleeding risk	1–2
High comorbidity burden (ASA ≥ 3)	Lower durability and higher failure rates; not absolute contraindication but requires counseling	3
Large prostate size (> 80 – 100 mL)	Feasible in select cases; longer operative time, more implants, less robust evidence for > 100 mL	4
Obstructive median lobe	No longer absolute contraindication; feasible in select patients with experienced operators	5
Device malfunction	Noted in post-marketing surveillance; underscores need for technical expertise	1
Active UTI, urethral stricture, etc.	Remain absolute contraindications; no new evidence to change this	6

Abbreviations: ASA, American Society of Anesthesiologists; UTI, urinary tract infection.

Long-term durability and retreatment

UroLift provides rapid symptom relief and preservation of sexual function, but its long-term durability is generally less than that of tissue-resective procedures such as TURP or laser therapies.^{2,16,19,25–27} The annual surgical reintervention rate after UroLift is approximately 6%, with cumulative retreatment rates of 8% to 15% at 2 to 3 years.^{27,28} Retreatment is most commonly managed with TURP or laser procedures, and outcomes after retreatment are generally favorable.^{20,27} The need for retreatment is higher after UroLift than after more invasive procedures, and this should be incorporated into shared decision-making and patient counseling.²⁹

Sexual function outcomes

UroLift is distinguished among BPH therapies by its robust preservation of ejaculatory and erectile function, with rates of *de novo* sexual dysfunction near zero and possible small improvements in erectile function over time.^{2,16,19,25,33–37} This profile is superior to TURP and laser-based procedures, which are associated with high rates of ejaculatory dysfunction and a small but real risk of erectile dysfunction.^{2,33–35,38} Compared to other minimally invasive therapies, UroLift is at least equivalent, and possibly superior, in preserving sexual function.^{25,35–37} Sexually active men who prioritize maintenance of ejaculation and erectile function, particularly those with prostates in the guideline-recommended size range and without significant median lobe obstruction, benefit most from this profile.^{2,19,33–37}

Patient preferences and quality-of-life considerations

Patient preferences and QoL considerations are central to the selection of UroLift over other therapies. The desire to preserve sexual function, achieve rapid recovery, avoid prolonged catheterization, and minimize perioperative morbidity are key drivers of patient choice.^{2,3,17,19,33,40} UroLift is typically performed as an outpatient procedure under local anesthesia, with minimal perioperative morbidity and a rapid return to normal activities.^{3,17,19,33,40} While UroLift may offer slightly less symptom improvement and a higher risk of retreatment compared to TURP, its favorable profile in terms of quality of life, sexual health, and recovery experience makes it an attractive option for men who prioritize these outcomes.^{2,3,17,19,29,33,40}

Special populations and complex histories

UroLift can be considered in select patients with prior prostate cancer treatment, including those who have undergone radiation or surgery, provided that standard anatomical and clinical selection criteria are met.²⁴ Early reports and ongoing studies suggest that UroLift may be feasible and safe in patients with prior pelvic radiation, but robust long-term data are lacking, and careful patient selection is critical.^{41,42} In individuals with complex urological histories or significant comorbidities, the risk of treatment failure is higher, and the durability of benefit is reduced, necessitating individualized counseling and close follow-up.^{21,43,44}

Management of retreatment after UroLift failure

Patients who require retreatment after UroLift failure have several management options, with TURP and laser-based procedures (such as HoLEP) being the most common and effective.^{20,29} Repeat UroLift may be considered in select cases, but the evidence for its long-term efficacy is limited.²⁷ Device explantation is reserved for implant-related complications. Outcomes after retreatment are generally favorable, with significant symptom improvement and a low risk of serious complications when appropriate surgical techniques are employed.^{5,20,29}

Management option	Indications/Considerations	Technical notes/Outcomes	References
Repeat UroLift	Selected patients with favorable anatomy, prior response	Limited data on durability; accounts for ~33% of reinterventions	1
TURP	Most common retreatment; persistent/recurrent obstruction	Effective; technical adaptation for implant removal required	1,2
HoLEP	Alternative to TURP, especially for larger prostates	Safe with careful morcellation; risk of morcellator jamming	1,2
Device explantation	Device-related complications (migration, erosion, symptoms)	Endoscopic removal; may be combined with TURP/HoLEP	1
Other MIST (e.g., Rezūm)	Limited evidence post-UroLift	Not standard; outcomes not well characterized	3,4

Abbreviations: HoLEP, holmium laser enucleation of the prostate; MIST, minimally invasive treatment; TURP, transurethral resection of the prostate.

Safety and efficacy in large prostates and complex anatomy

There is no high-quality evidence supporting the safety or efficacy of UroLift in men with prostates > 100 mL.^{1,2,4,6} The available data suggest that UroLift may be feasible in selected patients with prostates up to 100 mL, but outcomes in those with very large prostates are unknown and likely to be less predictable.^{4–6} The presence of significant IPP or a prominent median lobe remains a relative contraindication, although emerging data support the use of UroLift in selected cases with experienced operators.^{9–11,14} For patients with very large prostates or marked IPP, alternative surgical options such as endoscopic enucleation or TURP should be considered.^{1,7}

Emerging contraindications and patient factors

Recent post-marketing surveillance and real-world studies have not identified new absolute contraindications to UroLift, but have revealed important patient factors that may affect candidacy and outcomes. The risk of significant bleeding appears higher in real-world practice than in clinical trials, particularly in patients with unmodifiable bleeding risk or on chronic anticoagulation.^{22,23} High comorbidity burden is associated with reduced efficacy and higher retreatment rates, warranting careful patient selection and counseling.²¹ The presence of an

obstructive median lobe is no longer an absolute contraindication, but requires individualized assessment and surgical expertise.⁹ Larger prostate size is not an absolute barrier, but outcomes are less predictable beyond 100 mL.⁴ Device malfunction, while uncommon, highlights the importance of procedural proficiency.²²

Conclusion

The ideal candidate for UroLift is a man with moderate-to-severe LUTS due to BPH, a prostate volume between 25 cc and 75 cc, and no significant median lobe obstruction, who has failed or is intolerant of medical therapy and who wishes to preserve sexual function and minimize perioperative morbidity. UroLift is particularly well suited for sexually active men who prioritize maintenance of ejaculation and erectile function, and for those seeking rapid recovery and avoidance of prolonged catheterization. Careful preoperative assessment of prostate size, anatomy, comorbidity burden, and bleeding risk is essential to optimize outcomes. While UroLift can be considered in select patients with larger prostates, obstructive median lobes, prior prostate cancer treatment, or complex urological histories, these cases require individualized assessment and may be associated with higher retreatment rates or technical challenges. Shared decision-making, incorporating patient preferences and the most current evidence, is essential to optimizing treatment selection in men with BPH.

This synthesis reflects the current consensus in the medical literature and clinical guidelines, particularly those of the AUA, and incorporates the most recent evidence from RCTs, systematic reviews, and real-world studies.^{1,2,4,9,17,24,29,25–28,33–37,40,41}

Topic	Recommendation	LoE	GoR
Prostatic Urethral Lift (PUL)	Offer prostatic urethral lift to men with LUTS due to BPO interested in preserving ejaculatory function and/or avoiding anesthesia, who accept less de-obstruction with a greater need for retreatment (compared to TURP), in prostates between 30–80 mL without an obstructive median lobe or bladder neck obstruction.	I	A

Abbreviations: BPO, benign prostatic obstruction; GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; TURP, transurethral resection of the prostate.

Temporary Intraprostatic Devices—iTIND

Prostate volume and iTIND outcomes

The efficacy and safety of temporary implantable nitinol device (iTIND) are closely linked to prostate volume. The AUA guideline, published by the American Urological Association, recommends iTIND for men with prostate volumes between 25 cc and 75 cc, provided there is no obstructive median lobe. This recommendation is grounded in the inclusion criteria of pivotal randomized controlled trials and prospective studies, which consistently enrolled patients within this volume range and excluded those with larger prostates or median lobes due to higher rates of treatment failure and retreatment.^{1–4}

Clinical outcomes in men with prostate volumes between 30 cc and 80 cc are robustly supported by the literature. In this group, iTIND has demonstrated significant and durable improvements in IPSS, $Q_{\max}$, and QoL, with benefits maintained for up to 3 years.^{2,5} The safety profile is favorable, with most adverse events being mild and transient, and sexual function is consistently preserved.^{2,5,7,8}

For men with prostate volumes between 25 cc and 30 cc, the available evidence suggests that outcomes are comparable to those observed in patients with slightly larger prostates. Studies that included patients with prostates as small as 15–16 mL found no significant difference in efficacy or safety within the 25–30 cc subgroup, provided that other selection criteria were met.^{2,6} The principal predictor of poor outcome in this group is the presence of an obstructive median lobe, not the small prostate volume itself.³

There is a lack of evidence supporting the use of iTIND in prostates larger than 75–80 cc. All major studies excluded such patients, and expert consensus does not recommend iTIND for this population.^{1,9,10}

Anatomical features: median lobe and intravesical prostatic protrusion

The presence of an obstructive median lobe or significant IPP is a well-established contraindication to iTIND therapy. The device's mechanism of action—remodeling the prostatic urethra by exerting radial force—does not adequately address the “ball-valve” effect caused by a median lobe or IPP, leading to persistent obstruction and higher rates of treatment failure.^{3,12,13} All major clinical trials and the AUA guideline exclude patients with these anatomical features.^{1–4} Failure analyses confirm that the presence of a median lobe is the strongest predictor of poor outcome and need for retreatment, with no other baseline variable (including age, prostate volume, or symptom severity) showing a similar association.³

Careful preoperative assessment, including imaging to evaluate for IPP or median lobe, is essential for appropriate patient selection. For patients with these anatomical features, alternative therapies such as TURP or Aquablation should be considered.^{1,10}

Anatomical feature	Impact on iTIND efficacy/Suitability	Evidence/Guideline statement
Median lobe (obstructive)	Strong predictor of treatment failure; contraindication	AUA: iTIND/TIPD should only be offered in absence of obstructive median lobe; clinical trials show high failure rate in presence of median lobe
Intravesical prostatic protrusion	Associated with poor outcomes; exclusion criterion	IPP reflects median lobe; not addressed by iTIND mechanism; radiological assessment recommended
Lateral lobe enlargement only	Suitable for iTIND if within volume criteria	Durable symptom relief and preserved sexual function in absence of median lobe/IPP

Abbreviations: AUA, American Urological Association; IPP, intravesical prostatic protrusion; iTIND, temporary implantable nitinol device; TIPD, temporary implantable prostatic device.

Symptom severity and quality of life

iTIND has been primarily studied in men with moderate-to-severe LUTS, typically defined as IPSS ≥ 10 . Across multiple studies, the degree of improvement in IPSS and QoL is clinically meaningful and consistent, regardless of baseline symptom severity within the moderate-to-severe range.^{2,5} Baseline IPSS does not predict response or safety outcomes, and the magnitude of improvement is similar across the spectrum of moderate-to-severe symptoms.⁵ There is insufficient evidence to support the use of iTIND in men with only mild LUTS (IPSS < 10), as these patients were systematically excluded from clinical trials.^{2,5,14}

Sexual and ejaculatory function are preserved following iTIND, with no significant change in International Index of Erectile Function (IIEF) or Sexual Health Inventory for Men (SHIM) scores at 3 months or 12 months, regardless of age, prostate volume, or baseline sexual function.¹⁵ This preservation of function is a key advantage of iTIND over more invasive therapies.^{2,5,15–17}

Prior BPH treatments and iTIND candidacy

iTIND is most appropriate for men who have failed or are intolerant of medical therapy (e.g., α -blockers, 5 α -reductase inhibitors).^{2,6,8} Prior failure of medical therapy does not negatively impact the efficacy or safety of iTIND, and these patients represent the primary target population for the device.^{2,6,8}

Patients with a history of prior prostatic surgery or MISTs are generally excluded from iTIND studies, and the safety and efficacy of iTIND in this context are unknown.^{2–4,9,18} Anatomical alterations from previous interventions may compromise device efficacy and safety, and expert consensus does not recommend iTIND for these patients.^{9,19–20}

Comorbidities and contraindications to other therapies

iTIND is particularly suitable for patients with significant comorbidities, such as cardiovascular disease, need for ongoing anticoagulation, or frailty, who are at increased risk from more invasive procedures.^{2,5,7–9} The procedure can be performed under light sedation or local anesthesia, does not require interruption of antithrombotic therapy,

and is associated with a low risk of perioperative complications.³ These features make iTIND an attractive option for patients who are unfit for surgery or who wish to avoid the side effects of medical therapy.^{9,18}

The principal contraindications to iTIND, as established by guidelines and major studies, include the presence of an obstructive median lobe, prostate volume outside the studied range (< 25 cc or > 75–80 cc), prior prostatic surgery, high PVR urine (> 250 mL), active UTI, and significant bladder or sphincter dysfunction.^{1,2,6,7,9}

Selection criteria for iTIND	References
Male, age ≥ 50 years	1–7
Moderate-to-severe LUTS (IPSS ≥ 10)	1–7
Prostate volume 25–75 mL (most studies; up to 80 mL in some)	1–7
Q_{max} < 12 mL/s	1–7
No obstructive median lobe	1–7
PVR < 250 mL	2–7
No prior prostate surgery	2–7
No confounding bladder/sphincter dysfunction, no active UTI, able to interrupt antithrombotic/antiplatelet therapy	2–7

Abbreviations: IPSS, International Prostate Symptom Score; iTIND, temporary implantable nitinol device; LUTS, lower urinary tract symptoms; PVR, post-void residual; Q_{max} , peak urinary flow; UTI, urinary tract infection.

Long-term efficacy, safety, and retreatment

Long-term data, including 3-year follow-up from prospective multicenter studies, demonstrate that iTIND provides durable symptom relief, improvement in urinary flow, and enhanced quality of life in well-selected patients.⁵ The mean IPSS reduction at 3 years is approximately 58% from baseline, with sustained improvements in QoL and Q_{max} .⁵ No late postoperative complications or new cases of sexual dysfunction have been reported between 12 months and 36 months.⁵ The retreatment rate is low, with all surgical retreatments occurring within the first two years and no new retreatments observed in the third year.⁵ The principal predictor of retreatment is the presence of an obstructive median lobe.³

Key outcomes (12–36 months)	References
IPSS reduction: 9–14 points (58% reduction from baseline)	1–7
Q_{max} increase: 7–8 mL/s (115% increase from baseline)	1–7
QoL improvement: 1.6–1.9 points (55.6% reduction from baseline)	1–7
PVR reduction: 9.4 mL (85% reduction from baseline)	4
No <i>de novo</i> sexual or ejaculatory dysfunction	1–7
Most adverse events mild/transient (Clavien I–II)	1–7
Rapid return to daily life (mean, 4.3 days)	5

Abbreviations: IPSS, International Prostate Symptom Score; PVR, post-void residual; Q_{max} , peak urinary flow; QoL, quality of life.

Patient subgroups: age, symptom severity, ethnicity

Current evidence does not identify any major patient subgroups—such as younger men, those with mild LUTS, or specific ethnicities—for whom iTIND outcomes differ significantly from the general population of appropriately selected BPH patients.^{2,5,15–17} Age, within the studied range, and baseline sexual function do not influence outcomes, and there is no evidence to suggest differential efficacy or safety in specific ethnic groups. The use of iTIND in men with mild LUTS or in unstudied demographic subgroups remains uncharacterized.^{2,5,14–17}

Durability (long-term efficacy and safety)	References
Symptom and flow improvements stable at 2–3 years	1–4
No late complications or deterioration in sexual function at 3 years	2–4
No additional treatment failures between 24–36 months	2
No intraoperative complications	1–6

Clinical decision tools and patient selection algorithms

There are currently no fully validated, widely adopted clinical decision tools or formal algorithms specifically designed for iTIND patient selection. Instead, the AUA guideline provides explicit, evidence-based criteria that function as a *de facto* decision algorithm.¹ These criteria include prostate volume between 25 cc and 75 cc, absence of an obstructive median lobe, moderate-to-severe LUTS (IPSS ≥ 10), failure or intolerance of medical therapy, and absence of prior prostatic surgery or significant bladder dysfunction.^{1–4,9} Some centers may use institution-specific checklists or flowcharts that mirror these criteria, but these are not standardized or externally validated.⁹

Rare or emerging contraindications

While the principal contraindications to iTIND are well established, several rare or emerging scenarios are not fully addressed in current guidelines or major studies. These include subtle or unrecognized IPP, bladder neck abnormalities, prostatic urethral diverticula or cysts, severe coagulopathy, immunosuppression, neurogenic bladder, metal allergy, prior MISTs, unusual prostate anatomy, and chronic catheterization.^{2,6,7,11} These situations are either unstudied or only briefly mentioned in the literature and may represent relative or absolute contraindications until further evidence is available.

Real-world retreatment rate and patient satisfaction beyond 3 years

The real-world retreatment rate with iTIND beyond 3 years is low in appropriately selected patients, with no new retreatments observed between 2 and 3 years in the largest prospective cohort to date.⁵ Patient satisfaction is high, as evidenced by durable improvements in symptoms, quality of life, and preservation of sexual function, with

no late complications reported.^{5,7} These outcomes have been reproduced in diverse, multicenter international settings, supporting the generalizability of the findings when strict selection criteria are applied.^{5,7}

Retreatment data	References
Surgical retreatment: 2–11% at 1–4 years	1–6
Most failures associated with protocol deviation (e.g., median lobe presence)	2–5
Re-intervention rate at 12 months: 0.03% (network meta-analysis)	6
Retreatment rates higher than TURP, comparable to other MISTs	4–6

Abbreviations: MISTs, minimally invasive treatments; TURP, transurethral resection of the prostate.

Conclusion

The iTIND device is best suited for men with moderate-to-severe LUTS due to BPH, prostate volumes between 25 cc and 75 cc, and no obstructive median lobe. The device is particularly appropriate for patients who have failed or are intolerant of medical therapy, those with significant comorbidities or contraindications to more invasive procedures, and those who wish to preserve sexual and ejaculatory function. The efficacy and safety of iTIND are well supported by prospective multicenter studies and the AUA guideline, with durable symptom relief, low retreatment rates, and high patient satisfaction observed through at least 3 years of follow-up. Strict adherence to patient selection criteria, especially the exclusion of patients with a median lobe or prior prostatic surgery, is essential to optimize outcomes. While rare or emerging contraindications may exist, these are not yet fully characterized in the literature. Ongoing research and real-world surveillance will continue to refine the optimal use of iTIND in the management of BPH.

Topic	Recommendation	LoE	GoR
Temporary Implantable Nitinol Device (iTIND)	Offer temporary implantable nitinol device (iTIND) to men with LUTS due to BPO interested in preserving ejaculatory function and/or avoiding anesthesia, who accept less de-obstruction with a greater need for retreatment (compared to TURP), in prostates between 25–70 mL without an obstructive median lobe.	III	C

Abbreviations: BPO, benign prostatic obstruction; GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; TURP, transurethral resection of the prostate.

Intraprostatic Balloon Treatment—Optilume BPH

Efficacy and safety outcomes of Optilume across patient subgroups

Prostate size, anatomy, and symptom severity

The pivotal PINNACLE study—a double-blind, randomized, sham-controlled trial—and the EVEREST-I open-label study provide the most robust data on Optilume in BPH. Both studies enrolled men aged 50 years or older with moderate-to-severe LUTS, prostate volumes between 20 grams and 80 grams, and prostatic urethra lengths of 30 mm to 55 mm. At 2 years, Optilume demonstrated a mean reduction in IPSS of 11.0 to 14.1 points, a 116.8% increase in $Q_{\max}$, and significant improvements in quality of life. These benefits were sustained through 2 years, with 67.5% of patients achieving a $\geq 30\%$ improvement in IPSS without retreatment in the PINNACLE study, and similar durability observed in EVEREST-I.^{1–3}

Importantly, the PINNACLE study reported that improvements in uroflowmetry measures were consistent across all prostate volumes within the 20 g to 80 g range, indicating that Optilume is effective for a broad spectrum of prostate sizes within this range.² However, there is no evidence supporting its use in prostates smaller than 20 g or larger than 80 g, and the device has not been validated in these anatomical extremes.

Both studies enrolled patients with moderate-to-severe LUTS (mean baseline IPSS, 22–23), and there is no evidence for its use in men with only mild symptoms (IPSS < 8).^{1,2,4}

Anatomical variants: median lobe and complex anatomy

The presence of a median lobe or other complex prostatic anatomical variants is a well-recognized factor influencing BPH management. However, neither the PINNACLE nor the EVEREST-I study stratified outcomes by median lobe status or other anatomical variants, nor did they explicitly include or exclude such patients.^{1–3} The clinical significance of a median lobe is well established in the literature, as it can cause bladder outlet obstruction via a “ball-valve” mechanism and is associated with a higher risk of medical therapy failure.⁵ While other MISTs such as UroLift and GreenLight photovaporization have demonstrated efficacy in patients with median lobes, there is no published evidence for Optilume in this subgroup. Therefore, the efficacy and safety of Optilume in patients with a prominent median lobe or significant intravesical prostatic protrusion remain uncharacterized, and use in these patients should be considered investigational.^{1–3,5–9}

Patients with prior failed BPH interventions

The pivotal Optilume BPH trials excluded patients with prior surgical or minimally invasive BPH interventions, such as TURP, laser therapies, or other MISTs.^{1,2,4} As a result, there is no published evidence regarding the

efficacy or safety of Optilume in patients with prior failed BPH procedures. The only related data come from studies of the Optilume drug-coated balloon in urethral stricture disease, which is a distinct clinical entity and not directly applicable to BPH.¹⁰ Until further research is available, use of Optilume in patients with prior failed BPH interventions should be considered investigational.

Patients with significant comorbidities

The PINNACLE and EVEREST-I studies did not provide detailed outcomes for patients with significant comorbidities such as ongoing anticoagulation, urinary retention, or advanced cardiovascular disease.^{1,2,4} Standard exclusion criteria for these trials omitted patients with uncorrected coagulopathies, recent cardiovascular events, or those at high risk for anesthesia or procedural complications. While the minimally invasive nature of Optilume suggests potential suitability for higher-risk patients, the absence of explicit data in these subgroups necessitates individualized risk assessment and shared decision-making. In contrast, other MISTs such as laser-based therapies have established safety profiles in patients on anticoagulation or with cardiovascular disease.^{11–14}

Long-term efficacy and retreatment rates

Both the PINNACLE and EVEREST-I studies provide 2-year follow-up data, which currently represent the longest available evidence for Optilume in BPH. The majority of patients maintain clinically meaningful improvements in symptoms and urinary flow without the need for retreatment. In the PINNACLE study, the retreatment rate at 2 years was approximately one-third, which is comparable to other MISTs.^{2,3} No device or treatment-related serious adverse events were reported beyond 12 months, and there was no negative impact on sexual function.

Outcome domain	PINNACLE Study (2 Years)	EVEREST-I Study (2 Years)	References
Symptom score (IPSS)	23.4 → 11.0 (mean)	22.3 → 8.2 (mean)	1,2
Q _{max} (mL/s)	8.9 → 19.0 (mean)	10.9 → 17.2 (mean)	1,2
PVR (mL)	83.7 → 65.9 (mean)	63.1 → 45.0 (mean)	1,2
Responder rate	67.5% (≥ 30% IPSS improvement, no retreatment)	Not directly reported; sustained benefit	1,2
Retreatment rate	~32.5% (implied by responder definition)	Not directly reported	1,2
Sexual function	No negative impact	No negative impact	1,2
Serious adverse events	None beyond 12 months	None between 1–2 years	1,2
Common adverse events	Hematuria, UTI (mild, self-limited)	Hematuria, UTI (mild, self-limited)	1,2

Abbreviations: IPSS, International Prostate Symptom Score; PVR, post-void residual; Q_{max}, peak flow rate; UTI, urinary tract infection.

Guideline and expert consensus on patient selection

The AUA guideline amendment from 2023 recognizes the emergence of new MISTs, including drug-eluting catheters and balloon dilation devices such as Optilume, but does not provide specific recommendations for their use due to the need for further robust data.¹⁵ The AUA emphasizes that patient selection for new devices should be guided by the inclusion and exclusion criteria of pivotal clinical trials until more real-world and comparative effectiveness data are available. This position is echoed by expert consensus statements, which advocate for a cautious, evidence-based approach to patient selection, prioritizing safety and efficacy while acknowledging the limitations of the current evidence base.^{16–18}

Expert consensus highlights that, for now, Optilume should be considered for men aged 50 years or older with moderate-to-severe LUTS due to BPH, prostate volumes between 20 grams and 80 grams, and prostatic urethra lengths of 30 mm to 55 mm, who have failed or are intolerant to medical therapy and do not have active infection, prior prostate surgery, significant urethral pathology, or a history of prostate or bladder cancer.^{1,2,4,15–18} Extension of use to broader or higher-risk populations should be undertaken judiciously, ideally within the context of clinical studies or registries, and with full disclosure to patients regarding the uncertainties involved.

Contraindications and less effective scenarios

Based on the available evidence, several patient populations and clinical scenarios emerge where Optilume is either contraindicated or where its efficacy and safety are unproven or potentially diminished:

- Prostate size < 20 g or > 80 g: Not included in trials; device not validated outside this range.
- Prior prostate surgery or urethral procedures: Excluded from trials; altered anatomy may increase risk or reduce efficacy.
- Active urinary tract infection, urethral stricture, or bladder stones: Excluded from trials; increased risk of complications.
- History of prostate or bladder cancer: Excluded from trials; safety of paclitaxel delivery unknown.
- Prostatic urethra length < 30 mm or > 55 mm: Device designed for specific urethral length; not studied outside this range.
- Severe bladder dysfunction or high post-void residual: Not included in trials; limited benefit if detrusor underactivity present.
- Uncontrolled coagulopathy or anticoagulation: General surgical risk; not specifically addressed in trials.
- Allergy to paclitaxel: Device delivers paclitaxel; risk of hypersensitivity.^{1,2,4}

Patient population/Scenario	Contraindicated or less effective?	Rationale/Evidence	References
Prostate size < 20 g or > 80 g	Less effective/Unstudied	Not included in trials; device not validated outside this range	1–4
Prior prostate surgery or urethral procedures	Contraindicated/Unstudied	Excluded from trials; altered anatomy may increase risk or reduce efficacy	1–4
Active UTI, urethral stricture, or bladder stones	Contraindicated	Excluded from trials; increased risk of complications	1–4
History of prostate or bladder cancer	Contraindicated/Unstudied	Excluded from trials; safety of paclitaxel delivery unknown	1–4
Prostatic urethra length < 30 mm or > 55 mm	Less effective/Unstudied	Device designed for specific urethral length; not studied outside this range	3,4
Severe bladder dysfunction or high PVR	Less effective/Unstudied	Not included in trials; limited benefit if detrusor underactivity present	1–4
Uncontrolled coagulopathy/anticoagulation	Contraindicated	General surgical risk; not specifically addressed in trials	1–4
Allergy to paclitaxel	Contraindicated	Device delivers paclitaxel; risk of hypersensitivity	3,4

Abbreviations: PVR, post-void residual; UTI, urinary tract infection.

Comparative effectiveness and ongoing research

There are currently no published or ongoing head-to-head RCTs directly comparing Optilume to other MISTs such as UroLift, Rezūm, or Aquablation in terms of efficacy, safety, or patient selection.^{19–23} The available evidence for Optilume is limited to comparisons with sham procedures, and the device has not been included in network meta-analyses or indirect comparisons due to the absence of eligible studies. The AUA guideline panel and expert consensus statements recognize this evidence gap and emphasize the need for robust comparative data to inform clinical practice.^{15–18}

Real-world and registry data

As of the most recent literature, there are no published real-world registry or post-marketing surveillance data evaluating the outcomes of Optilume in broader or unstudied BPH populations, including those with large prostates, prior failed interventions, or high-risk comorbidities.^{24,25} The available evidence is limited to highly selected patient populations enrolled in prospective clinical trials, and the safety and efficacy of Optilume in broader or higher-risk groups remain uncharacterized.

Off-label or investigational use

A comprehensive review of the literature reveals no published case series, cohort studies, or expert reports describing off-label or investigational use of Optilume in BPH patients outside the strict clinical trial criteria,

such as those with a prominent median lobe, prior prostate surgery, or severe urinary retention.^{1,2,4,17,26–28} The absence of such data underscores the need for further research in these populations.

Summary: the optimal BPH patient for Optilume

Based on the current clinical evidence, guideline recommendations, and expert consensus, the Optilume BPH Catheter System is best suited for men aged 50 years or older with moderate-to-severe LUTS due to BPH, prostate volumes between 20 grams and 80 grams, and prostatic urethra lengths of 30 mm to 55 mm, who have failed or are intolerant to medical therapy and do not have active infection, prior prostate surgery, significant urethral pathology, or a history of prostate or bladder cancer. The therapy provides significant and durable improvements in symptoms and urinary flow, with a favorable safety profile and preservation of sexual function through at least 2 years of follow-up. Use in broader or higher-risk populations, including those with large prostates, prior failed interventions, prominent median lobes, or significant comorbidities, remains investigational and should be approached with caution until further data are available. The American Urological Association and expert consensus recommend that patient selection for Optilume should adhere to the inclusion and exclusion criteria of the pivotal clinical trials until more robust real-world and comparative effectiveness data are available.^{15–18}

Conclusion

The Optilume BPH Catheter System represents a promising addition to the armamentarium of minimally invasive therapies for BPH, offering durable symptom relief and functional improvement with a favorable safety profile in appropriately selected patients. However, its use should be restricted to the populations studied in the pivotal trials, and clinicians should exercise caution in extrapolating trial results to broader or higher-risk groups. Ongoing research and real-world data collection are needed to further define the optimal patient selection and comparative effectiveness of Optilume relative to other MISTs.

Topic	Recommendation	LoE	GoR
Drug-Coated Balloon Dilation: Optilume BPH	Offer drug-coated balloon dilation (Optilume BPH) as an option in men with LUTS due to BPO interested in preserving ejaculatory function and/or avoiding anesthesia, who accept less de-obstruction and will likely have a greater need for retreatment (compared to TURP), with prostates under 80 mL without a median lobe and without bladder neck obstruction.	III	C

Abbreviations: BPO, benign prostatic obstruction; GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; TURP, transurethral resection of the prostate.

Prostate Artery Embolization

Patient selection criteria for PAE

The AUA guideline, published by the American Urological Association, provides the most authoritative and up-to-date recommendations regarding prostate artery embolization (PAE). The AUA states that PAE may be offered for the treatment of LUTS/BPH, but only by clinicians specifically trained in this interventional radiology procedure and after a thorough discussion of potential risks and benefits with the patient. PAE is not recommended as a first-line therapy or as a replacement for more established MISTs or TURP, but rather as an option for select patients, particularly those who are not ideal candidates for surgery due to comorbidities, advanced age, or patient preference for a minimally invasive approach.¹

The key selection criteria for PAE, as outlined by the AUA and supported by the broader medical literature, include:

- Moderate-to-severe LUTS (typically IPSS ≥ 20 and QoL score ≥ 3) refractory to at least 6 months of medical therapy.¹⁻³
- Prostate volume generally greater than 40–50 mL, with the greatest benefit observed in larger prostates, although no strict lower size cutoff is mandated.^{1,4,5}
- Favorable prostatic artery anatomy as determined by preprocedural imaging (computed tomography angiography [CTA] or magnetic resonance angiography [MRA]), ensuring that the arteries are accessible and amenable to embolization.^{1,6-8}
- Absence of prior surgical or invasive prostatic procedures, as these patients were excluded from most clinical trials and outcomes are less predictable.^{1,9,10}
- High surgical risk or significant comorbidities, making the patient a poor candidate for TURP or other surgical interventions.¹¹⁻¹³
- Patient preference for a minimally invasive procedure, especially if preservation of sexual function is a priority.^{2,14}
- Contraindications to PAE include unfavorable vascular anatomy, active urinary tract infection, uncorrected coagulopathy, severe allergy to iodinated contrast, and suspected or confirmed prostate cancer.^{1,15-19}

Efficacy and safety across patient subgroups

Prostate volume

PAE has demonstrated efficacy across a wide range of prostate volumes. Systematic reviews and cohort studies indicate that both patients with moderate (40–80 mL) and large (> 80 mL) prostates experience significant and durable improvements in LUTS and quality of life after PAE, with no significant difference in adverse event rates.^{4,20}

However, the magnitude of symptom improvement and the likelihood of clinical success are greater in patients with larger prostates.^{12,21} Patients with small prostates (< 40 mL) may experience less robust improvement, and careful counseling is warranted in this subgroup.^{1,4,5,22}

Symptom severity

PAE is most effective in men with moderate-to-severe LUTS who have failed or are intolerant to medical therapy. RCTs and systematic reviews consistently report significant reductions in IPSS and improvements in QoL, with benefits comparable to TURP in terms of patient-reported outcomes.^{2,14} Patients with the highest baseline IPSS tend to experience the greatest absolute improvement, although they may also have a higher risk of clinical failure.^{23,24}

Comorbidities and age

PAE is particularly well suited for elderly patients and those with significant comorbidities, including cardiovascular disease, diabetes, and high Charlson Comorbidity Index scores. Large registry analyses and cohort studies have shown that comorbidities do not adversely affect PAE outcomes, provided the prostatic arteries are accessible.^{11,20} Age alone is not a contraindication, and substantial improvements in LUTS and QoL have been observed in patients over 70 years of age.^{11,20}

Urinary retention and high-risk populations

PAE is effective in patients with chronic urinary retention due to BPH, especially those who are catheter dependent and have preserved bladder contractility. High rates of catheter independence (83%–95%) have been reported, with durable improvements in symptom scores and QoL.^{13,25,26} The safety profile in these high-risk populations is favorable, with low rates of major complications and minimal impact on sexual function.^{20,27}

Sexual function and quality of life

PAE is associated with a low risk of new-onset sexual dysfunction and offers better preservation of ejaculatory function compared to TURP. Randomized trials and systematic reviews report similar or improved erectile function and significantly lower rates of retrograde ejaculation with PAE.^{2,14,28} Patient-reported QoL improves substantially after PAE, with benefits comparable to TURP and superior to medical therapy.^{2,14,27,29,31}

Prior failed therapies

While the AUA guideline does not currently recommend PAE for patients with prior failed MISTs or surgical interventions due to insufficient evidence, emerging retrospective data suggest that PAE can be a safe and effective salvage therapy in this population, with significant improvements in LUTS and QoL and a low risk of adverse events.^{9,10} However, these findings are based on small, nonrandomized studies, and further research is needed.

Small prostate volumes and atypical anatomy

PAE can be performed in patients with small prostates or atypical anatomy, but the expected clinical benefit is generally lower in men with prostates < 40 mL, and the likelihood of achieving optimal symptom relief increases with larger baseline gland size.^{1,4,5,22} Median lobe enlargement and internal prostatic architecture do not appear to significantly impact outcomes if the prostatic arteries are accessible.^{4,22} Unfavorable vascular anatomy remains a major technical limitation and may preclude successful or bilateral embolization.^{1,6,18}

Comparative effectiveness: PAE vs. TURP and other therapies

RCTs and systematic reviews consistently show that PAE and TURP yield similar improvements in patient-reported symptom scores and QoL at short- and intermediate-term follow-up (up to 2 years).^{2,32,33,35} TURP achieves greater improvements in objective measures such as maximum urinary flow rate, post-void residual volume, and prostate volume reduction.^{2,32,33,35} PAE is associated with a lower risk of perioperative complications, including bleeding, need for transfusion, and urinary incontinence, and a lower incidence of sexual side effects, particularly ejaculatory dysfunction.^{2,14,28}

However, PAE has a higher rate of retreatment or reoperation over time. Meta-analyses and real-world studies report 5-year retreatment rates for PAE of approximately 24%, compared to 8% for TURP.^{36,37} Other minimally invasive therapies, such as prostatic urethral lift (PUL) and water vapor thermal therapy (WVTT), have intermediate retreatment rates and may be preferred in select patients.^{38–40}

Long-term efficacy and durability

Long-term data (≥ 5 years) indicate that PAE provides durable symptom relief and QoL improvement for most men, but with a substantially higher retreatment rate compared to TURP and some other minimally invasive therapies.⁴¹ TURP remains the reference standard for maximal and durable symptom control, with the lowest long-term retreatment rates, but at the cost of higher perioperative morbidity and greater impact on sexual function.^{2,33,39,41,42,44}

Technical and anatomical predictors of success

The most influential technical and anatomical predictors of procedural success or failure in PAE are the degree of pelvic arterial tortuosity, severity of atherosclerotic disease, prostatic artery diameter and origin, vessel elongation and bifurcation angles, and the presence of anatomical variants.^{18,31,45–51} Preprocedural imaging with CTA or MRA is invaluable for procedural planning, particularly in patients with complex anatomy. Operator experience significantly improves technical efficiency, though clinical outcomes are robust even in less experienced hands when protocols are followed.^{18,31,49} Achieving bilateral embolization is a key technical goal, as it is associated with superior clinical outcomes.⁵¹

Cost-effectiveness

Cost-effectiveness analyses using U.S. Medicare data and Markov models demonstrate that PAE is a cost-effective alternative to TURP, providing similar patient-reported outcomes at a lower overall cost, despite higher retreatment rates.^{52,53} Compared to other minimally invasive therapies, PAE is economically competitive, though WVTM may offer the lowest procedural and follow-up costs in some settings.^{54–56} The cost-effectiveness of PAE is influenced by procedural costs, retreatment rates, and the cost of managing adverse events, and may vary across healthcare systems.^{52–54,56}

Patient subgroup/Characteristic	PAE efficacy & safety summary	Key considerations/Outcomes	References
Moderate-to-severe LUTS, failed medical treatment	High efficacy, safe	Comparable to TURP for symptoms/QoL	1–4
Large prostate volume (> 40–50 mL)	Greater symptom improvement, durable	Best outcomes, lower retreatment	5–9
Small prostate volume (< 40 mL)	Less robust improvement, higher retreatment	Careful selection/counseling needed	1,5,9,10
Elderly, high comorbidity	High efficacy, safe	No increased risk if arteries accessible	6,7,11,12
Urinary retention, catheter dependent	High catheter-free rates, safe	Best if bladder contractility preserved	12–14
Prior failed MISTs/prostate surgery	Emerging evidence, safe/effective in select patients	Not guideline endorsed, case-by-case	15,16
Atypical anatomy (median lobe, etc.)	Similar outcomes if arteries accessible	Preprocedural imaging essential	5,10
Unfavorable vascular anatomy	Lower technical success, higher risk	May preclude PAE	1,17–20
Sexual function preservation priority	Lower risk of dysfunction than TURP	High patient satisfaction	1,2,4,21
Cost-effectiveness	Cost-effective vs. TURP, competitive vs. MISTs	Lower cost, higher retreatment	22–25

Abbreviations: LUTS, lower urinary tract symptoms; MISTs, minimally invasive treatments; PAE, prostate artery embolization; QoL, quality of life; TURP, transurethral resection of the prostate.

Emerging and investigational indications

Several emerging and investigational indications for PAE are being explored outside current guideline recommendations. These include use as first-line therapy in treatment-naïve patients, management of BPH-related gross hematuria, treatment of catheter-dependent urinary retention, application in patients with very large prostates or high surgical risk, and as an alternative to combination medical therapy in resistant or intolerant patients.^{1,11,30,32,57} Ongoing randomized trials are needed to validate these indications and inform future guideline updates.

Contraindications and populations with reduced efficacy

Absolute contraindications to PAE include inability to access the prostatic arteries due to unfavorable vascular anatomy, active urinary tract infection, uncorrected coagulopathy, and severe allergy to iodinated contrast.^{1,15–19} PAE is less effective in men with small prostates, predominant bladder dysfunction, or prior prostatic surgery. Cardiovascular comorbidities and advanced age do not preclude PAE if technical access is feasible.¹² Careful patient selection, multidisciplinary evaluation, and operator expertise are essential to optimize outcomes and minimize risks.^{1,16,18,51}

Conclusion

Prostatic artery embolization is best suited for men with moderate-to-severe LUTS due to BPH who have failed or are intolerant to medical therapy, particularly those with larger prostates, high surgical risk, or a strong preference for minimally invasive therapy and preservation of sexual function. PAE is effective and safe across a broad range of patient profiles, including elderly and comorbid populations, and provides durable symptom relief and quality-of-life improvement, though with higher retreatment rates than TURP. Careful patient selection, preprocedural imaging, and multidisciplinary care are critical to optimizing outcomes. PAE is a cost-effective alternative to TURP and other minimally invasive therapies in most healthcare settings. While emerging evidence supports expanded indications, current guidelines recommend PAE primarily for patients who meet the established selection criteria, with ongoing research needed to further refine its role in BPH management.

Topic	Recommendation	LoE	GoR
Prostate Artery Embolization (PAE)	Offer prostatic artery embolization to men with LUTS due to BPO interested in preserving ejaculatory function and/or avoiding anesthesia, who accept less de-obstruction with a greater need for retreatment (compared to TURP), in prostates greater than 40 mL with ideal gland configurations undefined.	II	B
	Perform PAE only in collaboration with experienced interventional radiologists and not without involvement of a urologist.	II	B

Abbreviations: BPO, benign prostatic obstruction; GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; TURP, transurethral resection of the prostate.

Emerging Therapies—Transperineal Laser Ablation

Patient selection: prostate size and anatomy

The optimal candidates for transperineal laser ablation (TPLA) are men with symptomatic BPH and prostate volumes between 30 mL and 100 mL, with the strongest evidence for those in the 40 mL to 70 mL range. Most published studies and systematic reviews have included patients within this size range, demonstrating significant improvements in IPSS, $Q_{\max}$, and QoL, as well as preservation of ejaculatory function and low complication rates.¹⁻⁹ There is limited evidence for the efficacy and safety of TPLA in prostates larger than 100 mL, and most series have excluded such patients or have not reported outcomes stratified by this subgroup.^{1-7,10} Therefore, TPLA should be considered investigational in men with very large prostates (> 100 mL).

Anatomical features such as the presence of a median lobe or significant IPP are important considerations. Most studies have not systematically reported outcomes based on these features, but the consensus is that TPLA is feasible in patients with small or moderate median lobes, provided that safe fiber placement can be achieved under ultrasound guidance.^{1-4,11} Large, highly protruding median lobes or severe IPP may increase the risk of incomplete ablation or procedural complications, and TPLA should be approached with caution in these cases.^{6,7,10}

Impact of prior BPH treatments

TPLA is most commonly performed in patients who have failed or are intolerant to medical therapy, such as α -blockers or 5 α -reductase inhibitors. Prior medical therapy does not negatively impact candidacy or outcomes for TPLA; in fact, most patients in published series were on medical therapy at the time of intervention and experienced significant improvements in symptoms and were able to discontinue medications postprocedure.^{2,4,11}

The evidence regarding TPLA in patients with prior TURP or other MISTs is limited. Most studies have excluded such patients or have not reported outcomes in this subgroup.^{2,4,5,10-12} The altered anatomy and potential for fibrosis after prior interventions may complicate fiber placement and increase the risk of incomplete ablation or complications. Therefore, TPLA should be considered with caution in patients with prior TURP or MISTs, and individualized assessment with detailed imaging is essential.

Comorbidities and contraindications

TPLA is particularly attractive for patients with significant comorbidities who are poor candidates for traditional surgery. The procedure is performed under local anesthesia with or without conscious sedation, minimizing the risks associated with general or spinal anesthesia.^{1,4,5,9,11} The literature consistently reports low rates of perioperative bleeding and a lack of major hemorrhagic complications, even in populations likely to include patients on antiplatelet or anticoagulant therapy.^{4,5,11,13} While most studies do not explicitly stratify outcomes by anticoagulation status, the overall safety profile supports the use of TPLA in patients at increased bleeding risk.

Patients with urinary retention are not excluded from TPLA, and the procedure has been shown to facilitate catheter independence in most cases.^{1,4,5,11} However, a minority may experience transient or recurrent retention, typically managed with temporary recatheterization.

Absolute contraindications to TPLA include active urinary tract infection and uncorrected coagulopathy, which should be treated or optimized prior to the procedure.^{4,5,11} Severe, uncorrected bladder dysfunction (e.g., acontractile detrusor) may limit the benefit of TPLA, and prostate cancer is not an indication for the procedure.^{4,5,11} The safety and efficacy of TPLA in prostates > 100 mL remain uncertain.

Comorbidity/Condition	Compatibility with TPLA	Evidence/Notes	References
Anticoagulation/Antiplatelet	Generally compatible	Low bleeding risk; most studies report no major hemorrhagic complications	1–6
High surgical risk	Compatible	Local anesthesia; low perioperative morbidity; suitable for comorbid patients	1–4,6–8
Urinary retention	Compatible	Most patients achieve catheter independence; transient retention possible	2,3,6,7,9,10
Active UTI	Contraindicated (relative)	Should be treated prior to TPLA	1–4,6
Uncorrected coagulopathy	Contraindicated (relative)	Optimize prior to procedure	1–4,6
Severe bladder dysfunction	Caution	May limit benefit; not absolute contraindication	1–4,6
Prostate cancer	Not indicated	TPLA not for malignancy	1–4,6
Prostate > 100 mL	Limited data	Most studies include prostates < 100 mL	1,2,7

Abbreviations: TPLA, transperineal laser ablation; UTI, urinary tract infection.

Functional outcomes: symptom relief, sexual function, and durability

TPLA provides significant and durable improvements in LUTS, as measured by IPSS, Q_{max} , QoL, and PVR. Systematic reviews and prospective studies report reductions in IPSS of 40% to 73% at 12 months, with corresponding improvements in Q_{max} and QoL.^{2–8} These benefits are sustained in long-term follow-up, with a median of 57 months in the largest cohort, and are accompanied by durable reductions in prostate volume and PVR.⁵

Preservation of sexual function, particularly antegrade ejaculation, is a key advantage of TPLA. Randomized trials and cohort studies consistently report high rates of preserved ejaculation (95%–100%) and no significant deterioration in erectile function, as measured by International Index of Erectile Function 5-item version (IIEF-5) and Male Sexual Health Questionnaire–Ejaculatory Dysfunction (MSHQ-EjD).^{1,2,4–9,15,16} In direct comparison to TURP, TPLA preserved antegrade ejaculation in 96% of patients, compared to only 28% in the TURP group.¹⁵ These outcomes are robust across a range of prostate sizes and patient ages.

The durability of TPLA is supported by low retreatment rates in long-term follow-up. In the 57-month cohort, no patients required retreatment for recurrent symptoms or failure of the initial procedure.⁵ This compares favorably to other MISTs, where retreatment rates of 5% to 15% at 5 years have been reported.

Procedural safety and complication rates

TPLA is associated with a low rate of perioperative and postoperative complications, with most adverse events being minor (Clavien-Dindo grade I–II) and self-limited.^{2–7,10,12} The most common complications are transient urinary tract infection, acute urinary retention, and, rarely, prostatic abscess. Serious complications (Clavien-Dindo grade III or higher) are rare, and there are no reports of significant late-onset strictures, incontinence, or persistent sexual dysfunction in the available studies.^{2–7,10,12}

When compared to TURP, TPLA demonstrates a more favorable safety profile, particularly regarding perioperative bleeding, need for transfusion, and sexual side effects.^{7,17–19} TPLA is performed via a transperineal approach under local or conscious sedation, with no reported cases of significant intraoperative bleeding or need for transfusion.^{1–3,5–7,10,12} Compared to other MISTs such as Rezūm and PAE, TPLA appears to offer similar or lower complication rates.^{12,19}

Long-term outcomes and retreatment

Long-term data for TPLA are encouraging, with sustained improvements in LUTS, QoL, and objective urodynamic parameters for at least 5 years.⁵ Sexual function is preserved over long-term follow-up, and the retreatment rate is very low in the available long-term cohort.^{5,7} There is no evidence of an increased risk of late complications, such as bladder neck contracture or chronic urinary retention, in the available data.^{5,7}

Special populations: large prostates, anatomical variants, and prior radiation

The performance of TPLA in patients with very large prostates (> 100 mL) or severe anatomical variants (large median lobe, severe IPP) is not well established. Most studies have included patients with prostate volumes up to 100 mL, and there is a lack of robust data for larger glands.^{1–7,10} TPLA may be feasible in select patients with small or moderate median lobes, but large, highly protruding median lobes or severe IPP is considered a relative contraindication due to technical challenges and potential for suboptimal outcomes.^{6,7,10}

There is currently no direct, high-quality evidence evaluating the efficacy and safety of TPLA in BPH patients with prior pelvic radiation or prostate cancer treatment. Indirect evidence from studies of focal laser ablation in mixed cohorts suggests that laser-based debulking can be effective and preserve sexual function, but complication rates may be higher in this population, particularly for infection and prolonged catheterization.¹⁴ Until more robust data are available, TPLA should be considered experimental in these settings.

Technical and operator-dependent factors

The safety and efficacy of TPLA are highly dependent on operator skill in imaging, fiber placement, energy delivery, and complication management. Real-time ultrasound guidance is essential for accurate fiber placement and avoidance of critical structures.^{1,11,34} The number and positioning of fibers, as well as energy delivery, must be tailored to gland size and configuration.^{3,4,20} The learning curve for TPLA is not well defined, but outcomes are best in centers with standardized protocols and experienced operators.^{6,7,10} Technical limitations are most pronounced in patients with large prostates, complex anatomy, or prior interventions.

Patient-reported outcomes, preferences, and satisfaction

Patient-reported outcome measures (PROMs) and quality-of-life domains are central to the evaluation of BPH therapies. TPLA provides substantial and durable improvements in IPSS, QoL, and functional outcomes, with a safety and sexual function preservation profile that is superior to TURP and at least equivalent to other MISTs such as Rezūm.^{2–9,12,15} The main domain where TPLA is inferior to TURP is the absolute magnitude of improvement in urinary flow and symptom scores, but this is offset by a much lower risk of ejaculatory and sexual dysfunction.^{15,21,22}

Patient satisfaction rates following TPLA are high, with most patients reporting marked relief of symptoms, improved daily functioning, and rapid return to normal activities.^{2–5,7,9,12,23} The outpatient, minimally invasive nature of TPLA, combined with rapid recovery and preservation of sexual function, is highly valued by patients.^{23,24} In direct comparison to other MISTs, TPLA offers a similar or faster improvement in patient-reported symptoms and QoL, with high satisfaction rates.¹²

Attribute/Outcome	TPLA	Other MISTs (e.g., Rezūm)	TURP	References
Patient satisfaction	High, durable	High, comparable	High, but lower for sexual function	1–8
Symptom relief (IPSS, QoL)	Significant, rapid, durable	Significant, comparable	Maximal, but slower recovery	1–9
Recovery time	Outpatient, rapid return	Outpatient, rapid return	Inpatient, longer recovery	2,4–6,10
Return to normal activities	Days to 1 week	Days to 1 week	Weeks	2,4–5

Abbreviations: IPSS, International Prostate Symptom Score; MISTs, minimally invasive treatments; QoL, quality of life; TPLA, transperineal laser ablation; TURP, transurethral resection of the prostate; UTI, urinary tract infection.

Cost-effectiveness

While direct, high-quality cost-effectiveness analyses of TPLA are not yet available, the available evidence suggests that TPLA is likely to be a cost-effective option for BPH, particularly in outpatient and

resource-constrained healthcare settings. Its low procedural and complication costs, combined with durable functional outcomes and low retreatment rates, position it favorably relative to TURP and other MISTs such as prostatic urethral lift and photoselective vaporization.^{1,3,4,6–8,12,19,25} The ability to perform TPLA as an outpatient procedure under local anesthesia reduces direct costs and resource utilization.

Predictors of outcomes and complications

There are no validated molecular or laboratory biomarkers that predict outcomes or complication risk with TPLA. The most important predictors are anatomical and imaging based, specifically prostate size (optimal 30–100 mL), gland morphology, and the presence or absence of significant median lobe or IPP.^{1–5,10,11,14} Imaging findings that suggest challenging anatomy—such as large prostates, severe median lobe, prior surgical changes, or significant calcifications—are associated with higher risk of complications and less predictable outcomes.

Imaging finding	Predicts better outcome	Predicts higher complication risk	References
Prostate volume 30–100 mL	Yes	No	1–11
Prostate volume > 100 mL	Uncertain	Possible	1–11
Small/moderate median lobe	Yes	No	1–4,6,9–11
Large median lobe/severe IPP	No	Yes	1–4,6,9–11
Irregular gland morphology/fibrosis	No	Yes	1–4,6,9–12
Prior surgical intervention (TURP, etc.)	No	Yes	1–4,6,9–12
Significant calcifications	No	Yes	1–4,6,9–12

Abbreviations: IPP, intravesical prostatic protrusion; TURP, transurethral resection of the prostate.

Conclusion

Transperineal laser ablation is best suited for men with symptomatic BPH and prostate volumes between 30 mL and 100 mL, particularly those who have failed or are intolerant to medical therapy and who wish to preserve sexual function. The procedure is compatible with a wide range of comorbidities, including anticoagulation and high surgical risk, and is feasible in patients with urinary retention. TPLA offers significant and durable improvements in LUTS, with high rates of preserved sexual function and a low rate of complications. The main limitations are in patients with very large prostates, severe anatomical variants, or prior pelvic interventions, where evidence is limited and procedural risk may be higher. Careful preoperative imaging, individualized procedural planning, and operator expertise are essential to optimize outcomes. Patient satisfaction and quality of life are high, with rapid recovery and early return to normal activities. TPLA is likely to be a cost-effective option in appropriate healthcare settings. Further research, including randomized controlled trials and long-term comparative studies, is needed to refine patient selection and optimize the role of TPLA in the BPH treatment algorithm.

Ultrasound Ablation

Guideline-based indications and patient selection criteria

The AUA guideline, as published by the American Urological Association in its 2023 amendment, does not currently recommend transurethral ultrasound ablation (TULSA) or high-intensity focused ultrasound (HIFU) as standard-of-care options for BPH. The guideline emphasizes that while many MISTs, including ultrasound-based ablation techniques, are in development, robust comparative data and long-term outcomes are required before these can be incorporated into formal treatment algorithms. The AUA highlights the need for ongoing benchmarking of new technologies against established therapies and stresses that patient selection criteria for these modalities remain to be clearly defined as further evidence emerges.¹

Current evidence from prospective and retrospective studies suggests that TULSA and HIFU are most appropriate for men with moderate-to-severe LUTS (typically IPSS ≥ 12) who have failed or are intolerant of medical therapy and are seeking alternatives to traditional surgery. Ideal candidates for TULSA are those with prostate volumes generally in the range of 40 mL to 80 mL, without significant median lobe hypertrophy or large intravesical prostatic protrusion, and who wish to preserve sexual function. TULSA requires no contraindications to MRI or general anesthesia, as the procedure is MRI guided and performed under anesthesia.²⁻⁴ HIFU is best suited for men with moderate-to-severe LUTS and prostate volumes typically less than 80 mL, without significant prostatic calcifications or rectal disease, and who can tolerate anesthesia.⁵⁻⁹

Prostate size ranges: optimal and limiting factors

Prostate size is a critical determinant of eligibility and expected outcomes for both TULSA and HIFU. Clinical studies of TULSA have generally included patients with baseline prostate volumes in the range of 45 mL to 66 mL, with optimal outcomes observed in glands between 30 mL to 80 mL. Prostates smaller than 30 mL may not provide sufficient tissue for meaningful ablation, while those larger than 80 mL may exceed the ablation envelope or require prolonged treatment times, potentially increasing the risk of complications or incomplete treatment.^{2-4,10}

For HIFU, most studies have included patients with prostate volumes up to 75 mL, with optimal outcomes in glands ≤ 60 mL. Larger prostates are associated with higher retreatment rates and less complete ablation, and some protocols have combined HIFU with pretreatment TURP to debulk larger glands.^{6-9,11} Both modalities are generally not recommended for prostates < 30 mL or > 80 mL, as the risk-benefit ratio may not favor intervention in these extremes.^{12,13}

Modality	Optimal prostate size range	Limiting prostate size	Clinical evidence/Consensus	References
TULSA	30–80 mL	< 30 mL or > 80 mL	Most studies include 45–66 mL; limited data for > 80 mL; technical feasibility and safety best in 30–80 mL	1–4
HIFU	≤ 60–75 mL	< 30 mL or > 75 mL	Most studies include ≤ 75 mL; optimal outcomes ≤ 60 mL; higher retreatment rates in larger glands	5–9

Abbreviations: HIFU, high-intensity focused ultrasound; TULSA, transurethral ultrasound ablation.

Symptom severity and prior treatment history

Both TULSA and HIFU are primarily indicated for men with moderate-to-severe LUTS (IPSS ≥12) who have failed or are intolerant of medical therapy. Clinical trials of TULSA have included men with median IPSS scores of 17–18, demonstrating substantial improvements in symptom burden and urinary flow rates postprocedure. The degree of baseline symptom severity predicts the magnitude of improvement, with greater benefit seen in those with higher IPSS scores.^{2,3,14} HIFU studies have similarly enrolled patients with moderate-to-severe LUTS, with significant reductions in IPSS and improvements in QoL.^{6–8,15,16}

Prior medical therapy does not negatively impact the efficacy of TULSA or HIFU, and the ability to discontinue BPH medications postprocedure is a consistent finding.^{2,3} Most studies have focused on treatment-naïve patients or those without prior prostate surgery, but limited data suggest that selected patients with prior interventions may still benefit, provided that anatomic considerations are addressed.¹⁰

Comorbidities and contraindications

Eligibility and safety for TULSA and HIFU are influenced by several comorbidities and contraindications. Both procedures carry a risk of bleeding, particularly in patients on chronic anticoagulation. Most centers recommend temporary interruption of anticoagulation, if feasible, to minimize bleeding risk, though robust data in this population are lacking.^{2,3,5,17} Patients with significant urinary retention or high post-void residuals are at increased risk for perioperative complications, and those with complete retention or indwelling catheters are often excluded from early-phase trials.^{2,3,18,19}

TULSA and HIFU have both been studied in men with concurrent prostate cancer and BPH, with evidence supporting their safety and efficacy in organ-confined, low- to intermediate-risk disease.^{10,14,17,19,20} However, high-risk or metastatic prostate cancer is a contraindication. Other contraindications include uncorrected urinary tract infection, significant rectal pathology (for HIFU), MRI incompatibility (for TULSA), and severe comorbidities precluding anesthesia.^{2–4,17,19}

Efficacy, safety, and patient-reported outcomes

TULSA has demonstrated robust efficacy in prospective studies, with median IPSS reductions of 70% to 82%, $Q_{\max}$ increases of 60% to 100%, and prostate volume reductions of 30% to 40% at 12 months. These improvements are accompanied by preservation of continence and sexual function, with most adverse events being mild to moderate and resolving with conservative management.^{2,3,14} HIFU provides significant improvements in IPSS (50%–60% reduction) and $Q_{\max}$ (30%–54% increase) at 6 to 12 months, but is associated with higher retreatment rates and a greater risk of transient urinary retention and delayed recovery of continence, especially when combined with other therapies.^{6–8,15,18,19,21,22}

Patient-reported outcomes are favorable for TULSA, with marked improvements in symptom scores, quality of life, and preservation of urinary and sexual function.^{2,3,10,14} HIFU also improves symptoms and quality of life, but the risk of persistent or recurrent symptoms requiring retreatment is higher, and the impact on sexual function is more variable.^{6–8,15,19,21,22}

Modality	Efficacy (IPSS/ $Q_{\max}$)	Durability	Safety	Patient-reported outcomes	Ideal subgroups	References
TULSA	IPSS ↓ 70%–82%, $Q_{\max}$ ↑ 60%–100% at 12 mo	Sustained at 12 mo, longer-term data pending	Mostly mild/moderate AEs, rare serious events, preserves continence/sexual function	Marked symptom/QoL improvement, stable sexual function, preserved continence	Moderate LUTS, prostate < 75 mL, prioritizing continence/sexual function, concurrent CaP	1–5
HIFU	IPSS ↓ 50%–60%, $Q_{\max}$ ↑ 30%–54% at 6–12 mo	44% retreatment at 4 yr, efficacy wanes over time	Mild/moderate AEs common, higher risk of stricture, incontinence, ED (device dependent)	Symptom/QoL improvement, higher risk of ED/incontinence, higher retreatment	Moderate LUTS, prostate < 75 mL, not candidates for surgery, lower priority on sexual function	6–12

Abbreviations: AEs, adverse events; CaP, prostate cancer; ED, erectile dysfunction; HIFU, high-intensity focused ultrasound; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms; mo, months; $Q_{\max}$, maximum urinary flow rate; QoL, quality of life; TULSA, transurethral ultrasound ablation; yr, years.

Long-term efficacy, safety, and retreatment

Long-term data for TULSA are limited, with the most extended follow-up available in mixed cancer/BPH cohorts up to 48 months. These studies report sustained improvements in IPSS and quality of life, with continence preserved in 96% of patients and stable erectile function. The retreatment rate for TULSA in BPH-specific populations remains undefined, but early data suggest a lower need for secondary intervention compared to HIFU.⁴ HIFU, in contrast, has a well-documented high retreatment rate, with 43.8% of patients requiring TURP

within 4 years and a gradual decline in symptom relief over time.⁶ Most adverse events for both modalities are mild and transient, with rare serious complications.

Modality	Long-term efficacy (≥ 4 yr)	Retreatment rate (≥ 4 yr)	Durability of symptom relief	Safety profile	References
TULSA	Sustained IPSS/QoL improvement up to 48 mo in mixed cohorts; BPH-only data limited to 12–16 mo	Not precisely reported for BPH; low in available series	Symptom relief durable up to 4 yr in mixed cohorts; BPH-only long-term data lacking	Mostly mild/moderate AEs; continence and sexual function preserved; rare serious events	1–5
HIFU	IPSS improvement (53% at 12 mo) sustained in responders; Q _{max} benefit declines over 4 yr	43.8% required TURP within 4 yr	Symptom relief wanes over time; high retreatment rate	Mild/moderate AEs common; most transient; low severe complication rate	6–9

Abbreviations: AEs, adverse events; BPH, benign prostatic hyperplasia; HIFU, high-intensity focused ultrasound; IPSS, International Prostate Symptom Score; mo, months; Q_{max}, maximum urinary flow rate; QoL, quality of life; TURP, transurethral resection of the prostate; yr, years.

Cost-effectiveness and resource utilization

Economic analyses for TULSA and HIFU are limited. Established treatments such as TURP and laser therapies (HoLEP, PVP) are supported by robust cost-effectiveness data, demonstrating favorable long-term outcomes and resource utilization. TURP and HoLEP are both cost-effective for severe BPH, with 5-year costs per patient of \$6,328–\$6,670 and \$6,532, respectively, and high quality-adjusted life years (QALYs).^{24–30} Minimally invasive therapies such as WVT and PUL offer lower upfront costs but may be associated with higher retreatment rates.^{29,30}

TULSA requires MRI-compatible facilities and specialized equipment, likely increasing procedural costs and resource utilization compared to office-based therapies. HIFU also requires specialized ultrasound equipment and is associated with higher retreatment rates, further increasing cumulative costs. Neither modality has established cost-effectiveness relative to TURP or laser therapies due to the lack of long-term data and economic modeling.^{2,24–29,31}

Real-world adoption and accessibility

The real-world adoption of TULSA and HIFU for BPH remains limited, with availability largely confined to specialized tertiary centers with the requisite infrastructure and expertise. In Germany, HIFU has historically dominated the focal therapy landscape, but its share has declined as newer modalities, including TULSA, have increased in prevalence. By 2019, only six centers in Germany offered TULSA, and the majority of focal therapy procedures were performed in a small number of high-volume centers.³² In the United States, adoption is further

constrained by regulatory and reimbursement barriers, with most procedures performed in the context of clinical trials or as self-pay interventions.^{1,33} Key barriers to broader adoption include the need for advanced imaging and ablation technology, limited provider experience, inconsistent reimbursement, and the investigational status of these modalities in major guidelines.^{3,4,17,32,33}

Ongoing clinical trials and recent evidence

Recent and ongoing clinical trials have provided important preliminary data supporting the safety and efficacy of TULSA for BPH. A prospective phase 2 study published in 2025 evaluated MRI-guided TULSA in 30 men with BPH, demonstrating significant improvements in prostate volume, PSA, urinary flow rates, and symptom scores at 12 months, with a favorable safety profile and preservation of continence and sexual function.³ Earlier phase 1 data and retrospective analyses corroborate these findings.^{2,4,10} For HIFU, recent studies have focused on its use in combination with other therapies or in the context of prostate cancer, with limited new data for BPH-specific populations.¹⁸ Both modalities remain investigational, and further large-scale, long-term studies are needed to define their optimal role in BPH management.¹

Patient perspectives and preferences

Patient preferences in BPH treatment are highly individualized and influenced by perceived efficacy, risk of complications, impact on sexual function, and recovery experience. Studies of TULSA report high rates of satisfaction, with patients valuing the dual benefit of symptom relief and preservation of functional status, as well as the ability to discontinue BPH medications postprocedure.^{2,10,14} For HIFU, the appeal lies in the procedure's noninvasive nature and favorable short-term safety profile, but concerns about recovery and retreatment may limit its appeal.^{7,18} A large conjoint analysis found that the risk of complications was the most important attribute influencing treatment choice, followed by efficacy, recovery difficulty, and risk of ejaculatory dysfunction.³⁴ Qualitative research highlights that men often reach a “tipping point” in their decision to seek intervention, and their preferences are shaped by both clinical outcomes and the anticipated impact on daily life, sexual function, and independence.³⁵ The AUA emphasizes the importance of individualized, patient-centered counseling and shared decision-making as new technologies are integrated into BPH management.¹

Guideline updates

As of July 2025, there have been no substantive updates or changes in the major urological society guidelines, including those of the American Urological Association, regarding the use of TULSA or HIFU for BPH since the 2024 publication of the 2023 guideline amendment. Both modalities remain investigational, and their use should be considered only in the context of clinical trials or specialized centers with appropriate expertise and infrastructure.¹

Conclusion

TULSA and HIFU represent promising, minimally invasive options for select men with moderate-to-severe LUTS due to BPH, particularly those with prostate volumes in the 30 mL to 80 mL range who desire preservation of urinary and sexual function and are seeking alternatives to traditional surgery. The current evidence supports their safety and efficacy in well-selected patients, but both modalities remain investigational, with limited long-term data and high retreatment rates for HIFU. The American Urological Association does not currently recommend TULSA or HIFU as a standard-of-care option for BPH, emphasizing the need for further robust data and ongoing benchmarking against established therapies. Patient selection should be individualized, taking into account symptom severity, prostate size, comorbidities, and patient preferences, and these modalities should be offered primarily in the context of clinical trials or specialized centers. Ongoing research and future guideline updates are anticipated to further clarify the role of TULSA and HIFU in BPH management.^{1–3,10,11,14–16,21–36}

Topic	Recommendation	LoE	GoR
Ablative Therapies: Ultrasound and Laser	Discuss emerging therapies like transurethral ultrasound ablation (TULSA), transrectal ultrasound ablation (HIFU), or transperineal laser ablation (TPLA) as options to men with LUTS due to BPO interested in participating in a clinical trial, who accept an undefined likelihood of preserving ejaculatory function, to currently have the procedure under anesthesia, and likely have a greater need for retreatment (compared to TURP), with ideal prostate sizes and configurations yet to be defined.	IV (Expert Opinion/ emerging data)	D

Abbreviations: BPO, benign prostatic obstruction; GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; TURP, transurethral resection of the prostate.

Temporary Intraprostatic Devices/Stents

Temporary prostatic stents: devices and clinical context

Temporary prostatic stents are designed to maintain urethral patency and relieve bladder out obstruction due to BPH. The most studied devices in this category, aside from UroLume and iTIND, include the Allium™ Triangular Prostatic Stent (TPS), Memokath/Memotherm, FloStent™, and emerging devices such as Zenflow, Butterfly, Urocross, Exime, and ProVee. These stents are typically constructed from nitinol or silicone, are placed under local anesthesia, and are intended for temporary use, with indwelling times ranging from weeks to months or, in some cases, years depending on the device and patient context.^{1–6}

Published indications and ideal patient selection criteria

The AUA provides the most current and authoritative guidance on patient selection for temporary implanted prostatic devices (TIPDs), which include temporary prostatic stents. According to the AUA, TIPDs may be offered to patients with LUTS/BPH provided the prostate volume is between 25 cc and 75 cc and there is no obstructive median lobe.⁷ This recommendation is based on expert opinion and the inclusion/exclusion criteria of pivotal clinical trials, which generally exclude patients with larger prostates or significant median lobe hypertrophy due to concerns about device efficacy and risk of migration or incomplete relief of obstruction.^{7,8}

Ideal candidates for temporary prostatic stents are men with moderate-to-severe LUTS (IPSS, ≥ 10), reduced peak urinary flow ($Q_{\max}$, < 12 mL/s), and objective evidence of bladder outlet obstruction, who are either unfit for or unwilling to undergo standard surgical interventions.^{2,7} These patients may have significant comorbidities (e.g., cardiovascular or pulmonary disease be on chronic anticoagulation) or have a limited life expectancy. Additionally, men who wish to avoid the sexual side effects associated with surgery or long-term pharmacotherapy may be considered.^{2,7,9} Patients should have preserved detrusor function, as significant bladder dysfunction or high post-void residuals (> 250 mL) are associated with poor outcomes.^{10,11}

Contraindications and patient factors limiting suitability

Several contraindications and patient factors make temporary prostatic stents unsuitable for certain BPH patients. The most critical anatomical contraindication is the presence of an obstructive median lobe, which is associated with higher failure rates and poor stent positioning.^{7,8} Prostate size outside the 25 cc to 75 cc range is also a contraindication, as smaller prostates may not provide sufficient anchoring and larger prostates may not be adequately decompressed.^{7,8,11}

Other contraindications include active urinary tract infection, urethral strictures, bladder stones, prior prostatic surgery, significant detrusor underactivity, and neurogenic bladder.^{10,13} Patients with uncorrected bleeding disorders or those unable to interrupt anticoagulation are at increased risk of periprocedural bleeding.¹⁰ Frail

patients or those with limited life expectancy may be considered for stenting as a palliative measure, but the risk-benefit ratio must be carefully assessed.^{12,13}

Device-specific differences in patient selection

While the AUA provides unified class-level criteria, individual devices have been studied in populations with slightly different characteristics, and their design features may influence patient selection. For example, the Memokath stent is often used in elderly, high-risk patients and may be considered in prostates slightly outside the standard range, reflecting its use in populations where other interventions are contraindicated.^{4,12,14} The Allium TPS and FloStent adhere more strictly to the guideline criteria, with additional emphasis on the absence of prior prostatic surgery and significant detrusor underactivity.¹⁻³ The Exime stent, made of silicone is particularly suited for elderly patients with urinary retention who have failed a trial without catheter and are not candidates for surgery.⁵

Device	Prostate volume	Median lobe	Prior surgery	Detrusor function	Age/Comorbidity	Indwelling time	References
Memokath	~25–75 cc (flexible in frail/elderly)	Exclude significant	Exclude	Exclude underactivity	Often elderly, high comorbidity	Months–years (flexible)	1–4
Allium TPS	25–75 cc	Exclude	Exclude	Exclude	45–80 years, moderate comorbidity	Months (temporary)	2,5,6
FloStent	25–75 cc	Exclude	Exclude	Exclude	≥ 45 years, moderate comorbidity	Up to 1 year (temporary)	2,7
Exime	≤ 120 cc (most 25–75 cc)	Minimal protrusion	Exclude	Exclude	Elderly, urinary retention	Weeks–months (temporary)	8

Clinical outcomes and complication rates compared to other BPH management options

Temporary prostatic stents provide moderate symptom relief and improved urinary flow in men with BPH, with a favorable safety profile characterized by a low incidence of major complications but a relatively high rate of minor adverse events and re-interventions. In a systematic review of 38 studies, the mean improvement in IPSS at 12 months was 9.85 points, with a mean increase in Q_{max} of 6.62 mL/sec, and a catheter-free rate of 85.2%.⁴ The overall complication rate was 30.8%, with the most common complications being urinary tract infections (17.2%), stent calcification (12.6%), irritative symptoms (12.2%), and acute urinary retention (10.4%). The stent failure rate (removal or repositioning) was 14.8% at 12 months.⁴

Compared to other minimally invasive therapies, such as prostatic urethral lift (PUL), water vapor thermal therapy (WVTT/Rezūm), and prostatic arterial embolization (PAE), temporary stents offer similar or slightly less improvement in symptom scores and flow rates, but with a higher rate of minor complications and retreatment.^{15–17}

TURP remains the gold standard for symptom relief and flow rate improvement, but is associated with higher rates of major complications and sexual dysfunction.^{15–17}

Long-term clinical outcomes and durability

Long-term (> 2 years) data for temporary prostatic stents are limited. The most robust evidence pertains to metallic stents such as Memokath/Memotherm, which have demonstrated sustain symptom relief for several years in select, high-risk patients, but are associated with a significant risk of device migration, removal, and other complications.^{4,12,14,18} For newer generation stents, including Allium TPS and FloStent, published data are limited to 12 months, and there is a clear need for prospective studies with longer follow-up.^{1–4} The American Urological Association notes the lack of robust long-term data for these devices and emphasizes the importance of ongoing research.⁷

Device/Study	Follow-up duration	Complication rate (> 2 yr)	Retreatment/Removal rate (> 2 yr)	References
Memokath/Memotherm	Mean, 6.8 yr	Migration 14%, other complications not fully quantified	Removal 14% (Bozkurt); 0%–48% (Armitage, variable quality)	1,5
Allium TPS	12 months	No migration/obstruction at 1 yr	Not reported beyond 1 yr	1,6
FloStent, Zenflow, Butterfly, Urocross, Exime	No > 2-yr data	Unknown	Unknown	1,7–9

Patient-reported outcomes and quality of life

Temporary prostatic stents are associated with significant improvements in patient-reported outcomes and quality of life, comparable to other minimally invasive therapies and, in the short term, to TURP.^{4,15–17} The preservation of sexual function is a consistent advantage of temporary stents and other MISTs.^{7,19} The mean improvement in IPSS at 12 months is clinically meaningful, and the majority of patients report satisfaction with the procedure, particularly those who retain the stent for the intended duration.^{1,3,4}

Cost-effectiveness and healthcare resource implications

Temporary prostatic stents offer a cost profile characterized by low initial procedural costs due to their office-based, local anesthesia approach, and minimal perioperative resource utilization.^{4,20,21} However, their higher rates of retreatment and minor complications increase long-term healthcare resource use and may offset some of the initial cost savings compared to more durable interventions such as TURP or WVTT.^{4,20,21} While direct cost-effectiveness data for these stents are lacking, extrapolation from related MISTs suggests that their overall economic value is moderate, with the greatest benefit realized in patients who are poor candidates for surgery or who prioritize minimally invasive, reversible therapy.^{7,20–22}

Treatment Modality	Procedural setting	Anesthesia type	Index cost (USD)	Retreatment rate (1 yr)	Major complications	Minor complications	Long-term cost-effectiveness	References
Temporary prostatic stents	Office based	Local	Likely \$2,500 to \$4,000*	~15%	Rare	Common (UTI, irritative)	Moderate (higher retreatment offsets low index cost)	1–3
WVTT (Rezūm)	Office based	Local	\$2,655	~2%	Rare	Moderate	High (most cost-effective)	2–4
PUL (UroLift)	Office based/OR	Local/General	\$9,580	~10%	Rare	Moderate	Moderate (higher cost, moderate QALYs)	2,3
TURP	OR/inpatient	General/Spinal	\$6,328	< 5%	Higher	Moderate	Moderate (higher QALYs, higher cost)	2,3

Abbreviations: OP, operating room; PAE, prostatic arterial embolization; PUL, prostatic urethral lift; QALYs, quality-adjusted life years; TURP, transurethral resection of the prostate; UTI, urinary tract infection; WVTT, water vapor thermal therapy.

Real-world adherence and satisfaction

Real-world adherence to temporary prostatic stents is high, with approximately 85% of patients remaining catheter free at 12 months and most reporting significant symptom relief and satisfaction.^{1,3,4} These rates are superior to those observed with pharmacological therapy and comparable to other minimally invasive surgical therapies, though the risk of minor complications and need for retreatment are somewhat higher.^{4,23–25} Patient satisfaction is driven by meaningful improvements in symptoms and quality of life, as well as preservation of sexual function.^{1,3,7}

Patient subgroups: who derives the greatest benefit or risk?

Temporary prostatic stents are best suited for elderly or high-risk patients unfit for surgery, men with urinary retention who have failed catheter trials, and those with moderate-to-severe LUTS and preserved bladder function who desire a reversible, minimally invasive option.^{7,12,14} The greatest risks are seen in patients with detrusor underactivity, prior prostatic surgery, significant urethral pathology, or unfavorable prostate anatomy.^{7,12,14} In elderly or frail patients, stenting offers a valuable alternative to chronic catheterization, with lower rates of infection, pain, and urinary leakage, and higher patient satisfaction.^{5,14} However, these same patients may be at higher risk for stent-related discomfort, irritative symptoms, and early removal.¹³

Device-specific features influencing selection and outcomes

Stent material, design, and intended indwelling time are central determinants of both patient selection and clinical outcomes. Nitinol-based, polymer-covered stents such as Allium TPS are generally preferred for patients seeking reversible, minimally invasive relief of BPH symptoms, while silicone stents such as Exime may be advantageous in elderly or high-risk patients with urinary retention.^{1–6} Design features such as anti-encrustation coatings, anchoring mechanisms, and flexibility influence the risk of migration, encrustation, and patient comfort, and should be matched to the patient’s clinical scenario and anticipated duration of use.^{2–6}

Conclusion

Temporary prostatic stents, excluding UroLume and iTIND, are a valuable option for select BPH patients, particularly those who are unfit for or unwilling to undergo surgery, and have moderate-to-severe LUTS, preserved bladder function, and prostate volumes between 25 cc and 75 cc without an obstructive median lobe. The American Urological Association recommends careful patient selection based on these criteria, with additional consideration of device-specific features and patient comorbidities. While temporary stents offer meaningful symptom relief, improved quality of life, and preservation of sexual function, they are associated with higher rates of minor complications and retreatment compared to some other minimally invasive therapies. The greatest benefit is seen in elderly, high-risk patients and those with urinary retention who would otherwise require chronic catheterization. Ongoing research is needed to further define the long-term efficacy, safety, and cost-effectiveness of these devices, and to refine patient selection for optimal outcomes.^{1–3,7,12,14}

Topic	Recommendation	LoE	GoR
Temporary Prostatic Stents (TPS)	Offer temporary prostatic stents to men with LUTS due to BPO interested in preserving ejaculatory function and/or avoiding anesthesia, who accept less de-obstruction with an expectation for retreatment (compared to TURP), with ideal prostate sizes undefined and without an obstructive median lobe.	IV (Expert Opinion/emerging data)	D
	Discuss TPS as an option in men with LUTS due to BPO who are unsuitable for surgery and/or anesthesia.	IV (Expert Opinion/emerging data)	D
	Counsel that results from one temporary prostatic stent cannot be extrapolated to others, as each stent has a unique design, specific indications, and has been studied in different patients.	IV (Expert Opinion/emerging data)	D

Abbreviations: BPO, benign prostatic obstruction; GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; TURP, transurethral resection of the prostate.

Permanent Intraprostatic Devices/Stents

Patient selection criteria for permanent prostatic stents or implants

Guideline-based indications and quantitative selection parameters

Recent systematic reviews converge on several key indications for permanent prostatic stents or implants. The ideal candidate is a man with moderate-to-severe LUTS due to BPH who has failed or is intolerant to medical therapy (e.g., α -blockers, 5 α -reductase inhibitors, or combination therapy) and is not a candidate for, or declines, standard surgical interventions such as TURP or laser enucleation. Quantitatively, the optimal prostate volume for stent placement is typically between 25 cc and 75 cc, with a mean of 48 cc reported in large series, and a prostatic urethral length of approximately 40 mm. Patients should have preserved detrusor contractility, as confirmed by urodynamic studies, and no significant median lobe enlargement or intravesical prostatic protrusion, which are associated with higher failure and complication rates.¹⁻⁴

Permanent stents are particularly indicated in men with significant comorbidities (e.g., severe cardiopulmonary disease, chronic anticoagulation) that preclude anesthesia or surgery, and in those with chronic urinary retention who are catheter dependent but have preserved bladder contractility. In these populations, stent placement can achieve catheter-free status in approximately 85% of cases, with a mean improvement in IPSS of 10 points and a mean increase in $Q_{\max}$ of 6.6 mL/sec at 12 months.^{3,5,6}

Contraindications and special considerations

Absolute contraindications to permanent prostatic stents include active urinary tract infection, significant detrusor underactivity or acontractile bladder, allergy to device materials (e.g., nitinol, titanium), and uncorrected coagulopathy. Relative contraindications include a prominent median lobe, prostate size outside device specifications (typically < 25 cc or > 80 cc), prior pelvic irradiation, a short prostatic urethra (< 2.5 cm), and a history of complex urethral or prostatic surgery. Patients with recurrent or refractory urinary tract infections, bladder calculi, or unrecognized malignancy are at increased risk for device-related complications and should be carefully evaluated prior to stent placement.^{3,7,8}

In patients with atypical or complex anatomy, such as those with prior pelvic trauma, congenital anomalies, or significant anatomical distortion, the risk of technical failure, migration, encrustation, and the need for re-intervention are higher. Careful endoscopic and radiological assessment is essential to determine suitability and to customize device selection and sizing.^{3,7,8}

Influence of comorbidities

Permanent prostatic stents are uniquely suited for patients on chronic anticoagulation, as the procedure can be performed under local anesthesia with minimal bleeding risk and without the need to interrupt anticoagulation therapy. Frailty, advanced age, and limited life expectancy are not contraindications; rather, they are common indications for stent use, as the primary goal is to improve quality of life and avoid the morbidity of chronic catheterization.^{3,5,6,8} In contrast, neurogenic bladder or significant detrusor underactivity is a contraindication, as stents do not address impaired contractility and may result in persistent retention.^{3,7,9}

A summary of comorbidities influencing suitability is provided in the following table, which details the impact of specific conditions on patient selection and the rationale for each:^{3,5–8}

Comorbidity/Condition	Influence on suitability	Rationale/Comments	References
Chronic anticoagulation	Favors suitability	Stents can be placed under local anesthesia with minimal bleeding risk	1–3
Neurogenic bladder/detrusor underactivity	Contraindication/relative contraindication	Stents do not address impaired contractility; risk of persistent retention	1,4,5
Prior pelvic/prostatic surgery	Relative contraindication	Altered anatomy, risk of hyperplasia, encrustation, migration; individualized assessment needed	5,6
Frailty/advanced age/limited life expectancy	Favors suitability	Minimally invasive, improves quality of life, especially in those unfit for surgery	1–3,6
Active UTI, bladder calculi, or cancer	Contraindication until treated	Risk of infection, encrustation, or tumor seeding	1,2
Large median lobe/short prostatic urethra	Relative contraindication	Increased risk of migration, incomplete relief	1,5
History of pelvic irradiation	Relative contraindication	Poor tissue healing, increased risk of complications	5,6

Abbreviation: UTI, urinary tract infection.

Comparative outcomes, risks, and long-term data

Functional outcomes and complication rates

Permanent prostatic stents provide significant and durable improvements in LUTS for well-selected patients. In systematic reviews encompassing over 2,600 patients, the mean improvement in IPSS is approximately 10 points, with a mean increase in $Q_{\max}$ of 6.6 mL/sec and a mean reduction in PVR of 147 mL at 12 months. The catheter-free rate is 85% at 1 year, and these benefits are sustained in the majority of patients who retain a functional stent beyond the initial years.^{3,5,6,8,10}

However, the overall complication rate is 31%, with urinary tract infections occurring in 17%, stent calcification or encrustation in 13%, irritative voiding symptoms in 12%, and acute urinary retention in 10%. Stent migration rates range from 10% to 14%, and device failure (removal or repositioning) occurs in 15% to 23% of patients within the first year, increasing to one-third or more over 5 years.^{3,5,10,11} The majority of complications are minor and manageable, but stent removal can be technically challenging, especially in cases of tissue ingrowth or encrustation.^{3,7,10}

Long-term studies, such as the 12-year UroLume series, demonstrate that mean symptom scores remain improved (from 20.4 at baseline to 10.8 at 12 years), with a mean $Q_{\max}$ of 11.5 mL/sec and a mean PVR of 80 mL at 12 years. However, 47% of stents were removed during follow-up, primarily due to migration, malposition, or symptom progression.¹⁰ In the Memokath series, 23% of stents were removed for failure over 8 years, and an additional 4% were removed as no longer required.^{5,6,8}

Comparative efficacy with other BPH therapies

When compared to TURP and other MISTs, permanent prostatic stents offer less robust and less durable symptom relief but have a favorable risk profile in high-risk populations. TURP typically results in IPSS improvements of 13–15 points and $Q_{\max}$ increases of 6–10 mL/sec, with retreatment rates of 3–8% at 2–5 years. MISTs such as water vapor therapy (Rezūm), prostatic urethral lift (PUL), and prostatic artery embolization (PAE) provide intermediate efficacy, with IPSS improvements of 9 points to 12 points and $Q_{\max}$ increases of 3 mL/sec to 6 mL/sec, but with higher retreatment rates (4–21% at 1–2 years).^{12–17}

Permanent stents are associated with higher rates of device-related complications and reintervention compared to TURP and most MISTs, but they are uniquely suited for patients who are not surgical candidates. The preservation of sexual function is a notable advantage of newer stent designs, with minimal impact on erectile or ejaculatory function reported in the literature.^{2,18–20}

Long-term durability and patient-reported outcomes

Long-term (> 5 years) data indicate that permanent prostatic stents provide sustained symptom relief in a substantial proportion of patients, particularly those with limited life expectancy or high surgical risk. However, the cumulative risk of device failure and the need for removal or revision increases over time, with up to 47% of stents removed within 12 years in some series.¹⁰ Patient-reported quality of life and satisfaction are generally high when the stent functions as intended, especially in those previously dependent on indwelling catheters. However, satisfaction declines if complications necessitate removal or if symptoms recur.^{3,5,8,10,21}

Device-specific technical considerations and selection

Technical attributes and customization

Device-specific technical considerations are central to the selection and success of permanent prostatic stents. Modern stents such as Memokath/Memotherm, FloStent, and Allium TPS are designed for office-based placement under local anesthesia using a flexible cystoscope, minimizing procedural risk and facilitating use in frail or anticoagulated patients.^{3,5,6,18,22,23} Retrievability is a key advantage of these devices, with Memokath and FloStent designed for straightforward removal or repositioning using standard urological equipment, even after prolonged indwelling times.^{22,23}

Imaging compatibility is ensured by the use of radiopaque, MRI-safe materials (e.g., nitinol, titanium), allowing for confirmation of stent position and follow-up assessment. Device migration and encrustation remain the most common technical complications, with migration rates of 10% to 13% and encrustation rates of 13% reported in long-term studies.^{3,5,11} Polymer-covered stents such as Allium TPS are designed to minimize tissue ingrowth and encrustation, offering potential advantages in patients at high risk for these complications.¹⁸

The ability to customize stent length and diameter to match the patient's prostatic urethra is essential for optimal outcomes. Inadequate sizing or poor anatomical fit is a recognized cause of device failure and may necessitate early removal or replacement.^{3,5,23}

A summary of device-specific technical considerations is provided in the following table, which details the ease of placement, retrievability, imaging compatibility, migration/encrustation risk, and customization options for major devices:^{3,5,18,22–25}

Device/Feature	Ease of placement	Retrievability	Imaging compatibility	Migration/Encrustation risk	Customization/Sizing	References
Memokath/Memotherm	Office based, local anesthesia, flexible cystoscope	High (collapsible, easy removal with cold saline)	Radiopaque, MRI safe (minor artifact)	Migration 10%–13%, encrustation possible	Multiple lengths, trimmable	1–3
UroLume	Office based, local anesthesia	Moderate (tissue ingrowth may complicate removal)	Radiopaque, MRI safe	Higher risk of migration/encrustation	Multiple sizes	1
FloStent	Office based, flexible cystoscope	High (retrievable up to 1 year with standard tools)	Radiopaque, MRI safe	Early data: low migration/encrustation	Multiple sizes	4
Allium TPS	Office based, local anesthesia	Designed for easy removal (polymer cover)	Radiopaque, MRI safe	Designed to minimize encrustation	Multiple sizes	1,5
Covered nitinol stents with barbs	Office based, 18-F delivery system	High (removal set), barbs may complicate removal	Radiopaque, MRI safe	Barbs reduce migration, encrustation possible	Customizable	6,7

Abbreviations: MRI, magnetic resonance imaging.

Device-specific selection criteria and advantages

UroLume and Memokath/Memotherm are best suited for elderly, frail patients with significant comorbidities who are not surgical candidates and have failed or are intolerant to medical therapy. Memokath/Memotherm offers the advantage of easy removal and repositioning, with durable symptom relief in high-risk patients.^{3,5,6,8} Allium TPS, a polymer-covered nitinol stent, is designed to minimize tissue ingrowth and encrustation, making it suitable for patients with a history of stent-related complications or those at high risk for encrustation.¹⁸ FloStent and other emerging nitinol-based stents offer promising safety and efficacy profiles, with high technical success rates and favorable risk profiles in early studies, but long-term data are still emerging.²²

Device selection should be individualized based on prostate size, anatomy, prior treatment history, and patient preferences. In patients with complex anatomy or prior interventions, flexible and easily retrievable stents such as Memokath or Allium TPS may offer advantages, but the risk of migration and encrustation remains elevated.^{3,5,7,18,23}

Real-world effectiveness, cost-effectiveness, and health economic outcomes

Real-world registry and post-marketing data

Recent real-world registry and post-marketing surveillance data confirm that permanent prostatic stents are effective in relieving obstructive symptoms and improving urinary function in men with BPH who are poor candidates for surgery. The mean improvement in IPSS is approximately 10 points, with a mean increase in $Q_{\max}$ of 6.6 mL/sec and a mean reduction in PVR of 147 mL at 12 months. The catheter-free rate is 85%, and the overall complication rate is 31%, with most adverse events being minor and manageable.^{3,5,6,8,10,11,22}

Device-specific studies, such as the FloStent feasibility study, report no serious complications over 1 year of follow-up, with all adverse events resolving without sequelae and successful device retrieval using standard urological equipment.²² These findings are consistent with earlier registry data on Memokath and UroLume, which also demonstrate low rates of major complications but highlight the importance of careful patient selection to minimize the risk of migration, encrustation, and infection.^{3,5,6,8,10,11}

Cost-effectiveness and health economic outcomes

Permanent prostatic stents are a cost-effective option for high-risk or frail patients who are not candidates for standard surgical therapies. The primary economic advantages include low procedural costs, avoidance of anesthesia and hospitalization, reduction in catheter-associated morbidity and costs, and significant improvements in quality of life. In long-term studies, the majority of high-risk patients treated with stents reported sustained improvements in symptom scores and quality of life, with a high proportion dying with a functional stent *in situ* rather than requiring further intervention.^{5,6,8}

Direct procedural costs for permanent stents are generally lower than those for TURP or laser enucleation, as stent placement is typically performed under local anesthesia in an outpatient or office-based setting. The main economic disadvantage is the potential for retreatment, but this is less impactful in populations with limited life expectancy.^{3,5,6,8} Compared to other minimally invasive therapies, permanent stents offer similar or greater economic value in high-risk populations, although direct comparative cost-effectiveness data are limited.^{14,26,27}

Implementation, monitoring, and future directions

Stepwise implementation and monitoring

The selection and implementation of permanent prostatic stents should follow a stepwise approach:

First, confirm the diagnosis of BPH with moderate-to-severe LUTS refractory to medical therapy, using standardized scoring systems such as the IPSS and objective measures ($Q_{\max}$, < 12 mL/sec; PVR, > 100 mL; prostate volume, 25–75 cc).^{3,5,12,28} Second, assess for contraindications, including active infection, significant detrusor underactivity, prominent median lobe, and allergy to device materials. Third, evaluate comorbidities and anatomical factors, including prior interventions, prostate size, and urethral length, to guide device selection and customization.^{3,5,7,23}

Stent placement should be performed under local anesthesia using a flexible cystoscope, with intraoperative imaging to confirm correct positioning. Postprocedural monitoring includes clinical assessment, uroflowmetry, and imaging to confirm stent position and function. Patients should be followed at 1, 3, 6, and 12 months postprocedure, and annually thereafter, with prompt evaluation for symptoms of infection, migration, or obstruction.^{3,5,6,10,23}

Future research and ongoing trials

As of August 2025, there are no published randomized controlled trials directly comparing permanent prostatic stents (excluding UroLift) to other minimally invasive or surgical BPH therapies. The current evidence base consists primarily of single-arm studies, retrospective cohorts, and nonrandomized prospective series. Ongoing and future research should prioritize the inclusion of permanent prostatic stents in randomized, head-to-head trials against both established surgical therapies and other minimally invasive modalities to inform evidence-based patient selection and optimize clinical outcomes.^{2,3,16,22}

Conclusion and actionable recommendations

Permanent prostatic stents or implants (excluding UroLift) are best suited for men with moderate-to-severe LUTS due to BPH who have failed or are intolerant to medical therapy and are not candidates for, or decline, standard surgical interventions. The optimal candidate has a prostate volume of 25 cc to 75 cc, a prostatic urethral length of approximately 40 mm, no significant median lobe enlargement, preserved detrusor contractility, and no active infection or significant urethral pathology. Chronic anticoagulation, frailty, advanced age, and limited life expectancy favor suitability, while neurogenic bladder, significant detrusor underactivity, prior pelvic irradiation, and complex anatomy are relative or absolute contraindications.

Permanent stents provide clinically meaningful improvements in symptom scores, urinary flow, and quality of life, with a catheter-free rate of 85% at 1 year and sustained benefits in well-selected patients. The overall complication rate is 31%, with migration and encrustation being the most common device-related issues. Device selection should be individualized based on technical attributes, retrievability, and customization options, with modern stents such as Memokath, FloStent, and Allium TPS offering advantages in ease of placement and removal.

Permanent prostatic stents are a cost-effective and efficient option for high-risk or frail patients who are not candidates for standard surgical therapies, providing significant improvements in quality of life and reducing the morbidity and costs associated with chronic catheterization. Ongoing surveillance and further prospective studies are needed to define the long-term outcomes and optimal patient selection for these evolving technologies.

In summary, permanent prostatic stents or implants should be considered for carefully selected men with BPH who are unfit for surgery, have moderate prostate volumes, preserved bladder function, and no significant anatomical contraindications. Thorough preprocedural assessment, individualized device selection, and close postprocedural monitoring are essential to maximize efficacy and minimize complications, as supported by the current medical literature.^{1–3,5,6,8,10,12,18,22,23}

Topic	Recommendation	LoE	GoR
Permanent Prostatic Stents (PPS)	Offer permanent prostatic stents to men with LUTS due to BPO interested in preserving ejaculatory function and/or avoiding anesthesia, who accept less de-obstruction and will likely have a greater need for retreatment (compared to TURP), with ideal prostate sizes undefined and without an obstructive median lobe.	IV (Expert Opinion/emerging data)	D
	Discuss PPS as an option in men with LUTS due to BPO who are unsuitable for surgery and/or anesthesia.	IV (Expert Opinion/emerging data)	D
	Counsel that results from one permanent prostatic stent cannot be extrapolated to others, as each stent has a unique design, specific indications, and has been studied in different patients.	IV (Expert Opinion/emerging data)	D

Abbreviations: BPO, benign prostatic obstruction; GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; TURP, transurethral resection of the prostate.

Procedural Videos



Optilume® Procedural Video

Source: SIU Academy®.



Rezūm™ Procedural Video

Source: SIU Academy®.

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Intraprostatic Balloon Treatment—Optilume BPH

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Ultrasound Ablation

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COMMITTEE

06

**PREDICTIVE MODELS—
NOMOGRAMS FOR
PATIENT OUTCOME AND
SUCCESS CRITERIA**

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Table of Contents

Definition of Predictive Models and Nomograms	303
Introduction	303
Predictive Models: Definition, Purpose, Construction, Validation	303
Definition	303
Purpose	303
Construction	304
Validation	304
Nomograms: Definition, Purpose, Construction, Validation	304
Definition	304
Purpose	304
Construction	304
Validation	305
Application in male LUTS	305
Models and Nomograms for Medical Therapy	305
Monoparametric and multiparametric models	305
Monoparametric models	305
Based on objective parameter	305
Based on subjective parameter	306
Multiparametric models	307
Predictive models—nomograms for patient outcome and success criteria	309
Models and Nomograms for Invasive Therapy	311
Transurethral resection of the prostate (TURP)	311
Predictive models for functional outcomes	311
Predictive models for complications and mortality	312
Photoselective vaporization of the prostate (PVP)	313
Aquablation	313
Enucleation techniques	314
Models and Nomograms for Minimally Invasive Treatment	317
Prostatic artery embolization (PAE)	317

Table of Contents

Water vapor thermal therapy (WVTT)—Rezūm	318
Prostatic urethral lift (PUL)	318
Temporary implantable nitinol device (iTIND)	319
Clinical Utility	319
Future Directions: AI, Biomarkers, and Beyond	321
Artificial intelligence and machine learning	322
Integration of biomarkers and multi-omic data	322
Patient-centered data and digital health integration	322
Data infrastructure and model validation	323
Ethical and Regulatory Considerations	323
Conclusion	323
Statements and recommendations	324
References	325

Definition of Predictive Models and Nomograms

Introduction

Predictive models and nomograms are essential tools in clinical decision-making, particularly in managing male lower urinary tract symptoms (LUTS). The management of LUTS has evolved with the development of predictive models and nomograms designed to guide individualized therapy.

These tools integrate patient-specific parameters, such as prostate volume, symptom severity, and uroflowmetry data, to estimate treatment outcomes more accurately.^{1–4} By doing so, they support clinical decision-making, reduce trial-and-error prescribing, and improve patient satisfaction with medical or surgical interventions. By integrating clinical, demographic, and biological data, these models assist urologists in estimating the likelihood of particular clinical outcomes or the progression of disease.

This chapter aims to explore the role of predictive models and nomograms in optimizing management of LUTS. It will review the development, validation, and clinical application of these tools in guiding individualized treatment strategies. By integrating patient-specific parameters, predictive models can enhance treatment selection, improve understanding of expected outcomes, and refine the patient-physician discussion. Additionally, this chapter will highlight current challenges, the need for external validation, and future directions for refining these models to ensure broader clinical applicability. In the case no predictive models are available for some therapies, individual factors that can affect treatment outcomes will be discussed.

Predictive Models: Definition, Purpose, Construction, Validation

Definition

A predictive model is a statistical or machine learning (ML) tool designed to forecast a specific outcome based on one or more predictor variables.^{5,6} Predictive models can be broadly categorized into:

- Regression-based models: such as Logistic regression and Cox regression
- ML-based models: such as decision trees, random forests, support vector machines, and neural networks

These models have demonstrated clinical utility in guiding treatment strategies for LUTS and in evaluating the outcomes of interventions.

Purpose

The primary purpose of predictive models is to estimate the probability or risk of a particular outcome, which may include disease presence, disease progression, treatment response, or complications following an intervention.⁶

These models support diagnostic accuracy and therapeutic decision-making, as demonstrated in studies predicting bladder outlet obstruction⁷ and improvement post-treatment.⁸

Construction

Predictive models are constructed through a process of data collection, variable selection, model building, validation, and performance assessment. The model-building process often involves regression techniques where predictors are assigned coefficients based on their statistical significance and influence on the outcome.⁵ ML methods like deep neural networks (DNN) are increasingly used to improve predictive accuracy.⁸

Validation

Validation is critical for assessing the reliability and generalizability of predictive models. Internal validation, such as bootstrapping or cross-validation, ensures the model's robustness within the original dataset. External validation involves testing the model on independent datasets to evaluate its applicability to broader populations.⁶

Nomograms: Definition, Purpose, Construction, Validation

Definition

A nomogram is a graphical representation of a predictive model that provides a straightforward, user-friendly tool for estimating probabilities of clinical events.⁵ Typically, nomograms are constructed from regression models and presented as a series of scales, allowing clinicians to score individual predictors and calculate cumulative probabilities. Studies have shown their utility in predicting outcomes related to LUTS.⁷

Purpose

Nomograms translate complex statistical models into accessible, visual tools that can be readily applied in clinical practice. They are particularly valuable for patient counseling, shared decision-making, and individualized treatment planning.⁹

Construction

Creating a nomogram involves developing a predictive model using appropriate statistical techniques, followed by graphical representation of the model's predictive power. The scale for each predictor is often linear or logarithmic, depending on its influence on the outcome.⁵

Validation

As with predictive models, nomograms require rigorous validation to ensure their accuracy and reliability. Calibration plots, decision curve analysis, and concordance indices (C-index) are commonly used to assess their performance.^{6,10}

Application in male LUTS

Predictive models and nomograms are particularly useful in the context of male LUTS for:

- Risk stratification
- Treatment selection
- Outcome prediction

Models and Nomograms for Medical Therapy

Predictive models and nomograms are particularly valuable in stratifying patients based on their likelihood of response to the available pharmacologic therapies (either monotherapies or combinations).¹ Several validated nomograms have been developed using large-scale datasets from clinical trials and real-world studies to predict symptom progression, treatment efficacy, and the risk of acute urinary retention or surgery. The importance of risk stratification tools in optimizing medical therapy selection has also been highlighted by the European Association of Urology (EAU) and American Urological Association (AUA) guidelines.^{2,3}

Monoparametric and multiparametric models

Predictive models can be broadly categorized based on the number of factors they consider. Monoparametric models rely on a single predictive factor, while multiparametric models integrate multiple factors to generate predictions. Both approaches play a significant role in the field of predictive modeling, with the goal of accurately forecasting outcomes and guiding personalized interventions. The decision to use monoparametric or multiparametric models depends on the complexity of the clinical situation and the available data.

Monoparametric models

Based on objective parameter

Kawachi and colleagues explored the treatment outcomes of α -blocker (naftopidil/tamsulosin) for LUTS, revealing the predictive potential of single clinical parameters.⁴ While their study compared two medications, it also highlights how individual factors influence treatment success. Critically, the authors found a history of acute urinary retention (AUR) significantly impacts naftopidil (NAF) therapy. Patients with a prior AUR had significantly higher failure rates, suggesting that AUR history is a strong monoparametric predictor for NAF.

Similarly, overactive bladder (OAB) symptoms predicted tamsulosin (TAM) failure. Patients with OAB saw significantly higher failure rates, making OAB presence a potential monoparametric predictor for TAM. These findings suggest that considering AUR history and OAB symptoms individually can inform treatment choices for α -blocker. While these monoparametric insights are valuable, they may represent a simplified view.⁴

Sakalis and colleagues investigated whether detrusor overactivity (DO) predicts response to combination therapy (tamsulosin + solifenacin) versus monotherapy (tamsulosin) in men with benign prostatic enlargement (BPE) and storage LUTS.⁵ Their study randomized patients to either treatment for 26 weeks, with assessments including bladder diaries, International Prostate Symptom Score (IPSS), pressure-flow studies, and ultrasounds. Results strongly support the concept of DO as a predictive factor. The finding that baseline DO predicts a better response to combination therapy aligns with the development of predictive models. Urodynamic studies, although more invasive, provide objective evidence of DO. This information could be incorporated into a multiparametric model, alongside other clinical factors, to predict which patients with storage LUTS and BPE are most likely to benefit from combination therapy versus monotherapy. The ability to identify responders beforehand allows for more personalized treatment approaches, potentially improving patient outcomes and reducing unnecessary exposure to combination therapy in those less likely to benefit.⁵

A study by Simon and colleagues, using data from the REDUCE trial, included 3,090 men with mild-to-no LUTS (IPSS <8).⁶ The study found that men with a prostate size between 40.1 mL and 80 mL had a 67% higher risk of developing incident LUTS compared to men with a prostate size of 40 mL or less in the placebo group. However, this increased risk was not observed in men treated with dutasteride, suggesting that dutasteride may negate the effect of prostate size on LUTS development. The findings emphasize that prostate size is a significant predictor of new LUTS in men with mild-to-no symptoms, particularly in those not receiving dutasteride. Consequently, men with larger prostates and mild-to-no LUTS may benefit from closer monitoring for the progression of LUTS symptoms. Nonetheless, the study cautions against the routine use of prophylactic treatment with 5 α -reductase inhibitors (such as dutasteride), due to potential side effects and the high number of patients needed to treat to prevent the onset of incident LUTS.⁶

A study using data from the 4-year REDUCE trial followed 1534 men with mild-to-no LUTS at baseline to determine whether prostate-specific antigen (PSA) independently predicted incident LUTS. Results showed that higher PSA levels were associated with an increased risk of developing LUTS, even after adjusting for age, prostate volume, and baseline IPSS scores. Men with PSA levels of 6–10 ng/mL had a significantly higher risk of LUTS progression compared to those with PSA levels of 2.5–4 ng/mL. The findings suggest that PSA may serve as a useful biomarker for identifying men at higher risk of LUTS progression and could help guide early intervention strategies.⁷

Based on subjective parameter

The study by D'agate and colleagues evaluated the impact of immediate versus delayed initiation of tamsulosin-dutasteride combination therapy on symptom progression in patients with moderate-to-severe LUTS associated with benign prostatic hyperplasia (BPH).⁸ Using clinical trial simulations (CTS) based on data from 10,238 patients

across six phase 3/4 trials, the study compared immediate combination therapy with delayed initiation. The results showed that delayed initiation of combination therapy significantly reduced clinical response rates. The study concluded that early initiation of combination therapy provides greater long-term symptom improvement compared to delayed initiation, particularly in patients at risk of disease progression.⁸ A meta-analysis of existing data found that baseline IPSS, duration of symptoms, and alcohol use were significant covariates affecting IPSS trajectories. Immediate combination therapy with tamsulosin and dutasteride demonstrated a sustained reduction in disease progression. The meta-analyzed model also identified different phenotypes of disease progression, highlighting the variability in individual responses to treatment.⁹

Multiparametric models

Due to the inclusion of multiple parameters, multifactorial nomograms incorporate both objective and subjective evaluation criteria.

Mishriki and colleagues highlight the power of combining multiple parameters in predicting medical treatment failure for LUTS.¹⁰ Their central finding states that patients with worse baseline flow rates and bother scores were more likely to fail medical treatment for LUTS/BPH and require transurethral resection of the prostate (TURP). By integrating flow rate and symptom scores, clinicians gain a more comprehensive understanding of the patient's condition and can better predict long-term outcomes. This information can guide more informed treatment decisions, potentially reducing the need for unnecessary medical therapy in patients who are ultimately likely to require surgery. The ability to identify these individuals early allows for more timely intervention and potentially better patient outcomes.¹⁰

Kozminski and colleagues, using data from the MTOPS trial, developed a nomogram for predicting BPH progression, further illustrating the power of multiparametric models by combining multiple readily available clinical factors. Instead of relying on a single measure, the nomogram integrates age, symptom burden, impact on quality of life, and PSA level into a comprehensive risk assessment.¹¹ By calculating a total score and assigning patients to risk quartiles, the nomogram predicts the 4-year risk of BPH progression in patients who do not receive treatment.

The MTOPS nomogram highlights the advantages of multiparametric models. By considering the interplay of multiple factors, it provides a more nuanced and accurate prediction compared to single-parameter assessments. This facilitates personalized management, allowing clinicians to tailor treatment strategies based on individual risk profiles. The nomogram also empowers patients by providing a clearer understanding of their long-term prognosis and potential treatment benefits. While requiring some calculation, this nomogram demonstrates the practical applicability and clinical value of multiparametric models in optimizing LUTS management.¹¹

The Prostatic Inflammation Nomogram Study (PINS) aimed to develop a noninvasive method for predicting prostatic inflammation in men with LUTS, recognizing the limitations of relying solely on clinical symptoms.¹² The PINS nomogram exemplifies a multiparametric approach by combining readily available clinical data

(age, PSA, prostate volume) with specific LUTS-related information. This enables a more comprehensive assessment of the likelihood of prostatic inflammation compared to relying solely on individual parameters or symptom assessment.

The nomogram provides a probability of prostatic inflammation based on the summed points for each parameter. This noninvasive prediction can aid clinical decision-making. For instance, men with a higher probability of inflammation might benefit from specific anti-inflammatory therapies or closer monitoring, even without biopsy confirmation. The nomogram also helps stratify patients for research purposes, enabling targeted studies on the role of inflammation in the development and progression of LUTS.

The PINS nomogram showcases the power of multiparametric models in urological practice. By integrating multiple factors, it offers a more nuanced and potentially more accurate prediction of prostatic inflammation compared to traditional approaches. This facilitates personalized management, reducing reliance on invasive procedures, such as biopsies, in select cases. It also emphasizes the growing role of noninvasive predictive tools in optimizing patient care for LUTS and associated conditions.¹²

The study by Luciani and colleagues aimed to develop a predictive tool to identify patients at risk for pharmaceutical or surgical interventions for BPH-related LUTS over a 10-year follow-up.¹³ The study retrospectively analyzed 107 male patients with mild-to-moderate LUTS who were initially treated with phytotherapy. Two outcomes were evaluated: treatment switch from phytotherapy to α -blockers or 5 α -reductase inhibitor (5-ARI), and clinical progression (acute urinary retention or need for surgery). Key predictors for these outcomes included age, IPSS, maximum flow rate (Q_{max}), PSA, and post-void residual (PVR). The study proposed thresholds of > 75% and > 40% for high risk, and < 25% and < 5% for low risk of pharmaceutical or surgical interventions, respectively.¹³

An important predictive model was developed to predict treatment response in terms of IPSS and the risk of AUR or BPE-related surgery, based on large datasets and using as predictors baseline patient-specific factors such as prostate volume, IPSS scores, urinary flow rate, and post-void residual volume that commonly define the risk of disease progression.

Data from the CombAT trial and phase 3 dutasteride studies was used and generalized least squares models (for longitudinal IPSS) and a Cox proportional-hazards model for time to first AUR/surgery were developed.¹⁴ The nomogram could provide information on treatment responses (placebo, dutasteride, tamsulosin, or combination therapy) for different individual profiles. An interactive web-based tool (www.bphtool.com) was created to facilitate visualization of the estimated response to treatment (IPSS change from baseline and cumulative incidence of AUR or BPH-related surgery) for the selected combination of inputs that defines an individual profile.¹⁴

The researchers extended this work by developing similar models to predict the impact of treatments on different symptom types (storage, voiding, and nocturia), and quality of life (QoL) in men with prostate enlargement at risk of disease progression. The findings indicate that combination therapy (dutasteride + tamsulosin) provides

superior symptom relief and reduces the risk of acute urinary retention or surgery compared to monotherapy.¹⁵ The studies underlined the ability of predictive models to improve our understanding of how risk factors for disease progression interact and affect response to different treatments, reinforcing the importance of an individualized approach to LUTS/BPE management.^{14,15}

Hadi *et al.* used ML algorithms to develop a model that could predict the treatment response of OAB patients (men and women) to antimuscarinics and mirabegron based on training data from the FAITH registry.¹⁶ Treatment response to mirabegron or antimuscarinics was classified as “more effective” and “less effective” combining efficacy, persistence, and safety outcomes. Baseline overactive bladder symptom scores (OABSS), incontinence type, planned treatment, overactive bladder questionnaire (OABq) health-related QoL scores, and urgency were identified as the significant risk factors and were included in the final model. The final algorithm was integrated into an online application for intended use as an educational assessment tool.¹⁶

A multivariable linear regression model to predict the individual treatment response to mirabegron using patient baseline characteristics was developed analyzing data from eight global phase 2/3, double-blind, randomized, placebo- or active-controlled trials of mirabegron in adult patients (men and women) with OAB.¹⁷ Four baseline characteristics were notable as common predictive factors including the number of urgency episodes at baseline, prior OAB medication use, higher body mass index (BMI), and OAB symptom duration. It was concluded that the model could inform treatment decisions and help in setting realistic expectations for patients to support persistence and adherence, and ultimately treatment success.¹⁷

TABLE 1 provides a summary of key predictive models and nomograms used in optimizing medical therapy for male LUTS, highlighting their predictive factors, clinical applications, and treatment outcomes.

Predictive models—nomograms for patient outcome and success criteria

With the increasing emphasis on personalized medicine, the use of these predictive tools is gaining widespread acceptance. However, challenges remain, including the need for external validation, integration into electronic health records, and user-friendly implementation in routine clinical practice. Predictive models are not medical devices and are not intended either to substitute for medical advice or to dictate decisions. They can however contribute to inform healthcare professionals on personalized management of LUTS patients with different profiles and may be used during the discussion to support healthcare professionals and patients in making more personalized and data-driven decisions.

TABLE 1 Summary of Predictive Models and Nomograms for Optimizing Medical Therapy in Male LUTS

Model type	Study/Author	Key predictive factors	Outcome predicted	Clinical application
Monoparametric (Objective)	Kawachi <i>et al.</i> ⁴	AUR history, OAB symptoms	α -blocker (NAF/TAM) treatment success	Guides selection of α -blockers based on individual predictors
	Sakalis <i>et al.</i> ⁵	Detrusor overactivity (DO)	Response to combination therapy (tamsulosin + solifenacin)	Helps identify patients who benefit more from combination therapy
	Simon <i>et al.</i> ⁶	Prostate size (40.1–80 mL)	Risk of LUTS progression	Prostate size as a risk factor in LUTS development
	Patel <i>et al.</i> ⁷	PSA levels (6–10 ng/mL)	Incident LUTS risk	PSA as a biomarker for LUTS progression
Monoparametric (Subjective)	D'Agate <i>et al.</i> ⁹	IPSS, symptom duration, alcohol use	Impact of delayed combination therapy initiation	Supports early intervention in moderate-to-severe LUTS
Multiparametric	Mishriki <i>et al.</i> ¹⁰	Flow rate, symptom burden	Medical therapy failure, need for TURP	Identifies patients likely to require surgical intervention
	Kozminski <i>et al.</i> (MTOPS) ¹¹	Age, symptom burden, quality of life, PSA	BPH progression risk over 4 years	Provides comprehensive risk stratification for BPH progression
	Gravas <i>et al.</i> (PINS) ¹²	Age, PSA, prostate volume, LUTS factors	Prostatic inflammation probability	Reduces need for invasive procedures like biopsies
	Luciani <i>et al.</i> ¹³	Age, IPSS, $Q_{\max}$, PSA, PVR	Risk of pharmaceutical/surgical intervention	Identifies patients at high risk for treatment escalation
	Gravas <i>et al.</i> ¹⁴	Prostate volume, IPSS, urinary flow rate, PVR	Treatment outcomes for LUTS	Interactive web tool for personalized treatment selection
	Hadi <i>et al.</i> ¹⁶	Baseline OABSS, incontinence type, planned treatment, OABq HRQoL scores, and urgency	Treatment response to antimuscarinics and mirabegron	Educational or clinical decision-making aid
	Matta <i>et al.</i> ¹⁷	Baseline urgency episodes, prior OAB medication use, BMI, and OAB symptom duration	Treatment response to mirabegron	Informs treatment decisions and sets realistic expectations

Abbreviations: AUR, acute urinary retention; BMI, body mass index; BPH, benign prostatic hyperplasia; HRQoL, health-related quality of life; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms; NAF, naftopidil; OAB, overactive bladder; OABq, overactive bladder questionnaire; OABSS, overactive bladder symptom scores; PSA, prostate-specific antigen; PVR, post-void residual; $Q_{\max}$, maximum flow rate; TAM, tamsulosin; TURP, transurethral resection of the prostate.

Models and Nomograms for Invasive Therapy

All the available invasive therapies have been described and presented in [Chapter 4](#).

Given the prevalence of LUTS in our population, there is a wealth of research that goes into the various management options available, including randomized controlled trials (RCTs) and systematic reviews of prospective and retrospective cohort studies. Over the past decades, several prediction models and nomograms have been developed to predict functional outcomes and complications in patients undergoing invasive surgical procedures for benign prostatic obstruction (BPO). However, the majority of the models focus on the so-called “gold-standard treatment,” namely monopolar or bipolar TURP. There are only few predictive models for the other invasive therapies. This section will discuss the available nomograms for the different modalities, but it will also present the evidence regarding predictive factors in the absence of nomograms.

Transurethral resection of the prostate (TURP)

Predictive models for functional outcomes

Huang and colleagues conducted a prospective study with 182 patients to establish four predictive models for assessing functional recovery 6 months after TURP.¹ Recovery was evaluated based on changes in the IPSS, QoL, and $Q_{\max}$, with outcomes categorized as none, fair, good, or excellent. A favorable outcome was defined as achieving a “good” or “excellent” level. The most accurate model incorporated multiple variables: urge urinary incontinence (odds ratio [OR], 1.481; $P = .031$), IPSS storage score (OR, 2.576; $P = .041$), ratio of IPSS storage to voiding score (OR, 3.023; $P = .047$), ratio of transitional zone volume to total prostate volume (OR, 0.583; $P = .037$), resistive index (OR, 0.461; $P = .01$), bladder wall thickness (OR, 0.775; $P = .019$), ultrasonic estimation of bladder weight (OR, 0.281; $P = .024$), PdetQmax (OR, 0.352; $P = .035$), and bladder outlet obstruction index (BOOI) (OR, 0.199; $P = .016$). This model achieved an area under the curve (AUC) of 0.93, indicating excellent predictive performance.

In another study, DE Nunzio and colleagues defined a successful outcome as an increase in $Q_{\max}$ of at least 100% combined with a reduction in IPSS of at least 50% 3 months after monopolar TURP.² The authors’ multivariable regression analysis revealed that younger age (OR, 0.953; $P = .033$), higher preoperative IPSS scores (OR, 1.068; $P = .029$), and a high probability according to the previously developed and externally validated YAU nomogram for BOO prediction (OR, 1.063; $P = .001$) were associated with better functional outcomes. This prediction model demonstrated a moderate predictive accuracy with an AUC of 0.77.

Tian and colleagues introduced the P.R.OS.T.A.T.E. nomogram based on a retrospective analysis of 356 patients, with subsequent validation in 177 patients.³ In this model, treatment effectiveness was defined as achieving at least two postoperative improvements among IPSS, QoL, $Q_{\max}$, and prostate volume, rated as good or excellent at 6 months. Their analysis identified age (OR, 0.886; $P < .001$), IPSS (OR, 1.173; $P < .001$), intravesical prostatic

protrusion (IPP) (OR, 2.707; $P = .02$), bladder wall thickness (OR, 0.128; $P = .001$), peripheral zone thickness (OR, 0.516; $P = .037$), and transitional zone thickness (OR, 3.468; $P < .001$) as independent predictors. The nomogram achieved an AUC of 0.860 in the training cohort and 0.806 in the validation cohort.

Mourmouris *et al.*⁴ compared several ML algorithms to predict outcomes of transurethral surgery (bipolar vaporization, monopolar and bipolar TURP) in terms of percentage changes in IPSS and Q_{max} . They used baseline characteristics of 153 patients with age, prostate volume, method of operation, baseline Q_{max} , and baseline IPSS being identified as independent variables. It was found that a random forest model demonstrated the best performance, with correlation coefficients of 0.97 for the percentage increase in Q_{max} and 0.90 for the percentage decrease in IPSS.

More recently, a predictive model was developed by analyzing data from 250 patients who underwent TURP, 185 of whom had effective outcomes and 65 ineffective outcomes.⁵ Effectiveness was defined as a ratio of postoperative total IPSS (IPSS-T) to preoperative IPSS-T of 0.5 or less and a decrease in postoperative QoL score of 3 points or more. Univariate and multivariate analyses identified 6 independent predictive factors of surgical outcomes including IPSS-voiding/storage (IPSS-V/S) ratio, post-void residual urine ratio (PVR-R), disease duration, IPP, history of diabetes, and history of urinary retention. The AUC of the model was 0.894 and its sensitivity and specificity were 79.46% and 87.69%, respectively. Internal validation and the calibration curve indicated good agreement between the predicted and actual outcomes.⁵

Predictive models for complications and mortality

Urinary tract infections (UTIs) and bleeding are the most common complications after TURP. Lin and colleagues developed a nomogram to predict postoperative infections.⁶ Their multivariable model identified a positive preoperative urine culture (OR, 1.857; $P = .029$), longer operation time (OR, 2.319; $P = .016$), and a preoperative indwelling catheter duration exceeding 3 days (OR, 2.402; $P < .001$) as significant risk factors. Two nomograms were constructed: one including age, operation time, urinary bacterial load, catheter duration, and urine culture (AUC, 0.709), and another incorporating age, operation time, urinary bacterial load, and the presence of specific pathogens such as *E. faecium*, *K. pneumoniae*, or *P. aeruginosa* (AUC, 0.705).

For predicting postoperative bleeding requiring reoperation after monopolar TURP, Guo and colleagues identified BPH-related complications (including recurrent urinary retention, hematuria, UTIs, bladder stones, and upper urinary tract dilation with or without renal insufficiency; OR, 0.386; $P = .017$), the percentage of resected prostate tissue (OR, 0.156; $P = .047$), and prior suprapubic cystostomy (OR, 0.298; $P = .02$), with the nomogram yielding an AUC of 0.718.⁷

Lastly, Jeldres and colleagues established a nomogram to estimate 30-day postoperative mortality in a cohort of 7362 patients (mortality rate, 0.4%).⁸ Age (OR, 1.11; $P < .001$) and the Charlson Comorbidity Index (OR, 1.36; $P < .001$) emerged as independent predictors. The model was validated in a second cohort of 7362 patients, achieving an AUC of 0.83.

TABLE 2 provides an overview of the currently available prediction models and nomograms, along with their characteristics in this field.

Photoselective vaporization of the prostate (PVP)

To date, there are no prediction models or nomograms in the current literature that specifically predict outcomes for PVP. However, in a recent retrospective study published in 2024 by Zhou and colleagues, involving 426 patients who underwent either TURP or PVP (279 PVP, 147 TURP), a nomogram was developed to predict incomplete recovery (defined as IPSS > 10, QoL > 3, and a decrease in IPSS < 10 at 6 months postoperatively).⁹ The nomogram was created using data from 245 patients (157 PVP, 88 TURP). Age (OR, 1.07; $P < .001$), bladder compliance (OR, 2.37; $P < .001$), detrusor function (OR, 5.92; $P < .001$), and the severity of BOO (OR, 2.21; $P < .001$) were identified as independent predictors and incorporated into the model. This nomogram demonstrated an accuracy with an AUC of 0.83, and in the 181 patients (122 PVP, 59 TURP) used for validation, it achieved an AUC of 0.785.

Aquablation

Although no predictive models or nomograms currently exist for Aquablation, several studies have identified potential risk factors for both functional outcomes and complications using univariate analyses and descriptive statistics.

Plante and colleagues reported that men with an enlarged middle lobe, severe middle lobe obstruction, low baseline $Q_{\max}$, or elevated post-void residual (> 100 mL) experienced greater improvements in IPSS.¹⁰ In a retrospective study by Burton and colleagues, men without preoperative urinary retention were more likely to pass a void trial (93% vs. 60% in acute retention and 87% in chronic retention, $P < .001$) and had shorter mean times to spontaneous void (4 vs. 17 vs. 7.8 days, $P = .006$).¹¹

Regarding complications, Ringler and colleagues found that patients with prostates ≥ 150 mL had higher rates of serious adverse events (Clavien–Dindo grade III and IV: both 3% vs. 0.8%), greater retreatment rates (24.7% vs. 10.7%; $P = .043$), and a larger mean hemoglobin drop (2.45 vs. 1.54 g/dL; $P = .004$).¹² In a logistic regression model, Elterman and colleagues demonstrated that a larger postoperative hemoglobin drop was associated with larger prostates and the absence of cautery at the end of the procedure (all $P < .001$).¹³

Surgeon experience also appears to be a key factor: El Hajj and colleagues reported improved bleeding control (OR, 3.93) and better ejaculation preservation (OR, 4.69) after 20 to 30 cases.¹⁴ Furthermore, Nguyen and colleagues identified that penetration of the ejaculatory ducts (OR, 8.6; $P = .041$) and deeper resection below the verumontanum (OR, 1.92; $P = .015$) increased the likelihood of postoperative anejaculation.¹⁵

Enucleation techniques

This section is focused on the enucleation techniques for BPO including holmium laser enucleation of the prostate (HoLEP), thulium enucleation, bipolar enucleation of the prostate, diode laser enucleation, open prostatectomy (OP) and robotic-assisted simple prostatectomy (RASP).

Interestingly enough, there are only very few models to predict efficacy of the enucleation techniques. On the contrary, several publications have investigated possible risk factors for urinary incontinence (UI) and models have been constructed to predict postoperative UI. This can be explained by the fact that endoscopic enucleation of the prostate (EEP) is associated with a higher postoperative incontinence rate, particularly mixed incontinence compared to TURP.¹⁶ These predictive models on UI can be used to inform the individual patient about the risk of UI, set the expectations, and also identify patients who will benefit more from pelvic floor exercises and physiotherapy postoperatively resulting in optimization of available resources.

Lee *et al.* developed an artificial intelligence (AI) model to predict efficacy of HoLEP in terms of improvement in $Q_{\max}$ and voiding efficiency (VE) 1 month postoperatively. A dataset of 1142 patients assessed with urodynamic studies and treated with HoLEP was analyzed. The significant parameters for each one of the endpoints were reported to be: TRUS-prostate volume, serum PSA, uroflow PVR, uroflow $Q_{\max}$, and age (change in $Q_{\max}$), TRUS-transitional zone volume, serum PSA, age, IPSS voiding subscore, and uroflow PVR (change in VE). A deep neural network (DNN) for multiclass classification was employed. The improvement for each endpoint was categorized into 3 classes: for $Q_{\max}$, class I ranged from 0 to 15 mL/sec, class II from 15 to 20 mL/sec, and class III from 20 to 60 mL/sec; and for VE, class I ranged from 0 to 0.5, class II from 0.5 to 0.75, and class III from 0.75 to 1.0. For comparison, additional ML models such as extreme gradient boosting, random forest classification, and support vector machine were utilized. For the $Q_{\max}$ changes, the DNN achieved an AUC of 0.88, sensitivity of 0.78, and specificity of 0.89. For VE prediction, the AUC, sensitivity, and specificity were 0.82, 0.66, and 0.83, respectively. It was found that the DNN's predictive performance was superior to that of other ML models.¹⁷

A study evaluated the value of magnetic resonance imaging (MRI) and radiomics analysis in predicting the efficacy of bipolar transurethral enucleation of the prostate (B-TUEP). Good efficacy was defined as 2 or more indicators (IPSS, $Q_{\max}$, QoL) categorized as excellent or good; otherwise, efficacy was considered poor.¹⁸ Clinical and radiomic data from 137 patients who underwent B-TUEP were analyzed. Multivariate analysis identified $Q_{\max}$ and Transitional Zone Index (TZI) as independent predictors of short-term efficacy. The radiomics score was developed from 1702 radiomics features extracted from the prostate and transitional zone. Three prediction models were developed and validated based on clinical-radiological features, radiomic features, and their combinations. The combination model performed better, with an AUC of 0.838. Higher $Q_{\max}$, lower TZI, and higher radiomics score were associated with increased risk of poor efficacy. It appears that this model that combines clinical and radiomics features can assist urologists in making more individualized decisions.¹⁸ The main limitation of the study is that MRI is needed for all patients in order to predict the efficacy of B-TUEP in patients with enlarged prostates.

Smaller studies have investigated baseline characteristics of patients that can be used as factors to predict outcomes of surgical therapies without constructing a nomogram. In addition, these studies suffer from the small number of patients, the retrospective nature, the specific population, and the available parameters in the database. As an example, Watanabe *et al.* examined whether IPP, IPSS, IPSS-QoL, PVR, and the presence of OAB could classify patients treated with HoLEP in the poor or good therapeutic efficacy group. A multivariable analysis found that the preoperative presence of OAB and short IPP were independent risk factors for the poor therapeutic efficacy of HoLEP, but no prediction model was developed.¹⁹

Fong *et al.* constructed an ML model to predict postoperative UI after endoscopic enucleation with any source of energy.²⁰ In total 3828 patients from two endoscopic enucleation databases were analyzed. Energy sources included low-power holmium laser, high-power holmium laser, holmium laser with MOSES technology, thulium fiber laser, pulsed thulium-YAG laser, and bipolar and monopolar electrocautery. Six ML models were tested, and the extreme gradient boosting with manual fine-tuning (XGB) model was found to have the best performance, with an accuracy of 86.2%, sensitivity of 96.8%, specificity of 23.7%, PPV of 88.2%, and NPV of 55.9%. Several characteristics of the patients were examined and preoperative Q_{max} , prostate volume, age, preoperative PVR, and preoperative IPSS were ranked as the most important characteristics. The XGB model was ported onto a web interface and is available at <https://kyfong.shinyapps.io/glpmlshiny/>.

Similarly, another nomogram to predict early UI post-endoscopic enucleation was developed using data from 458 eligible patients from one institution who underwent either plasmakinetic or diode laser enucleation of the prostate.²¹ Univariate and multivariate logistic regression analyses identified the following independent predictive factors: 65 years $\leq$ age < 70 years, 75 years $\leq$ age, 25 kg/m² $\leq$ BMI < 30 kg/m², 30 kg/m² $\leq$ BMI, 5 years $\leq$ LUTS duration, and 75 mL $\leq$ prostate volume. The AUC was 0.764 and 0.775 in the training and validation sets, respectively, indicating satisfactory discrimination.²¹

TABLE 2 Overview of Available Prediction Models and Nomograms for Outcomes Following Transurethral Ablative, Non-Anatomical Procedures in Prostatic Bladder Outlet Obstruction

Author	Year	Type of surgery	Endpoint	Type of model	Included factors	Accuracy	Optimal cutoff	Sensitivity / Specificity	PPV / NPV	Validated
Jeldres <i>et al.</i> ⁸	2009	TURP	Mortality from any cause within 30 days postoperative	Nomogram	Age, Charlson Comorbidity Index	AUC, 0.83 (95% CI, not reported)	NA	NA	NA	Yes (external)
Huang <i>et al.</i> ¹	2015	TURP	Successful outcome at 6 months defined as excellent or good overall outcome in IPSS, QoL, Q _{max}	4 different prediction models	Urge urinary incontinence, IPSS storage score, IPSS storage / voiding ratio, transitional zone volume / total prostate volume ratio, resistive index, bladder wall thickness, ultrasonic estimation of bladder weight, PdetQmax, BOOI	AUC, 0.93 (95% CI, 0.89–0.96)	7.41 (ROC curve)	87.3% / 85.42%	94.4% / 75.6%	No
					Urinary tract infection, urge urinary incontinence, IPSS score, IPSS storage score, IPSS storage / voiding ratio	AUC, 0.69 (95% CI, 0.62–0.75)	6.11 (ROC curve)	69.4% / 64.6%	84.6% / 63.0%	
					Urge urinary incontinence, IPSS storage score, IPSS storage / voiding ratio, transitional zone volume, resistive index, bladder wall thickness, ultrasonic estimation of bladder weight	AUC, 0.79 (95% CI, 0.73–0.85)	7.09 (ROC curve)	84.3% / 75.0%	90.4% / 73.2%	
					Urge urinary incontinence, IPSS storage score, IPSS storage / voiding ratio, PdetQmax, BOOI	AUC, 0.83 (95% CI, 0.77–0.88)	5.84 (ROC curve)	81.3% / 83.3%	93.2% / 79.4%	
DE Nunzio <i>et al.</i> ³	2018	mTURP	Successful outcome at 3 months defined as a rise in Q _{max} of at least 100% and an IPSS reduction of at least 50%	Nomogram (geometrical figure not shown)	Age, IPSS, YAU nomogram probability	AUC, 0.77 (95% CI, 0.70–0.83)	75% (nomogram probability)	62% / 73%	81% / 52%	No
Guo <i>et al.</i> ⁷	2018	mTURP	Re-operation due to postoperative hemorrhage	Nomogram	BPH-related complications (<i>recurrent urinary retention, recurrent hematuria, recurrent UTI, bladder stones, and dilation of upper urinary tract with/without renal insufficiency</i>), percent of resected prostate, suprapubic cystostomy insertion for resection	AUC, 0.72 (95% CI, 0.62–0.82)	27% (nomogram probability)	60.5% / 81.5%	47.9% / 88.0%	No
Tian <i>et al.</i> ³	2022	TURP	Successful outcome at 6 months defined as excellent or good overall outcome in IPSS, QoL, Q _{max} , prostate volume reduction	Nomogram (P.R.O.S.T.A.T.E)	Age, IPSS, intravesical prostatic, bladder wall thickness, peripheral zone thickness, transitional zone thickness	AUC, 0.81 (95% CI, 0.73–0.88) (validation cohort)	177 (total nomogram score, validation cohort)	70.6% / 75.6% (validation cohort)	90.6% / 43.7% (validation cohort)	Yes (external)
Lin <i>et al.</i> ⁶	2023	TURP	Postoperative infection defined as positive blood culture or body temperature above 38.5 °C	Nomograms	<u>Two nomograms:</u> Age, operation time, amount of urine bacteria, preop indwelling catheter > 3 days, positive preoperative urine culture	0.71 (95% CI, 0.66–0.76)	NA	NA	NA	Yes (internal)
					Age, operation time, amount of urine bacteria, <i>E. faecium</i> , <i>K. pneumoniae</i> , <i>P. aeruginosa</i>	AUC, 0.71 (95% CI, 0.65–0.76)	NA	NA	NA	Yes (internal)
Zhou <i>et al.</i> ⁹	2024	TURP, PVP	Incomplete postoperative recovery at 6 months defined as IPSS > 10, IPSS decrease < 10, QoL > 3	Nomogram	Age, bladder compliance, detrusor function, bladder outlet obstruction (defined as BOOI > 40)	AUC, 0.79 (95% CI, 0.71–0.86) (validation cohort)	125.50 (total nomogram score, training cohort)	67% / 80%	NA	Yes (external)

Abbreviations: AUC, area under the curve; BPH, benign prostatic hyperplasia; BOOI, Bladder Outlet Obstruction Index; IPSS, International Prostate Symptom Score; NA, not available; NPV, negative predictive value; PdetQmax, detrusor pressure at maximum flow; PPV, positive predictive value; PVP, photoselective vaporization of the prostate; QoL, quality of life; Q_{max}, maximum urinary flow; ROC, receiver operating characteristic; TURP, transurethral resection of the prostate.

Models and Nomograms for Minimally Invasive Treatment

Many studies have evaluated the efficacy and safety profiles of different minimally invasive treatment (MIST) techniques, and several comparative studies between these modalities have been published. All the available MISTs have been described and are presented in [Chapter 5](#).

Many experts acknowledge that the precise indications for each MIST require careful consideration and that treatment outcomes vary significantly based on patient selection criteria. Therefore, predictive models could play a significant role in the shared decision-making process, as patients should be informed and be ready to accept that MISTs usually have lower efficacy and higher risk for retreatment compared to more invasive surgical options.

However, not all those therapies are at the same level of maturation and they are not supported by the same quality and volume of data. Some MISTs are rather new and “new,” by definition, implies the lack of high number of studies and long-term follow-up. In addition, the number of the patients in most of the studies is rather low. As a result, the literature is lacking predictive models for almost all the MISTs. This section will discuss the very few available predictive models for the different modalities, but it will also present the evidence regarding predictive factors in the absence of models.

Prostatic artery embolization (PAE)

A predictive model using ML was developed and internally validated to predict IPSS reduction 6 weeks post-PAE with n-Butyl Cyanoacrylate Liquid Embolic Agent using clinical and procedural tabular data. The model was able to perform binary classification, differentiating between favorable outcomes (IPSS reduction > 9) and unfavorable outcomes (IPSS reduction ≤ 9). The model achieved an accuracy of 0.676 (95% CI, 0.647–0.705), a precision of 0.666 (95% CI, 0.640–0.698) with an area under the precision–recall curve (AUPRC) of 0.851 (95% CI, 0.824–0.874) and an area under the receiver operating characteristic curve (AUROC) of 0.821 (95% CI, 0.790–0.848), reflecting excellent discriminatory ability. SHAP analysis identified pre-PAE IPSS, prior therapy, right embolization volume, preoperative quality of life, and age as the top five most influential features. The authors concluded that this study was rather a proof-of concept and cannot be considered as a clinically deployable decision-support system.¹

Zorzi *et al.* analyzed demographic, procedural, and clinical data of elderly, frail patients who were treated with PAE and applied univariate and multivariate regression models to identify potential factors that could predict clinical failure.² Clinical failure was defined as no improvement or worsening of symptoms based on IPSS at the follow-up evaluation. Almost one-third of the patients experienced clinical failure, which was significantly correlated with unilateral embolization. Multivariate regression analysis indicated that higher Charlson Comorbidity Index

(CCI), elevated PVR, and the use of larger microspheres ($\geq 300 \mu\text{m}$) were associated with unfavorable clinical outcomes, with odds ratios of 2.17 (95% CI, 1.4–3.38), 1.02 (95% CI, 1.01–1.03), and 26.83 (95% CI, 4.81–149.8), respectively ($P < .01$). Careful patient selection including consider factors such as CCI, and PVR, alongside with the technical aspects, seems to be able to optimize PAE outcome.²

Water vapor thermal therapy (WVTT)—Rezūm

A retrospective study on patients treated with Rezūm investigated several demographic and baseline parameters to identify predictors of achieving a minimal clinically important difference (MCID) at 3 months after treatment. MCID was defined as a $\geq 25\%$ improvement in IPSS. Potential predictors were evaluated through multivariate logistic regression analysis and only higher IPSS scores and larger prostate volumes were found to be independent predictors of achieving an MCID at 3 months.³ Each point increase in the baseline IPSS was associated with a 10% increase in the odds of achieving an MCID at 3 months (OR, 1.10; 95% CI, 1.04–1.17). Similarly, every 10-cc increase in baseline prostate volume was associated with a 30% increase in the odds of achieving an MCID at 3 months (OR, 1.03; 95% CI, 1.00–1.05). It was found that the optimal cutoff value for the two predictors was an IPSS ≥ 20 or a prostate volume ≥ 60 cc. Patients with moderate LUTS or smaller prostates were less likely to achieve MCID. Therefore, those patients may need to be counseled preoperatively on realistic expectations regarding LUTS improvements.

It is well known that patients treated with Rezūm are discharged with a Foley catheter to avoid acute urinary retention, and there is no consensus on the optimal length of catheterization, while up to 11% of patients will require recatheterization after the first trial without catheter (TWOC).⁴ Identification of predictors of TWOC failure would be very useful to offer individualized counseling to patients prior to Rezūm about the risk of recatheterization. A recent study analyzed age, imaging, number of injections, Q_{max} , PVR, IPSS, QoL, and adverse events at baseline and 3 months after treatment. Failed initial TWOC was defined as the incapacity to pass urine or measured PVR > 300 mL.⁵

Univariate logistic regression reported PVR, the number of injections per lateral lobe, and the number of total injections as predictors of failed TWOC. However, after multivariate logistic regression, preoperative PVR was the only independent risk factor predicting unsuccessful catheter removal after Rezūm (OR, 1.01; 95% CI, 1.00–1.01). On the other hand, the presence/treatment of a median lobe does not appear to increase this risk.⁵ This finding confirms the previous report that a baseline PVR of > 200 mL results in a larger proportion of patients who will fail TWOC compared to patients with a baseline PVR of < 200 mL and that patients with large PVR may require a catheter for an extended duration.⁴

Prostatic urethral lift (PUL)

A prospective, single-arm, multicenter study (PULSAR) evaluated the efficacy and safety of PUL in patients with AUR.⁶ Outcomes of PULSAR patients were compared with patients with AUR from the large real-world retrospective (RWRr) study of PUL and from the LIFT trial. Several factors were found to be associated with

PUL success in terms of spontaneous voiding. Logistic regression on combined PULSAR and RWRr data showed that younger patients < 70 years (mean responder age, 69.7; mean failure age, 72.7; OR, 2.04; $P < .01$) and shorter preprocedural catheter duration (mean responder duration, 53.2; mean failure catheter duration, 198.7; OR, 1.004; $P < .01$) predicted success. Higher bladder voiding efficacy (BE), though only measured in PULSAR, measured between postoperative days 3 to 7 (59%; mean failure voiding efficiency, 32%; OR, 1.02; $P = .02$) and as a continuous variable was a predictive factor of response to treatment in patients with AUR at 12 months post-PUL.⁶

Temporary implantable nitinol device (iTIND)

Similarly, another study investigated potential factors for predicting iTIND failure with a 2-year follow-up. A significant percentage of patients (58.33%) in the failure group had median lobes, which was found to be statistically significant. None of the other preoperative variables (age, prostate volume, IPSS scores, $Q_{\max}$, PVR, and PSA) could predict response to iTIND treatment.⁷

Clinical Utility

In the past decade, multiple options have emerged for the treatment of male LUTS. While medical treatment has remained almost unchanged and only a few alternative drug options—such as tadalafil and mirabegron—have entered the treatment cascade, interventional treatment has seen multiple new treatments competing with the established options. The challenge today is to identify the single best treatment option for the individual patient (personalized treatment) based on the principle of shared decision-making (SDM) while considering not only patient-specific clinical parameters but also the patient's expectations.

In past decades, the treatment cascade was outlined clearly. Once a patient became symptomatic, medical treatment was started. If complications arose or patients bother increased, primary ablative surgical therapy was the next logical step, and prostate volume was the major discriminator in deciding the type of treatment (TUR-P vs. open simple prostatectomy). Today, the challenge is completely different. Besides medical treatment, multiple MISTs and primary ablative surgical options are available and challenge the now historic treatment cascade.

Today, with the opportunity to provide each patient a personalized treatment that maximizes success and minimizes complications, independent nomograms are urgently needed to help urologists identify the optimal treatment option. The authors strongly believe that urologists must move beyond the rigid treatment cascade and instead offer patients the full range of available options whenever treatment advice is sought.

The optimal solution would be a single nomogram that integrates personal preferences, patient-specific parameters, and all treatment options—from medical therapy to MISTs to surgery—as outlined in international guidelines. Such a tool would provide one evidence-based recommendation for the best possible treatment, applicable to both treatment-naïve patients and those with prior interventions. Unfortunately, this nomogram does not yet

exist. There is no consensus on which patient-specific parameters, clinical tests, or personal preferences should be incorporated into decision-making.

Some success criteria exist for selecting medical therapy, but they are limited to α -blockers, 5-ARIs, and combination treatment, without accounting for newer options. As discussed above, both monoparametric and multiparametric approaches have been developed, focusing on patient-centered objective parameters. These may help urologists identify, for example, the most suitable α -blocker (Kawachi *et al.*),¹ the role of combination therapy in patients with detrusor overactivity (Sakalis *et al.*),² or when α -blocker and 5-ARI combination therapy is preferable to monotherapy (D'Agate *et al.*).³ Although helpful in daily practice, these success criteria apply only once the decision to initiate medical therapy has already been made. They do not account for patients' personal preferences or alternative treatment options—particularly MISTs—which may be considered as initial alternatives to medical therapy, even early in the treatment cascade.

As with medical management, no pretreatment nomogram exists to identify the most appropriate MIST or primary ablative intervention. Although several success criteria have been proposed for different treatment options, it remains unclear how treatment success should be defined and which pretreatment parameters must be assessed to support reliable recommendations. Unlike medical therapy, interventional outcomes are strongly influenced by the surgical learning curve and treatment availability—factors that have a major impact on both results and decision-making. Yet, these parameters have been largely ignored in the decision processes published to date.

The presence or absence of specific findings has been proposed as success criteria to predict treatment outcomes in interventional therapy. Anatomical considerations appear less relevant for primary ablative, non-anatomic techniques, such as TURP, PVP, or laser enucleation. The various factors used to predict outcomes with primary ablative techniques have been discussed in detail above (summarized in **TABLES 1 and 2**), highlighting a major limitation of these studies—the inconsistent definition of success, with 7 studies reporting 6 different endpoints. The only consensus is that all primary ablative surgical treatments improve bladder outlet obstruction, as confirmed by urodynamics. Ultimately, treatment choice still depends on availability and the experience of the operating center, which does not align with the principle of SDM or the goal of a pretreatment nomogram to identify the best management strategy before intervention.

In contrast to primary ablative techniques, several clinical findings have been identified that influence treatment success in MIST. Pretreatment—and even more importantly, preconsultation—identification of these parameters is crucial, as patient preference carries greater weight in the decision-making process for these treatment options. The available modalities and influencing parameters are discussed in detail above and in [Chapter 5](#), but it is important to note that prostate volume and anatomical factors—such as the presence, absence, and configuration of a median lobe, the degree of IPP, and potential bladder neck obstruction—affect treatment outcomes.

Today, a wide range of treatment options for male LUTS is available—from medical therapy to minimally invasive, anatomy-modulating, secondary ablative, and primary ablative surgical approaches—allowing us to offer personalized LUTS management. Each option carries its own advantages and risks, and to date, only limited

success criteria have been defined for individual treatments. Nonetheless, several clinical findings have been recognized as potential success criteria and may support clinical decision-making.

A single, objective, and independent pretreatment nomogram is still lacking. To develop a predictive “*one nomogram answers all questions tool*,” several steps must be undertaken:

1. Define objective diagnostic parameters that influence treatment outcomes.
2. Establish a clear definition of treatment success based on objective parameters.
3. Evaluate the outcomes of available treatment options using steps 1 and 2.
4. Integrate the results into a user-friendly electronic health record system.
5. Externally validate the findings through large-scale clinical use.
6. Apply the results in patient counseling (SDM) to optimize personalized treatment.

Implementing the steps outlined above highlights the challenges in developing the desired nomogram. Preclinical workups may be time-consuming and costly (e.g., urodynamics or MRI) and, in some cases, examiner dependent (e.g., ultrasound or cystoscopy), making them less pragmatic. Furthermore, the availability of treatment options and the surgical experience of the provider play a major role not only in shaping recommendations but also in influencing clinical outcomes and morbidity. To overcome these limitations, it may be necessary to establish specialized male LUTS centers that offer the full spectrum of treatment options delivered by dedicated, highly trained healthcare professionals. Alternatively, different centers could provide selected options, with patients migrating between them as needed.

Future Directions: AI, Biomarkers, and Beyond

Future research in predictive models and nomograms for male LUTS should prioritize external validation across diverse populations to enhance generalizability and clinical utility. Integration of these tools into electronic health records and the development of user-friendly interfaces will be essential for their adoption in routine clinical practice.

The future of predictive modeling in male LUTS is being reshaped by advancements in AI, novel biomarkers, multi-omic profiling, and real-world data integration. These innovations hold the promise of improving the accuracy, personalization, and clinical applicability of decision-support tools. This section outlines key emerging themes and strategic directions that are expected to define the next generation of predictive models and nomograms.

Artificial intelligence and machine learning

AI technologies—particularly machine learning (ML) and deep learning (DL)—are revolutionizing clinical prediction. These methods can identify complex, non-linear relationships among variables that may not be captured by traditional regression-based models. Applications in male LUTS include:

Application area	AI capabilities
Risk stratification	Predicts bladder outlet obstruction, treatment failure, postsurgical complications
Pattern recognition	Analyzes imaging, video urodynamics, wearable data
Real-time analytics	Updates predictions dynamically from live patient inputs

The development of federated learning models, where data are analyzed across institutions without centralizing sensitive patient information, may facilitate collaboration while preserving privacy.

Integration of biomarkers and multi-omic data

The inclusion of molecular data has the potential to significantly enhance predictive accuracy. Candidate approaches include:

Biomarker type	Predictive utility
Genomic markers	Stratifies drug metabolism and risk of progression
Proteomics/Metabolomics	Identifies inflammatory/fibrotic signatures
Urinary biomarkers	Provides noninvasive assessment of bladder outlet obstruction severity, inflammation

These biologically anchored parameters could complement traditional clinical variables and create truly individualized prediction models.

Patient-centered data and digital health integration

Patient-reported outcome measures (PROMs), digital voiding diaries, and mobile health apps offer valuable data streams for real-world modeling. Their inclusion can improve:

- **Patient stratification:** Differentiating patients based on symptom burden and QoL impacts.
- **Outcome prediction:** Mapping patient goals to treatment outcomes.
- **Adherence monitoring:** Identifying early warning signs of treatment failure or dissatisfaction.

Data infrastructure and model validation

The future success of predictive tools relies on not only model sophistication but also robust data pipelines. Key considerations include:

Component	Role in model ecosystem
Multinational data registries	Enables external validation across diverse populations
Standardized metrics	Aligns endpoints, definitions, and assessment tools
Transparent modeling	Builds trust through explainability and auditability
Health economic integration	Assesses cost-effectiveness and resource use implications

Ethical and Regulatory Considerations

As AI models enter clinical decision-making, governance frameworks must evolve to address:

- **Bias and fairness:** Ensuring model performance across age, ethnicity, and comorbidity subgroups.
- **Transparency and accountability:** Clarifying responsibility when AI tools inform medical decisions.
- **Regulatory approval:** Navigating emerging pathways for AI-assisted diagnostics under regulatory agencies.

Collaborations between clinicians, data scientists, ethicists, and regulators will be essential to embed these tools responsibly in routine care.

Conclusion

Predictive models and nomograms are powerful tools in clinical research and practice. Their application in male LUTS has the potential to improve diagnostic accuracy, enhance treatment planning, and ultimately lead to better patient outcomes. Aligning the use of predictive models and nomograms with the available guidelines promotes individualized patient care and supports shared decision-making in the management of male LUTS.

The integration of AI, novel biomarkers, and real-world patient data represents the next frontier in personalized LUTS management. These technologies offer the potential to transform static prediction into dynamic, adaptive decision-support systems. Future research should focus on building interoperable, validated, and patient-centered models that complement clinical judgment and enhance shared decision-making. As these tools mature, they will become indispensable in delivering precision care in male LUTS.

Statements and recommendations

Statement	Recommendation	LoE	GoR
Use of predictive models for individualized therapy	Validated predictive models and nomograms should be used to better inform patients and guide an evidence-based individualized management of male LUTS.	II	B
Stratification based on treatment response	Patients should be stratified based on their likelihood of response to different therapies, using only validated nomograms to optimize treatment selection and minimize unnecessary interventions.	II	B
Incorporation of monoparametric and multiparametric models	Clinicians may use both monoparametric (single-factor) and multiparametric (multi-factor) predictive models depending on the clinical scenario.	III	C

Abbreviations: GoR, Grade of Recommendation; LoE, Level of Evidence; LUTS, lower urinary tract symptoms.

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Models and Nomograms for Medical Therapy

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COMMITTEE

07

**MANAGING PATIENTS
WITH COMPLICATIONS
AND PERSISTENT
SYMPTOMS**

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Table of Contents

Introduction by <i>Enrico Finazzi Agrò, MD</i>	335
Epidemiology of Complications After BPO Surgery (Including MISTs)	335
Incontinence after BPO surgery by <i>Tufan Tarcan, MD</i>	335
Epidemiology and risk factors for SUI after BPO surgery	336
Treatment of SUI after BPO surgery	337
Other Complications After BPO Surgery by <i>Anastasios D. Asimakopoulos, MD</i>	341
Introduction	341
What mechanisms can BPH surgery cause sexual dysfunction (SD)?	341
Impact of the main BPH surgical treatments on sexual dysfunction	342
Transurethral incision of the prostate (TUIP)	342
Transurethral resection of the prostate (TURP)	342
Prostate enucleation/vaporization	343
Minimally invasive surgical therapies (MISTs)	344
What about orgasmic function after BPH-related surgery?	346
Conclusion	346
Persisting/de novo LUTS after BPO surgery (including MISTs)	348
Etiology of persisting/de novo LUTS by <i>Mikolaj Przydacz, MD</i>	348
Assessment of persisting/de novo LUTS by <i>Mikolaj Przydacz, MD</i>	349
Voiding symptoms	349
Storage symptoms	349
Management of persisting/de novo LUTS by <i>Mikolaj Przydacz, MD</i>	349
Short-term voiding symptoms	349
Short-term storage symptoms	350
Long-term voiding symptoms	350
Long-term storage symptoms	350
Conclusion	351
Medical therapy after BPO surgery by <i>Stephan Madersbacher, MD</i>	352
Prevalence of medical therapy after BPO surgery	352
Risk factors associated with LUTS-related pharmacotherapy after BPO surgery	352

Table of Contents

Reasons for the use of LUTS-related pharmacotherapy after BPO surgery	353
Conclusion	353
Surgical reintervention after BPO surgery by <i>Eleonora Rosato MD</i>	354
Introduction	354
Surgical treatment of urethral stricture after BPO surgery	355
Surgical treatment of incomplete prostate resection ore regrowing prostate adenoma	355
Prostatic artery embolization after MISTs surgery	356
Rezūm system after previous BPO surgery	356
HoLEP after BPO surgery	356
Conclusion by <i>Enrico Finazzi Agrò, MD</i>	358
References	360

Introduction

Surgery for treating benign prostatic obstruction (BPO) is intended to resolve lower urinary tract symptoms (LUTS), thus improving patients' quality of life (QoL).¹ For this reason, complications such as possible incontinence or a negative impact on sexual function, which may impair QoL in different but significant ways, are frustrating for both patients and surgeons.² In recent years, several minimally invasive treatments (MISTs) have been proposed to treat BPO, with the aim of reducing the risk of negative effects, particularly on sexual function, in comparison to standard treatments.² Similarly, the persistence of LUTS after surgery for BPO—whether due to the surgery itself or to other pathophysiological conditions—is related to a continuing impact on QoL, resulting in postoperative dissatisfaction of the patients and, at times, regret over having undergone the procedure.³

The aim of this chapter is to analyze complications and persistent LUTS after surgery for BPO, considering both standard treatments and newer MISTs. The goal is to provide data on the frequency, possible risk factors, and underlying pathophysiologies of these complications or persistent LUTS, thereby offering useful insights into the management of patients with such unfavorable outcomes.

Epidemiology of Complications After BPO Surgery (Including MISTs)

Incontinence after BPO surgery

Different types of urinary incontinence (UI) can be observed after BPO surgery, including stress UI (SUI), urgency UI (UUI), mixed UI, and overflow UI.⁴ Thus, UI after BPO surgery does not always indicate SUI or sphincteric injury, and it is mandatory to classify the type of UI through a thorough assessment. Urgency UI, which is not uncommon in the early postoperative period after catheter removal, is almost always transient.^{4,5} Preoperative detrusor overactivity-related UI may resolve in most patients after BPO surgery. Still, patients must be informed preoperatively that UUI may persist after BPO surgery in some patients. Persistent urgency or UUI may necessitate further treatment, but it should not be considered as a surgical complication.

Stress UI that was not present preoperatively may occur due to sphincteric weakening resulting from BPO surgery and is considered a surgical complication and an iatrogenic condition.^{4,5} *De novo* SUI after BPO surgery may be transient or persistent. Transient SUI typically resolves within 3 to 6 months postoperatively, whereas persistent SUI is defined as continuing beyond 6 months after BPO surgery.^{4,5}

The pathophysiology of transient or persistent SUI after BPO surgery is not yet fully understood. One hypothesis suggests that transient SUI may result from anatomical changes following enucleation and is influenced by the healing of the prostatic fossa after surgery.^{4,6} It is also associated with manipulation of the scope in front

of the striated sphincter area, and depends on prostate size, preoperative sphincter function, duration of the intervention, and surgical experience. Persistent SUI may be more related to definitive sphincter injury—that is, a purely iatrogenic cause—but can also result from preexisting very low sphincter function, severe bladder dysfunction, or a neurogenic background, all of which may worsen the condition postoperatively.

Epidemiology and risk factors for SUI after BPO surgery

Historical cohorts of transurethral resection of the prostate (TURP) and open prostatectomy (OP) cases have shown rates of 0% to 40% for short-term UI, respectively⁴. The European Association of Urology (EAU) guidelines report the prevalence of persistent UI after TURP to be 2.2%.¹

The type of surgery applied for treating BPO may influence the risk of SUI, which is attributed to direct external sphincter injury during surgery—a complication that frequently reflects the surgeon's level of experience.^{7,8} Interestingly, comparative data from randomized controlled trials (RCTs) evaluating the risk of UI after various types of surgical techniques for LUTS/BPO are scarce.⁹

A recent meta-analysis reported an overall UI rate of 8% after BPO surgery across all included studies, with high overall heterogeneity ($I^2 = 84\%$).¹⁰ The authors did not observe any significant change in the incidence of UI over the study period. Notably, the study did not include separate analyses of UI subtypes or specify the postoperative follow-up period for reporting UI due to considerable variability observed among the studies.

It is important to recognize that UI following BPO interventions significantly influences patients' QoL, with age identified as a significant risk factor.^{11,12} It is essential to determine a standardized reporting approach in future research to enhance our understanding of postoperative UI in the context of various BPO surgeries. Although the literature suggests a comparable UI rate among treatment modalities for BPO, there is a consistent trend toward symptom improvement over time.¹³ However, it should be noted that most patients undergo BPO surgery based on empirical assessment, typically relying on symptoms and non-invasive evaluation, without standardized urodynamic testing as recommended by the International Continence Society (ICS), including filling cystometry and pressure-flow study. Therefore, most patients with LUTS undergoing BPO surgery lack a definitive urodynamic diagnosis of BPO, making it difficult to evaluate the potential role of preoperative urodynamic parameters in the development of postoperative UI.

Certain preoperative factors have been associated with an increased risk of postoperative UI. For example, a retrospective multicenter study evaluating predictive factors for UI after holmium laser enucleation of prostate (HoLEP) in 2346 male patients reported UI in 14.5% of patients at 3 months and in 4.2% at 6 months postoperatively.¹⁴ The study identified the following predictors as being significantly associated with UI at 3 months after HoLEP: advanced age (> 70 years), elevated body mass index (BMI), preoperative urinary drainage, larger enucleated prostate weight, and limited surgeon experience (fewer than 40 cases). At 6 months, the significant risk factors for UI were found to be elevated BMI, increased whole gland volume, and a diagnosis of diabetes mellitus.

Different types of BPO surgery may be associated with diverse risks of postoperative UI. A recent study analyzed a national database of 274,808 patients who underwent surgery for male LUTS.¹⁵ The investigators found that 4% of patients experienced persistent UI. Multivariable analysis demonstrated that Holmium/Thulium laser enucleation of the prostate (HoLEP/ThuLEP) photoselective vaporization of the prostate (PVP), OP, and minimally invasive adenomectomy were associated with a significantly higher likelihood of UI compared to TURP. In contrast, procedures such as prostatic urethral lift (PUL), water vapor thermal therapy (Rezūm), robotic waterjet treatment (aquablation), and prostatic artery embolization (PAE) were associated with a lower likelihood of postoperative UI.¹⁵

Treatment of SUI after BPO surgery

Treatment of UI after BPO surgery starts with conservative management. According to a recent Cochrane review, there is a lack of high-certainty evidence regarding the use of conservative interventions for SUI following prostate surgery.¹⁶ Existing trials lack standardization regarding the pelvic floor muscle training (PFMT) technique, protocols for combining conservative treatments, outcome measures for assessing subjective and objective responses, QoL assessments, and reporting of adverse events.¹⁴ Still, PFMT is weakly recommended by the EAU guidelines or moderately recommended by the AUA guidelines as first-line treatment for SUI after BPO surgery.^{1,17}

The only medical treatment option for SUI after BPO surgery is duloxetine, a serotonin/norepinephrine reuptake inhibitor, which can be combined with PFMT. According to a recent review, duloxetine demonstrated good short-term cure and/or improvement in treating men with persistent SUI, as well as in reducing the time to achieve continence.¹⁸ However, some patients discontinue treatment due to adverse events. The overall certainty evidence is moderate to low, with heterogeneity across studies and methodological limitations. Therefore, the EAU guidelines have a weak recommendation for duloxetine and highlight the need for further studies to assess the long-term effectiveness of duloxetine.¹

There is consensus between the EAU and AUA guidelines that surgical interventions can be implemented when conservative options to treat SUI fail within 12 months of BPO surgery.^{1,17} However, the AUA guidelines further emphasize that surgery can be planned as early as 6 months after BPO surgery for patients with severe SUI and no improvement with conservative management. It is important to note that only a minority of patients with SUI after BPO surgery undergo surgical treatment. Indeed, nationwide series report surgical rates for SUI of around 0.5% after TURP and 0.3% after OP within 5 years of follow-up, suggesting that the actual rate of SUI might be much higher.¹⁹ In a recent study, Kim *et al.* reported significantly higher rates of surgery for SUI after HoLEP (0.31%) than after TURP (0.10%).²⁰

The surgical management of persistent SUI after BPO remains poorly studied, with most of the existing knowledge on male SUI management based on post-radical prostatectomy (PRP) SUI cases.^{4,5} Surgical options include bulking agents, adjustable or fixed male slings, peri-urethral balloons, and artificial urinary sphincters (AUSs). A thorough presurgical assessment is needed before deciding on any surgical intervention and should

include symptom and QoL assessment with validated instruments; physical examination including standing cough test; bladder diaries, particularly in the presence of other storage symptoms; pad testing to quantify UI; cystoscopy to rule out other pathologies; and noninvasive and invasive urodynamic studies to assess bladder-sphincter function.

While invasive urodynamic studies do not assess sphincteric function, they can reveal concomitant bladder dysfunction in up to 30% of cases, such as bladder noncompliance, detrusor overactivity (DO) and detrusor underactivity (DU).²¹ It should be kept in mind that this patient population is likely to develop bladder dysfunction secondary to long-lasting BPO, and its prevalence may be higher in elderly patients.

The choice of surgical treatment should be made after comprehensive patient counseling considering patient expectations and the pros and cons of the treatment options.

Bulking agents are the least invasive but also the least effective surgical options. A recent review reported significant variation in outcomes, with reported dry rates ranging from 0% and 83%. The evidence remained limited due to the relatively short follow-up in most studies.²² The EAU guidelines advocate the need for future studies in order to support recommendations for widespread use.⁴ Bulking agents appear to be more suitable for patients unfit for surgery or patients with mild SUI.

Male slings (fixed or adjustable) constitute an alternative to AUSs in patients with mild-to-moderate SUI. Unfortunately, data on male slings in the treatment of SUI after BPO surgery remain limited. Male slings carry the advantages of being less costly and less invasive compared to AUSs. Their success rates may be inferior to AUSs in severe SUI, especially in the long term and after radiotherapy. This limitation is particularly relevant in the management of SUI after radical prostatectomy (RP).

In retrospective, multicenter case series, 20 patients with SUI after TURP were treated with adjustable trans-obturator male system (ATOMS®) and followed up for a median of 38.5 months.²³ The satisfaction rate was 80%, with no patient having urinary retention after catheter removal. Complications occurred in 3 patients (15%), all of which were minor, and no urethral erosion was observed—even in 5 patients who had previous pelvic radiation. The authors proposed ATOMS as an alternative that may be especially suitable for patients with diminished dexterity, advanced age, and previous failed treatments.

A recent, retrospective, multicenter study assessed the results of ATOMS in 40 patients with SUI after TURP or HoLEP.²⁴ After device adjustment, 80% of patients were dry and total continence was achieved in 45%. After a median follow-up of 32.5 months, postoperative complications occurred in 7 patients (17.5%) and 2 devices were removed (5%, both after HoLEP).

Another retrospective, multicenter study investigated the outcomes and complications of adjustable continence therapy (ProACT™) for UI after TURP in 29 patients.²⁵ At last visit (median 21 months after implantation), continence had improved in 76% of patients, including 45% who were dry. The reintervention rate was 24%.

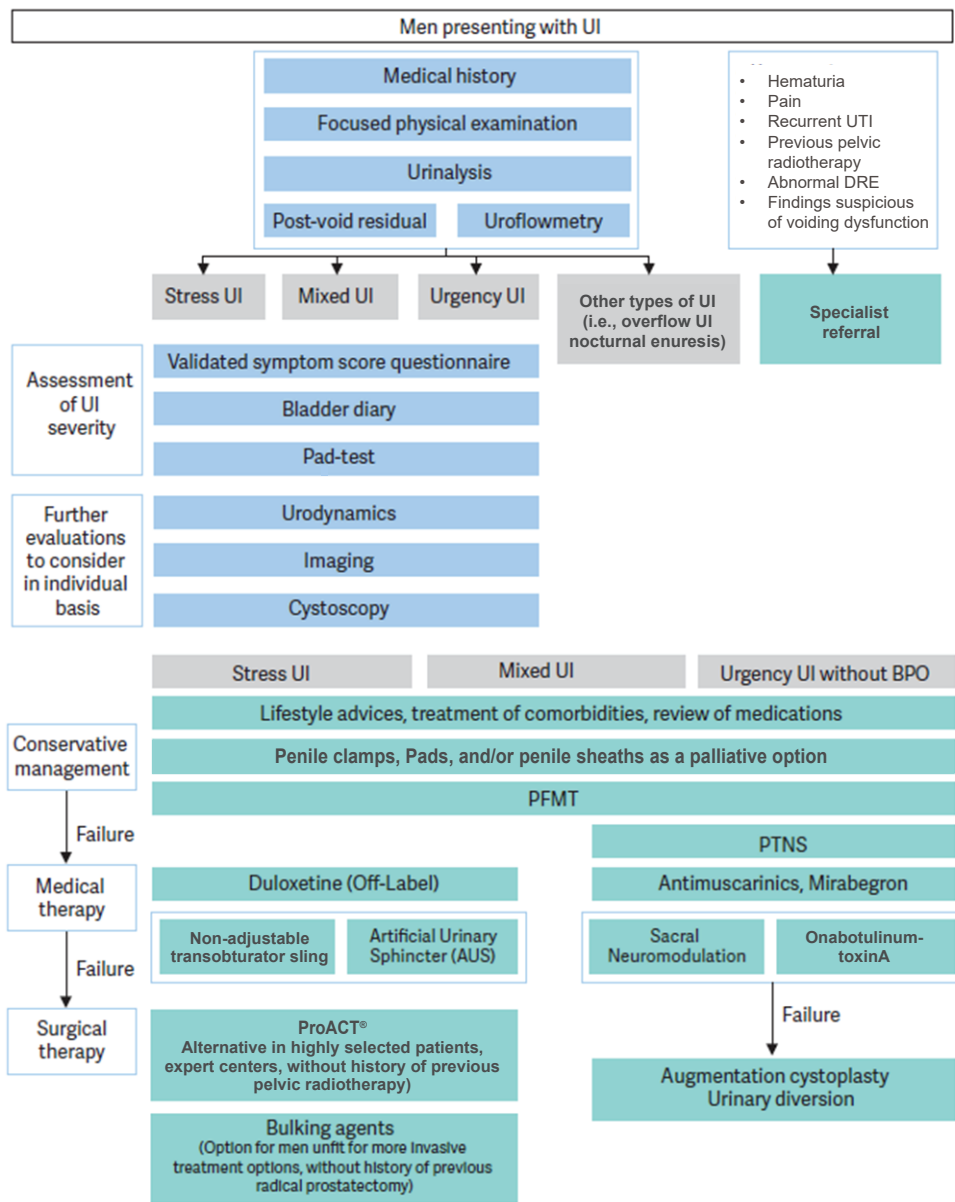
AUS is considered the gold standard for treating severe SUI after RP.^{17,26} Although there is limited evidence about the efficacy of AUS after BPO surgery, it may be reasonable to expect the same success.^{17,26} However, AUSs are also the most invasive option with well-known risks of infection, explantation, erosion, and mechanical dysfunction, all of which need to be discussed during preoperative patient counseling.

TABLE 1 Evidence and Recommendation of Urinary Incontinence (UI) After BPO Surgery

Topic	Recommendation	LoE	GoR
Advanced age, elevated BMI, preoperative UI, larger enucleated prostate weight, limited surgeon experience, and diabetes are reported to predict the risk of UI after BPO surgery.	Thorough evaluation to classify UI type (SUI, UUI, mixed, overflow). Do not assume SUI in all cases.	II	B
	Do not consider persistent UUI following BPO surgery to be a surgical complication.	II	B
	Persistent <i>de novo</i> SUI after BPO surgery should be considered as an iatrogenic condition caused by the sphincteric damage during surgery.	II	B
The first-line management of SUI after BPO surgery includes conservative treatment options.	Persistent SUI after BPO surgery mandates thorough assessment including ICS standard urodynamic testing before surgical treatment options are applied.	III	C
	Conservative treatment should be trailed up to 6–12 months before surgery (persistent SUI).	I Ib	C
	PFMT as first-line for SUI after BPO surgery.	III	C
	Duloxetine may be considered as adjunct to PFMT in men with persistent SUI.	III	C
The postoperative UI risk of different surgical options to treat BPO are to be clarified by further studies. There is limited evidence regarding the choice of several surgical options to treat SUI after BPO surgery.	Surgery may be considered after 6–12 months of failed conservative therapy.	IIa	B
	Surgical treatment should follow thorough assessment (QoL, cystoscopy, urodynamics).	II	B
	AUS is the gold standard for severe SUI, despite limited data in post-BPO setting.	III	C
	ProACT system shows moderate improvement, but reintervention risk is notable.	III	C
	Adjustable/fixed male slings can be considered for mild-moderate SUI.	III	C
	Bulking agents are least invasive but have variable and often poor results.	IV	D

Abbreviations: AUS, artificial urinary sphincter; BMI, body mass index; BPO, bladder outlet obstruction; DRE digital rectal examination; GoR, Grade of Recommendation; ICS, International Continence Society; LoE, Level of Evidence; PFMT, pelvic floor muscle training; ProACT, adjustable continence therapy; PTNS, percutaneous tibial nerve stimulation; QoL, quality of life; SUI, stress urinary incontinence; UI, urinary incontinence; UTI, urinary tract infection; UUI, urgency urinary incontinence.

FIGURE 1 Management of UI post-BPO surgery.



Abbreviations: BPO, bladder outlet obstruction; DRE digital rectal examination; PFMT, pelvic floor muscle training; ProACT, adjustable continence therapy; PTNS, percutaneous tibial nerve stimulation; UI, urinary incontinence, UTI, urinary tract infection.

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Other Complications After BPO Surgery

Introduction

The triple goal of BPO surgery is to alleviate bothersome LUTS, prevent disease progression, and avoid complications such as acute urinary retention.²⁷ When lifestyle changes, pharmacologic therapies, or nonsurgical interventions fail to improve symptoms or prevent progression, surgical therapies—such as transurethral surgery, simple prostatectomy, and minimally invasive surgical therapies (MISTs)—enter the discussion.²⁷

The choice of surgical treatment for a specific patient depends on several factors but is mainly guided by prostate volume, bleeding risk, and the patient's willingness to preserve erectile/ejaculatory function (EF/EjF).²⁷ Although data on sexual side effects from BPH surgery can be difficult to ascertain—as many studies are not designed to assess them specifically—patients today are increasingly aware that any surgical treatment may cause ejaculatory dysfunction (EjD), contribute to or worsen erectile dysfunction (ED), and potentially affect libido.^{27–31} One of the main concerns is that sexual side effects from surgical treatments are more likely to be permanent than those from medical treatments.

The aim of this section of the chapter is to provide an overview of the interplay between the main surgical treatments for BPH and their effects on sexual function.

What mechanisms can BPH surgery cause sexual dysfunction (SD)?

Male sexual function consists of different domains: sexual desire, EF, orgasmic function, EjF, and sexual satisfaction.³² However, with the exception of ED and EjD, there is a paucity of data in the literature concerning the other domains. Thus, the term SD in the context of BPH surgery typically refers to only ejaculatory and erectile dysfunction.²⁹ EjD in turn includes premature, retrograde, delayed, and painful ejaculation, and decreased force of ejaculation.³³

The mechanism of ejaculatory volume loss or reduction in BPH surgery is not fully understood. The term retrograde ejaculation is often used inaccurately. To date, there is no evidence to suggest that the observed effect is retrograde ejaculation rather than anejaculation.³⁴

Traditionally, surgical dogma has emphasized bladder neck closure to preserve male EjF. However, since cervical incision alone does not lead to loss of antegrade ejaculation, other explanations have been sought.^{32,34} Current perspectives and recent pelvic imaging research during ejaculation have shifted toward the importance of conserving the pericollicular tissue surrounding the veru montanum.³⁴ Anatomical studies have demonstrated that the ejaculatory ducts can be preserved with approximately 90% accuracy when a block of tissue 7.5 mm from the midline on either side of the veru montanum is preserved, coupled with up to 10 mm tissue proximal to the verumontanum (ejaculatory hood-sparing).^{35,36}

The development of ED after BPH surgery also lacks a clear explanation. The most concerning hypothesis involves thermal damage to the vascular-nervous bands that run along the prostate. It is also recognized that changes in ejaculation may have a negative effect on erection, orgasm, and overall sexual satisfaction.³²

On the other hand, improvements in urinary symptoms after BPH surgery may have a positive effect on sexual well-being, especially due to the discontinuation of drug treatments with adverse sexual effects.³⁷

Figure 2 summarizes the main mechanisms that may affect sexual function after surgery for BPH.

FIGURE 2 Main mechanisms that may affect sexual function after surgery for BPH.

Impact of surgical treatment for BPH on sexual satisfaction	
Beneficial impact	Negative impact
• Improvement of urinary function—alleviation of LUTS • Improvement of ejaculatory pain • Discontinuation of BPH medications	• Internal urinary sphincter injury—loss of antegrade ejaculation • <i>De novo</i> ejaculatory pain • Thermal effect on neurovascular bundles • Catheterization • Psychological impact of surgery, emotional trauma

Abbreviations: BPH, benign prostatic hyperplasia; LUTS, lower urinary tract symptoms.

Impact of the main BPH surgical treatments on sexual dysfunction

Transurethral incision of the prostate (TUIP)

A recent literature review reported a rate of so-called retrograde ejaculation of 21% after TUIP,³⁸ indicating that the technique offers a good likelihood of preserving ejaculation.

Transurethral resection of the prostate (TURP)

TURP remains the gold standard technique for surgical treatment of clinical BPH in prostates ranging between 30 mL to 80 mL with BPO. However, the impact of TURP on ED/EjD remains controversial and conflicting across studies.

Studies indicate an incidence rate of 62% to 75% for EjD and a 4% to 35% chance of developing ED after TURP.^{28,39–41} In addition to surgical factors, patient-related factors should also be considered. Patients with more severe LUTS at baseline, higher age, and those with lower preoperative nocturnal penile tumescence⁴¹ or metabolic syndrome⁴² had a higher likelihood of developing ED after TURP. Interestingly, more extensive TURP can also

lead to a higher incidence of ED and EjD in BPH patients without preoperative sexual dysfunction.⁴³ Patients with a lower seminal vesicle volume also appear to have a higher incidence of premature ejaculation after TURP.⁴³

However, other authors documented a significant improvement in EF in patients with preoperative ED undergoing TURP. In a recent review, Soans *et al.* reported a post-TURP EF improvement in 7 of 16 studies.³⁷ In a survey of 988 patients, Muntener *et al.* found a significant deterioration in EjF but noted a (nonsignificant) improvement in ejaculatory pain and EF.⁴⁴ In a study by Poulakis *et al.* including 500 patients, ED improvement was observed in 12% of patients after TURP.⁴⁵ Intraoperative capsular perforation and diabetes mellitus were highlighted as crucial factors contributing to postoperative EF deterioration. In another study, Favilla *et al.* identified age as the only statistically significant risk factor for ED following TURP, with higher ED rates observed for patients over 65 years old.⁴⁶

The impact of bipolar resection on SD has been compared to monopolar TURP in a few RCTs. Mamoukalis *et al.* randomized 279 men to either resection technique and found no significant difference in postoperative sexual function, with similar rates of both EF improvement and deterioration.⁴⁷ Similarly, in their RCTs, El-Assmy *et al.* reported no differences between monopolar and bipolar TURP across any aspect of sexual function.⁴⁸ A comprehensive meta-analysis showed similar levels of 12-month EF, as measured by the International Index of Erectile Function (IIEF-5), for both monopolar and bipolar TURP.⁴⁹

Prostate enucleation/vaporization

Recent studies consistently report a high incidence of EjD, particularly retrograde ejaculation, following HoLEP, with rates ranging from 70% to over 90%, depending on the technique used and the extent of tissue removal. On the other hand, EF is often unaffected. In a review of eight RCTs, Friebe *et al.* found that decreased EF was reported by 7.5% of patients after HoLEP and 7.7% patients after TURP.⁵⁰ Interestingly, 7.1% and 6.2% (range, 0%–19%) of patients after HoLEP and TURP, respectively, reported increased EF. Retrograde ejaculation was equally common after HoLEP (50%–96%) and TURP (50%–86%).

A Danish study involving 108 HoLEP patients reported that 70% had retrograde ejaculation at 6 months postoperatively, but the incidence of early morning erections increased from 45% to 62%.⁵¹ The study found that HoLEP did not significantly affect libido, erections, or sexual satisfaction. In a retrospective study of 346 patients who underwent HoLEP between November 2018 and February 2022, Roper *et al.* assessed sexual function using the Male Sexual Health Questionnaire–Ejaculatory Dysfunction (MSHQ-EjD) and the International Index of Erectile Function (IIEF-5).⁵² The authors found a significant decline in EjF postoperatively but no significant change in EF. Notably, patients did not report increased bother from the decline in EjF.⁵² A recent meta-analysis involving 10 articles with a total of 1435 patients investigated the impact of endoscopic enucleation of the prostate (EEP) versus TURP on EF and ejaculation. The EEP group showed higher IIEF-5 scores than the TURP group at both 48 months and ≥ 60 months. Additionally, no significant difference in retrograde ejaculation rate was found between EEP and TURP.⁵³

Emerging surgical techniques, such as selective median lobe enucleation or ejaculatory hood-sparing HOLEP, show promise in preserving EjF.^{30,54}

Photoselective vaporization of the prostate (PVP), particularly using GreenLight laser technology, has been associated with varying rates of EjD, with retrograde ejaculation incidence rates ranging from approximately 30% to 67%, depending on laser power and technique.^{55–57} In an RCT, Abolazm *et al.* compared the EjF and EF between standard prostate photoselective vaporization (24 patients) and ejaculatory hood-sparing vaporization (25 patients).⁵⁸ Antegrade ejaculation was reported in 85% of patients after hood sparing and in 31.6% of patients after standard prostate vaporization ($P = .001$). While both groups showed a decline in mean total IIEF-15 scores at 1 year, this was statistically significant only in the standard vaporization group ($P = .001$). All urinary outcomes showed a comparable significant improvement at all follow-up times. The authors concluded that hood-sparing GreenLight prostate photoselective vaporization is associated with superior sexual function outcomes while providing short-term symptom relief from obstruction comparable to that of standard prostate photoselective vaporization.⁵⁸

Minimally invasive surgical therapies (MISTs)

In the early days of less invasive treatment options—such as transurethral needle ablation and microwave thermotherapy—the target population was often represented by older patients who were unfit for conventional surgery. Today, however, a growing number of younger men are turning to MISTs, seeking to avoid standard surgical procedures that typically require general anesthesia, involve longer recovery times, and carry a considerable risk of sexual side effects.²

Transurethral microwave therapy (TUMT) and transurethral needle ablation (TUNA) of the prostate are not commonly used in contemporary practice and have been replaced by newer MISTs, such as UroLift, Rezūm, aquablation, prostate artery embolization, iTIND, and Optilume BPH.²

Prostate urethral lift (PUL)

PUL implants work by retracting the anterolateral lobes of the prostate toward the prostate capsule, thereby opening the urethral lumen. In an RCT published by Roehrborn *et al.*, 206 patients were randomized to receive either PUL or a sham procedure and were followed using patient-reported outcome measures (PROMs) for 5 years.⁵⁹ Within the treatment group, the authors documented statistically significant increases in IIEF-5 scores at 3, 6, and 24 months, compared to baseline, with concomitant improvement in EjF from baseline to 48 months and a decrease in ejaculatory bother scores from baseline to 60 months. In another RCT comparing PUL to TURP, EF remained stable in both treatment arms; however, ejaculation was preserved in 100% of the PUL group, compared to only 66% in the TURP group 2 years.⁶⁰ Small retrospective studies also confirm the finding that PUL is not associated with ED or EjD.^{61,62}

At present, PUL is the only surgical procedure for which the AUA and EAU guidelines on BPH include a specific recommendation regarding sexual function.^{1,17}

Prostatic artery embolization (PAE)

PAE consists of radiological embolization of arteries irrigating the prostate. Although promising, the technique remains investigational, to fully ascertain its long term effects. Carnevale *et al.* published a randomized study in 2016 comparing PAE to TURP.⁶³ At 1 year, a significant decrease in IIEF5 score was observed in the TURP group

but not in the PAE group. A reduction in ejaculation volume was reported in 10% of PAE cases compared to 100% of TURP cases. Multiple other investigations have reported an increase in IIEF scores following PAE, with no documented cases of new-onset ED.^{64–66} Overall, very little data is available to draw definitive conclusions about the sexual consequences of PAE.

Water vapor thermal therapy (Rezūm)

The Rezūm system involves delivering water vapor through endoscopically inserted intraprostatic needles. The system uses water vapor to effect cell necrosis and has shown promising outcomes in treating LUTS while preserving sexual function. In 2016, Roehrborn *et al.* published a prospective study of 130 patients with a 3-year follow-up.⁶⁷ EF, assessed using the IIEF, and EjF, assessed using the MSHQ-EjD, both remained stable at 3 years. Mcvary *et al.* evaluated the long-term impact of Rezūm on erectile function and EjF in 197 patients who were randomized in a 2:1 ratio to Rezūm or a sham procedure (136 treated, 61 sham) and followed for 5 years.⁶⁸ Sexual function was assessed using the IIEF-EF and MSHQ-EjD. The authors found no clinically relevant impact of Rezūm in ED and EjD. These findings were also confirmed by a first systematic review evaluating the safety and effectiveness of Rezūm in men with large prostate volumes ($\geq 80 \text{ cm}^3$).⁶⁹ Overall, the Rezūm system demonstrates long-lasting and prompt alleviation of LUTS with limited and transient effects on sexual function.

Aquablation

Aquablation (AQUABEAM System, PROCEPT BioRobotics Corporation, Redwood Shores, California, USA) is an ultrasound-guided, automated prostatic vaporization technique using a high-pressure water jet to ablate prostate tissue. The operator identifies the area to be vaporized under ultrasound guidance, which theoretically preserves supramontanal tissue to preserve ejaculation. The technique is supposed to prevent heat diffusion, and therefore theoretically prevent thermal damage to the neurovascular bundles. Gilling *et al.* reported the results from the randomized WATER versus TURP study for prostates between 30 cm^3 and 80 cm^3 .⁷⁰ No cases of ED were reported. Anejaculation occurred in 10% patients after Aquablation versus 36% after TURP ($P = .003$). The WATER II trial, a prospective, multicenter, single-arm, international clinical trial, explored Aquablation outcomes in patients with prostate volumes between 80 cm^3 and 150 cm^3 .⁷¹ The study found that mean IIEF-5 scores remained stable from baseline to 12 months, and no patient reported new-onset ED. The rate of preserved antegrade ejaculation in WATER II was slightly lower—81% in WATER II compared to 90% in WATER I for smaller prostates.

Initial findings from the WATER III trial were presented at the 2025 European Association of Urology (EAU) Congress in Madrid. The multicenter trial enrolled 202 men with prostates between 80 cm^3 and 180 cm^3 and randomized 98 participants to Aquablation and 88 to holmium/thulium laser surgery (HoLEP/ThuLEP).⁷² At 3-month follow-up, retrograde ejaculation occurred in 15% of Aquablation patients versus 77% in the laser group ($P < .001$). Among sexually active participants ($n = 89$), Aquablation patients reported higher satisfaction, with 85% maintaining antegrade ejaculation.⁷²

iTIND/Optilume BPH

The temporary implantable nitinol device (iTIND) is a minimally invasive treatment for BPO, designed to relieve LUTS by reshaping the prostatic urethra without removing tissue. Clinical studies have demonstrated

that iTIND effectively preserves sexual function, including ejaculation. Elterman *et al.* performed a multicenter, randomized, single-blinded, sham-controlled trial to assess the impact of iTIND on sexual function.⁷³ A total of 185 men with BPH (mean age, 61.1 years) were randomized 2:1 to receive either the iTIND implant or a sham procedure. Sexual function was evaluated using the Sexual Health Inventory for Men (SHIM) and the IIEF at baseline, and at 3 months and 12 months post-procedure. No significant changes in SHIM or IIEF scores were observed at 3 or 12 months compared to baseline, indicating preservation of EF and EjF. Men without baseline ED showed an improvement in total IIEF score of $+6.07 \pm 21.17$ points at 12 months ($P = .034$), suggesting potential enhancement in sexual function. No cases of treatment-related *de novo* ED or EjD were reported.

These preliminary data may support the use of iTIND as a treatment option for BPH patients concerned about maintaining sexual function.

Optilume BPH Catheter System is a relatively new minimally invasive treatment for BPO that combines balloon dilation of the prostatic urethra with localized delivery of paclitaxel, a drug that helps prevent tissue regrowth and avoid restenosis. The PINNACLE is a pivotal study evaluating the efficacy of Optilume BPH in alleviating LUTS and its impact on sexual function. In this 2:1 randomized trial, a total of 148 participants (100 Optilume vs. 48 sham) across 18 centers in the United States and Canada were enrolled. The study demonstrated sustained 2-year improvements in symptom relief and urinary flow, with no significant changes in EF or EjF, as measured by IIEF and MSHQ-EjD questionnaires.⁷⁴

What about orgasmic function after BPH-related surgery?

While postoperative sexual dysfunction has been widely studied in terms of EjD, less attention has been paid to the impact of surgery on orgasmic sensation. Bouchet *et al.* recently evaluated this outcome by comparing the results of question 10 of the IIEF-15 questionnaire before and after surgery in 104 patients.⁷⁵ According to the authors, orgasmic function remained stable in 34% of patients, improved in 30% of patients, and worsened in 36% of patients. Notably, patients who maintained good ejaculation force before surgery were at greater risk of experiencing impaired orgasm postoperatively. Thus, appropriate patient counseling should also include the potential adverse effects on orgasmic functions.

Conclusion

The management of BPO has evolved into a more complex, patient-centered endeavor, where preserving ejaculatory function is as critical as relieving urinary symptoms. At present, PUL remains the only surgical procedure for which there is a clear recommendation regarding sexual function in the AUA/EAU guidelines on BPH. However, other MISTs—such as UroLift, iTIND, Rezūm, and Aquablation—and the implementation of ejaculatory hood-sparing techniques in settings where MISTs are unavailable offer urologists an additional toolkit to meet patients' needs. Given the current availability of BPH treatment options that improve the likelihood of preserving ejaculation, it is imperative that men receive thorough counseling and are offered individualized therapy.

TABLE 2 Sexual Dysfunction After Surgical Treatments for BPO

Topic	Recommendation	LoE	GoR
BPO surgery and sexual dysfunction	Inform patients that BPO surgery may impact sexual function, particularly ejaculation.	I	A
	Provide thorough preoperative counseling regarding the potential impact of BPO surgery on all domains of sexual function.	I	A
	Inform patients that orgasmic function may improve, remain stable, or worsen after BPO surgery; worsening is more likely in patients with strong baseline EjF.	I	A
TUIP	Consider TUIP as a technique with a relatively low risk of ejaculatory dysfunction (~21%).	IIa	B
TURP	Inform patients undergoing TURP of the high risk of ejaculatory dysfunction (62%–75%) and the variable risk of erectile dysfunction (4%–35%).	I	A
	Be aware that risk factors for postoperative ED after TURP include age, LUTS severity, diabetes, and metabolic syndrome.	II	B
	Do not expect significant differences in sexual outcomes between monopolar and bipolar TURP.	I	A
HoLEP	Inform patients that HoLEP is associated with a high rate of ejaculatory dysfunction (70%–96%) but generally preserves erectile function.	I	A
	Consider ejaculatory hood-sparing HoLEP in sexually active men wishing to preserve ejaculation.	II	B
Greenlight PVP	Inform patients that GreenLight PVP results in variable rates of ejaculatory dysfunction (30%–67%), depending on laser settings and technique.	II	B
	Consider hood-sparing PVP to improve ejaculatory outcomes without compromising functional results.	II	B
Aquablation	Consider Aquablation as an option with low risk of anejaculation (10%–15%) and preserved erectile function.	I	A
Optilume	Consider Optilume for men wishing to maintain sexual function, as no significant changes in EF or EjF have been reported.	I	A
MISTs	Offer PUL to patients prioritizing sexual function preservation, as both erectile and ejaculatory functions are well preserved.	I	A
	Consider PAE in selected patients concerned about sexual side effects; available data show preserved EF and low rates of EjD.	III	C
	Inform patients that Rezūm is associated with stable erectile and ejaculatory function up to 5 years after treatment.	II	B
	Consider iTIND in sexually active men, as no <i>de novo</i> erectile or ejaculatory dysfunction has been reported.	II	B

Abbreviations: BPO, bladder outlet obstruction; ED, erectile dysfunction; EF, erectile function; EjD, ejaculatory dysfunction; EjF, ejaculatory function; GoR, Grade of Recommendation; HoLEP, holmium laser enucleation of the prostate; iTIND, temporary implantable nitinol device; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; MISTs, minimally invasive surgical treatments; PAE, prostatic artery embolization; PUL, prostatic urethral lift; PVP, photoselective vaporization of the prostate; TUIP, transurethral incision of the prostate; TURP, transurethral resection of the prostate.

Persisting/de novo LUTS after BPO surgery (including MISTs)

Although surgical treatments for BPO are generally effective in alleviating LUTS, a proportion of patients continues to experience bothersome symptoms postoperatively. Previous studies indicate that approximately 30% of individuals report ongoing urinary issues following surgery.²⁰ For example, up to 27% of men require pharmacological treatment for LUTS after undergoing TURP, highlighting the persistence of symptoms.⁷⁶ This ongoing symptom burden represents a notable clinical dilemma for both patients and urologists, particularly given the limited evidence available to inform diagnostic and therapeutic strategies.

Etiology of persisting/de novo LUTS

Persistent LUTS after BPO surgery have a multifactorial etiology, requiring comprehensive clinical assessment.⁷⁷ Effective management hinges on understanding the patient's baseline symptoms, the surgical intervention performed, and the nature and timing of postoperative symptoms. Potential causes include residual obstruction from incomplete resection or postoperative complications such as infection, bladder neck contracture, or urethral stricture. However, in many cases, persistent symptoms are more often attributed to bladder dysfunction, particularly detrusor overactivity or underactivity.⁷⁸

Chronic BOO leads to physiological changes such as detrusor muscle hypertrophy and bladder wall thickening, which disrupt bladder compliance and neural signaling.⁷⁷ These changes contribute to storage symptoms such as urgency and frequency—even after the obstruction is relieved—due to persistent OAB mechanisms.⁷⁹ In severe cases, long-standing BOO can result in detrusor underactivity and urinary retention, reflecting irreversible or slowly reversible bladder decompensation.⁸⁰

Initial evaluation should distinguish between voiding and storage symptoms and consider their timing post-surgery. Heiman *et al.* proposed a clinical framework categorizing patients into four groups based on symptom type and duration of postoperative symptoms:

1. short-term voiding symptoms, potentially due to incomplete resection, urethral stricture, bladder neck contracture, and detrusor underactivity;
2. short-term storage symptoms, associated with OAB or stress incontinence;
3. long-term voiding symptoms, associated with prostatic regrowth, urethral stricture, or bladder neck contracture; and
4. long-term storage symptoms, most commonly due to persistent OAB.³

This classification framework aids in tailoring diagnostic and therapeutic strategies according to symptom pattern and chronicity.

Assessment of persisting/de novo LUTS

A thorough evaluation is crucial for identifying the underlying causes of persistent LUTS following BPH surgery and guiding appropriate management. According to the AUA guidelines, assessment should begin with distinguishing between voiding and storage symptoms.⁸¹ A detailed clinical history, supported by validated tools, such as the IPSS, helps characterize symptom type and severity.⁸² Physical examination should include genital, rectal, and neurological assessment. Urinalysis and urine culture help rule out infection. Key diagnostic tests include PVR measurement, uroflowmetry, cystourethroscopy, and when needed, urodynamics—to differentiate between obstruction and bladder dysfunction.⁸¹

Voiding symptoms

For patients presenting with voiding symptoms, PVR and cystoscopy are essential to identify structural causes such as urethral stricture, bladder neck contracture, or residual prostatic tissue.⁸² Strictures and contractures are common complications of transurethral surgery, with incidence rates of 5% after TURP and 2% after HoLEP.⁸³ TURP accounts for 41% of iatrogenic urethral strictures, which typically manifest within the first 3 months postoperatively.^{84,85} If obstruction is ruled out but urinary retention persists, urodynamic studies can assess detrusor contractility and identify underactive bladder.

Storage symptoms

For patients with urgency, frequency, or nocturia, a comprehensive assessment including urinalysis, PVR, bladder diary, and urodynamic pressure-flow studies is critical. These tests help identify detrusor overactivity, underactivity, or pelvic floor dysfunction. As Kuo *et al.* emphasize, symptoms alone are insufficient for diagnosis—urodynamic testing is often necessary to determine the true etiology in patients with persistent symptoms.⁸⁶ A complete diagnostic approach minimizes unnecessary repeat procedures and enables tailored, effective treatment strategies.

Management of persisting/de novo LUTS

Effectively managing persistent LUTS after BPH surgery requires a personalized, multifaceted approach, targeting underlying causes based on thorough assessment, symptom timing, and both subjective and objective findings.

Short-term voiding symptoms

Persistent BOO following BPH surgery may result from incomplete resection, urethral stricture, or bladder neck contracture. Urethral strictures < 2 cm are typically managed with dilation or direct vision internal urethrotomy.⁸⁷ Strictures > 2 to 3 cm or failed endoscopic management warrant referral for urethroplasty.⁸⁷ Bladder neck contractures are treated primarily with transurethral incision/resection.⁸⁸ For recurrent cases, adding an 8-point steroid injection to scar resection achieves high success rates, approaching 93%.⁸⁹

Although uncommon, incomplete resections should prompt consideration of repeat surgery. Salvage HoLEP has demonstrated safety and efficacy in such cases, offering complete tissue removal and precise anatomical dissection, making it ideal for reoperations.⁹⁰ In these scenarios, full enucleation or aggressive TURP is recommended.

In patients with underactive bladders, conservative management such as timed or double voiding may be sufficient, provided there are no complications such as elevated PVR, infection, or renal impairment. In severe cases, intermittent or chronic catheterization may be needed. Notably, despite poor bladder contractility, HoLEP can remain an effective and durable option.⁹¹ If the initial surgery was non-enucleative, reoperation may lead to better outcomes. In cases of end-stage bladder dysfunction, urinary diversion may ultimately be necessary.

Short-term storage symptoms

Storage symptoms are common after BPH surgery but typically resolve within 6 to 12 weeks. When symptoms persist beyond this period, further evaluation is warranted.⁷⁷ After obstruction has been ruled out, initial management may include behavioral changes, pelvic floor therapy, and pharmacologic treatment with OAB medications.⁹² Emerging research also supports intradetrusor botulinum toxin administered during HoLEP for patients with severe storage symptoms. In a study by Huang *et al.*, this approach improved symptom scores without affecting outcomes; however, its use should be limited to select patients due to retention risks.⁹³ Urinary incontinence may also occur after BPH surgery and is discussed in detail in a separate section.

Long-term voiding symptoms

Obstructive symptoms occurring ≥ 1 year post-surgery are often due to prostatic regrowth, though late-onset urethral stricture or bladder neck contracture should be excluded. If residual or regrown tissue is confirmed, medical therapy with α -blockers and 5 α -reductase inhibitors (5-ARIs) may be initiated.⁸² If symptoms persist, repeat surgical intervention should be considered based on patient preference and clinical response.

Repeating endoscopic procedures is safe and yields outcomes comparable to initial treatments. Elshal *et al.* demonstrated similar safety and efficacy for HoLEP in patients with prior BPH surgery,⁹⁴ while Abdelaziz *et al.* reported no increase in complication rates with repeat TURP for regrowth.⁹⁵ Additionally, Gauhar *et al.* found Rezūm to be a safe and effective retreatment option, with symptom improvement and no complications at 3 months.⁹⁶ Late-presenting strictures or bladder neck contractures should be managed as outlined in previous sections.

Long-term storage symptoms

Patients with persistent or new storage symptoms > 1 -year post-surgery—despite lifestyle changes, pelvic floor therapy, and OAB medications—are considered to have long-term storage symptoms. In these cases, treatment options include intradetrusor botulinum toxin A (for patients able to manage PVR monitoring or self-catheterization) or neuromodulation for those with refractory OAB or medication intolerance.⁹²

Conclusion

With an aging population, optimizing both BPH surgery and postoperative care is becoming increasingly important. While most patients experience symptom relief, persistent LUTS remain a clinical challenge. Symptoms in the first 4 to 12 weeks often resolve with conservative care, but later-onset symptoms require further evaluation and potential intervention. Effective management demands a thorough understanding of the multifactorial causes of LUTS and all available treatment options. A patient-centered, shared decision-making approach—starting before surgery—can help improve outcomes and enhance quality of life.

TABLE 3 Management of Persisting/*De Novo* LUTS After BPO Surgery

Topic	Recommendation	LoE	GoR
Up to 30% of patients experience persistent LUTS after BPH surgery, often due to bladder dysfunction or residual obstruction.	Perform a comprehensive clinical assessment including symptom classification (voiding vs. storage), surgical history, and timing.	I	A
Symptom type and timing (voiding vs. storage; short- vs. long-term) guide diagnosis and treatment strategies.	Use validated tools (e.g., IPSS), PVR measurement, uroflowmetry, and urinalysis as first-line investigations.	I	A
Comprehensive evaluation is critical to identify underlying causes.	Perform cystoscopy and consider urodynamics in patients with persistent symptoms or unclear diagnosis.	II	B
Management should be individualized, ranging from reoperation to behavioral therapy, medications, or advanced interventions, all guided by shared decision-making with the patient.	For short-term storage (< 12 months) symptoms, initiate conservative/OAB therapy.	I	A
	For long-term storage symptoms, consider intradetrusorial injection of botulinum toxin A or sacral neuromodulation in refractory cases.	III	C
	In underactive bladder, adopt conservative strategies or CIC.	III	C
	For long-term voiding symptoms (>12 months), rule out regrowth or late strictures and manage accordingly.	II	B
	Alpha-blockers or 5-ARIs may be initiated in patients with suspected regrowth.	II	B
	Repeat BPO surgery (e.g., HoLEP) can be considered in case of incomplete resection or prostatic regrowth.	I	A
	Treat bladder neck contractures with transurethral incision/resection in recurrent cases.	II	B
	Manage strictures < 2 cm with dilation or DVIU; refer longer/recurrent strictures for urethroplasty.	I	A
	Consider repeat TURP/HoLEP or minimally invasive retreatment (e.g., Rezūm) in case of recurrent obstruction.	IIb	C

Abbreviations: 5-ARIs, 5 α -reductase inhibitors; BPH, benign prostatic hyperplasia; BPO, bladder outlet obstruction; CIC, clean intermittent catheterization; DVIU, direct vision internal urethrotomy; GoR, Grade of Recommendation; HoLEP, holmium laser enucleation of the prostate; IPSS, International Prostate Symptom Score; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; PVR, post-void residual; TURP, transurethral resection of the prostate.

Medical therapy after BPO surgery

Despite the well-documented long-term relief of symptoms following BPO surgery, recent studies suggest that a high proportion of patients either continue medication or resume LUTS-related pharmacotherapy after surgical treatment of BPO.⁷⁸ These findings contrast with outcomes reported in RCTs, where the primary endpoint is often the IPSS and secondary outcome measures include QoL, other PROMs, maximum flow rate, PVR, and surgical reintervention rates.⁷⁸ However, the use of medical LUTS therapy after invasive BPO treatment is rarely reported, despite the fact that discontinuation of LUTS-related medication is one of the primary goals of surgical treatment in men with BPO.⁷⁸ Thus, long-term freedom from LUTS-related pharmacotherapy should be considered as an important endpoint when assessing the efficacy of BPO surgery. This section is based in part from a recently published narrative review.⁷⁸

Prevalence of medical therapy after BPO surgery

As indicated above, the vast majority of available literature on this topic focuses on TURP. In the aforementioned review, Rieken *et al.* identified eight studies after TURP, three after laser vaporization, two on transurethral enucleation, two on TUIP, and one on open prostatectomy.⁷⁸ Lukacs *et al.* were among the first to describe the use of LUTS-related pharmacotherapy after surgery in a population-based setting.¹⁹ The authors investigated 310,834 patients who underwent surgical therapy (TURP, TUIP, TUNA, TUMT) between 2004 and 2008 in France. At 12 months postoperatively, the cumulative incidence of the use of plant extracts, 5-ARIs, α -blockers, and antimuscarinics was in the range of 25%, and this percentage increased to more than 35% at 5 years after surgery.¹⁹ A separate analysis for the various surgical approaches was not reported.¹⁹ Campbell *et al.* used datasets from the province of Ontario, Canada, to identify men older than 66 years who underwent their first TURP between April 2003 and March 2016.⁷⁶ The authors identified 58,038 men (median age, 75 years), with a median follow-up of 4.9 years. Following a 90-day washout period after TURP, α -blockers, 5-ARIs, and anticholinergics/ β -3 agonists were used by 27%, 20%, and 15% of men, respectively.⁷⁶ The cumulative probability of using these medications within the first 10 years after TURP was 38%, 28%, and 20%, respectively.⁷⁶

Risk factors associated with LUTS-related pharmacotherapy after BPO surgery

Regression analyses examining risk factors associated with medication use following BPO surgery were performed in three studies. Han *et al.* conducted a multicenter study involving 372 patients and found that age > 70 years, a history of diabetes mellitus, a history of cerebrovascular accident, and a history of medication use to be associated with a higher risk of use of any type of LUTS pharmacotherapy following TURP.⁹⁷ A population-based study on patients after TURP found age $\geq$ 75 years, a history of diabetes mellitus, absence of preoperative urinary retention, and preoperative use of OAB medications to be associated with a higher risk of antimuscarinic use or β 3-agonist use immediately after surgery.⁷⁶ Few studies have compared various surgical approaches in this respect. Ory *et al.* used a large-scale US-data base (TriNetX Analytics Network) to compare laser enucleation of the prostate (LEP) to TURP, prostate laser vaporization, Rezūm, and the UroLift procedure.⁹⁸ A total of 21,475 men who were receiving LUTS-related pharmacotherapy and subsequently underwent surgery were included: TURP

(n = 12,294), prostate laser vaporization (n = 5290), water vaporization (Rezūm; n = 397), prostate urethral lift (PUL, n = 1308), TUIP (n = 346), and LEP (n = 1840). LUTS-related pharmacotherapy use between 6 months and 2 years after surgery was 38% for laser enucleation of the prostate, 50% for water vaporization, 61% for TURP, 63% for prostate urethral lift, 65% for TUIP, and 66% for laser vaporization.⁹⁸ All surgical modalities showed higher odds of using medications when compared to LEP ($P < .001$).⁹⁸ This remained significant after propensity score matching for nine potentially confounding variables.⁹⁸

Reasons for the use of LUTS-related pharmacotherapy after BPO surgery

BPO is a urodynamic diagnosis, and it has been consistently shown that patients with BPO benefit more with surgery than those without. However, fewer than 50% of men with LUTS who undergo surgical intervention actually have evidence of BPO; the remaining patients have detrusor underactivity, detrusor overactivity, nocturia, or combinations thereof.⁹⁹ It is highly likely that urodynamic patterns other than BPO, which may persist after BPO surgery, contribute to the continued use of LUTS-related pharmacotherapy.⁹⁹ Several of the risk factors described above, such as advanced age (with age-related urodynamic changes), diabetes mellitus, a history of cardiovascular disease, and preoperative use of OAB medication also support this notion.^{76,78,97} This underscores the need for a thorough preoperative work-up, particularly in at-risk groups, including the use of frequency-volume charts and pressure-flow studies, as recommended by the EAU guidelines.⁹ Long-term data suggest that incomplete relief of BPH during surgery or regrowth of prostate tissue months or years later may be also related to the persistence or new onset of LUTS-related pharmacotherapy. Procedures involving immediate tissue removal, such as TURP, have been associated with higher medication discontinuation rates, resumption, and *de novo* initiation compared with delayed tissue removal procedures such as TUMT or TUNA.⁷⁸ The previously cited study by Ory *et al.* also supports this notion and suggests that a larger amount of tissue removal is associated with a lower risk of LUTS-related pharmacotherapy use after surgery.⁹⁸

Conclusion

The use of pharmacotherapy after TURP is common and appears to increase over time during the postoperative follow-up. The evidence pharmacotherapy use in this context remains limited. While similar trends may be observed with other surgical techniques, supporting data are still limited. Patients should be informed of this fact prior surgery. As most available evidence comes from retrospective studies, an underreporting in RCTs must be suspected. Therefore, pharmacotherapy use after BPO surgery should be considered a relevant endpoint in future studies evaluating techniques of BPO surgery and should serve as a quality outcome measure. Finally, the identification of various risk factors for LUTS-related pharmacotherapy after BPO surgery highlights the need for a more thorough work-up, including frequency-volume charts and urodynamics in at-risk groups.

TABLE 4 Use of Medical Therapy After BPO Surgery

Topic	Recommendation	LoE	GoR
Use of pharmacotherapy post-BPO surgery	Inform patients that LUTS-related pharmacotherapy is commonly resumed or continued after BPO surgery, particularly TURP.	I	A
	Consider age > 70 years, diabetes mellitus, cerebrovascular disease, and prior use of LUTS-related medications as risk factors for postoperative pharmacotherapy.	II	B
	HoLEP may result in a lower need for postoperative LUTS medication compared to TURP, TUIP, PUL, Rezūm, or laser vaporization.	III	C
	Counsel patients that surgical treatment does not guarantee freedom from LUTS medications over the long term.	I	A

Abbreviations: BPO, bladder outlet obstruction; GoR, Grade of Recommendation; HoLEP, holmium laser enucleation of prostate; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; PUL, prostatic urethral lift; Rezūm, water vapor thermal therapy; TUIP, transurethral incision of the prostate; TURP, transurethral resection of the prostate.

Surgical reintervention after BPO surgery

Introduction

As mentioned above, when persisting obstructive LUTS are present, evaluation should include PVR measurement and cystourethroscopy to identify anatomical abnormalities including urethral strictures, bladder neck contractures, or residual prostatic tissue either due to incomplete prostatic resection (short-term complication) or regrowth of prostatic tissue (long-term complication).⁸² Although rare in the short term, if incomplete resection is identified, patients should be scheduled for a repeat procedure with the aim of achieving a more thorough and effective resection. The reoperation rate after BPO surgery, as reported in the literature, often varies depending on the technique used.

Urethral strictures and bladder neck contractures can occur after BPO surgery, with incidence varying by procedure—5% after TURP and 2% after HoLEP.⁸³ Transurethral surgery is the leading cause of iatrogenic urethral stricture disease, accounting for 41% of cases.⁸⁴

For TURP, the estimated reoperation rate is approximately 1.8% per year, with cumulative rates reaching 12.0% to 15.5% at 8 years.^{100,101} Only one study specifically assessed whether monopolar or bipolar TURP had been performed.¹⁰² Kim *et al.* reported a 2% reoperation rate at 1 year for patients following TURP, compared to 0.7% for those treated with HoLEP.²⁰ Among laser therapies, PVP shows reoperation rates of 11% at 1 year and 22% at 10 years,^{103,104} while HoLEP shows lower retreatment rates, ranging from 0% to 4% at 5 years.^{9,105}

Among MISTs, PUL exhibits retreatment rates of 1.5% to 16% at 12 months and 7.5% to 20% at 2 years,^{106,107} and TUNA and TUMT demonstrate 1-year reoperation rates of 8% and 7%, respectively.¹⁰⁴ The Rezūm system shows a favorable reintervention rate of 4.4% at 5 years.¹⁰⁸

These data highlight the variability in procedural durability and the need for individualized treatment decisions based on patient characteristics and outcomes, although some techniques currently lack long-term efficacy and effectiveness data.

Surgical treatment of urethral stricture after BPO surgery

For urethral strictures < 2 cm, conservative or endoscopic treatments such as dilation or direct visual internal urethrotomy (DVIU) are recommended.^{87,109} Recent evidence supports using paclitaxel-coated balloons for strictures < 3 cm, showing higher success rates than DVIU.¹¹⁰ If strictures are > 2 to 3 cm or endoscopic treatments fail, referral to a urethroplasty specialist is advised.^{87,109} Bladder neck contractures are typically managed with transurethral incision or resection; recurrent cases may benefit from steroid injections or paclitaxel-coated balloon therapy.⁸⁹ Though rare, strictures or contractures can develop beyond 1 year post-surgery and should be treated accordingly.

Surgical treatment of incomplete prostate resection or regrowing prostate adenoma

Repeat surgical intervention to remove residual or recurrent obstructive tissue is recommended in accordance with patient-specific factors. In case of regrowth, the available literature lacks robust data comparing various salvage procedures for recurrent BPE.

Theoretically, ThuLEP has been considered potentially more suitable for identifying the correct enucleation plane due to the shallow penetration and precise cutting of thulium laser; however, this advantage does not appear to be reflected in studies.¹¹¹ In particular, only one study directly compared HoLEP and ThuLEP techniques, concluding that both holmium and thulium laser enucleation are safe and feasible, with similar efficacy following previous prostate surgery.¹¹¹

Kallidonis *et al.* demonstrated that salvage HoLEP after previous interventions for treating recurrent prostate adenoma is a feasible, safe, and efficient procedure.⁹⁰ In an analysis of BPE surgery utilization trends, Abdelaziz *et al.* compared complication rates between TURP and repeat TURP for regrowth, reporting no difference in complication rates and thereby proving the safety of repeat TURP for regrowth.⁹⁵

Several studies have found no significant differences in postoperative outcomes or complication rates between salvage and primary HoLEP procedures.^{102,108,111–113} However, Marien *et al.* reported a higher incidence of clot retention and urethral stricture at 6-month follow-up in the salvage group.¹¹² The shorter operative times observed in some cases may be attributed to both smaller residual prostate volumes and the involvement of

experienced endourologists.¹¹² Conversely, another study noted slightly longer operative times in the salvage group despite smaller prostates, likely due to more challenging surgical conditions. Nonetheless, salvage HoLEP was associated with reduced bleeding and better intraoperative visibility.¹¹¹

The use of minimally invasive techniques, such as the innovative MISTs or PAE, as salvage surgery remains poorly documented. The following paragraphs summarize all available evidence in the literature.

Prostatic artery embolization after MISTs surgery

Minimally Invasive Surgical Treatments (MIST), such as Rezūm, UroLift, and iTIND, offer alternatives to traditional surgical approaches for BPO treatment, aiming to reduce LUTS while minimizing sexual side effects.¹ On the other hand, PAE is a nonsurgical, image-guided endovascular technique that induces ischemic reduction of prostate volume by selectively occluding prostatic arteries. In a single study, Goyal *et al.* evaluated the efficacy of PAE in patients with persistent or recurrent LUTS following prior MIST procedures.¹¹⁴ The results demonstrated a significant reduction in median IPSS score (20 vs. 8, $P = .003$), a decrease in PVR (from 80 mL to 24 mL, $P = .01$), and an improvement in QoL scores. No major adverse events were observed, and clinical outcomes were comparable to those typically seen in treatment-naïve patients undergoing PAE.¹¹⁴

These findings support the role of PAE as an effective and safe salvage option for patients with refractory symptoms after MIST.

Rezūm system after previous BPO surgery

The study by Gauhar *et al.* on the use of Rezūm as a retreatment option for patients with recurrent LUTS after previous BPO surgery provides promising findings.⁹⁶ The research suggests that the procedure leads to clinical improvement in symptoms and favorable outcomes at 3 months, without complications. Rezūm can be safely repeated in cases where there is adenoma regrowth, offering a feasible treatment option with outcomes comparable to the initial procedure. However, when performing this technique as salvage surgery, it is crucial to follow the original injection protocol to avoid sphincter injury and potential incontinence. Additionally, in patients with prior UroLift, there is a theoretical risk that the implanted clips may loosen due to tissue apoptosis and resorption following treatment.⁹⁶

HoLEP after BPO surgery

Whether due to residual adenoma after obstructive surgery or recurrence of adenoma, most studies on salvage surgery after BPO surgery focus on HoLEP.

The physical properties of holmium laser to resect more tissue and to dissect along the true anatomical plane of the hyperplastic prostate in an analogous way to simple prostatectomy (SP), solidify HoLEP as an ideal treatment modality for reoperations in the setting of residual or recurrent BPE symptoms.⁹⁰ On the other hand, salvage HoLEP after previous interventions for BPE treatment could be technically challenging and may be associated with more adverse outcomes compared to the primary modality.¹¹²

Kallidonis *et al.* demonstrated that salvage HoLEP after previous interventions for recurrent prostate adenoma is a feasible, safe, and efficient procedure.⁹⁰ Elshal *et al.* evaluated patients undergoing HoLEP after a previous BPE procedure and found that patients had comparable safety and functional outcomes to those undergoing primary HoLEP.⁹⁴ However, salvage cases were associated with a lower morcellation rate and increased need for sharp dissection, resulting in higher energy consumption.⁹⁴

Salvage HoLEP after TURP

Several studies have evaluated the feasibility and effectiveness of salvage HoLEP following TURP. Khater *et al.* initially hypothesized that previous resection would lead to adhesions and fibrosis along the enucleation plane, increasing the risk of capsular perforation.¹¹⁵ Intraoperative findings contradicted the initial concerns, as the enucleation plane remained clearly identifiable, the procedure was technically smooth, and outcomes were comparable to primary HoLEP, with only a higher rate of bladder neck fibrosis noted, which had no effect on results. Jaeger and Krambeck as well as Becker *et al.* similarly confirmed that salvage HoLEP is feasible even after prior prostate surgery, including TURP.^{102,111}

Salvage HoLEP after laser surgery

PVP, HoLEP, and holmium laser ablation of the prostate (HoLAP) were reported as previous procedures in four studies.^{94,102,108,113} However, no study specifically focused on the impact of prior laser therapies on the outcomes of salvage HoLEP.

Salvage HoLEP after other endoscopic techniques and MISTs

Salvage HoLEP following prior treatments such as Rezūm, TUIP, TUNA, and TUMT has been reported in several studies.^{94,102,111–113} Oh *et al.* reported encountering an unclear enucleation plane in 3 of 35 patients undergoing salvage HoLEP after various prior interventions (TURP, PVP, TUNA), though they did not specify which prior surgery each patient had undergone.¹¹³

Salvage HoLEP after PUL was specifically examined in two studies.^{116,117} The authors concluded that salvage HoLEP is safe and effective, though technical challenges during morcellation were noted due to the presence of implants, including blade jamming and the need for additional maneuvers.^{116,117}

Finally, salvage HoLEP after prior placement of a permanent prostatic urethral stent (PPUS) has been described in a single study, with reported two cases by Banerjee *et al.*¹¹⁸ In both cases, the procedure was successfully performed alongside stent removal, taking advantage of the holmium laser's precise ablative, cutting, and hemostatic capabilities.

Salvage HoLEP after PAE

PAE is a radiological technique that fails to adequately improve LUTS in 20% to 36% of patients. Therefore, having an effective salvage option such as HoLEP is crucial in managing these cases.¹¹⁹

Two studies investigated PAE as the treatment before HoLEP.^{120,121} Li *et al.* used PAE as a planned first step before HoLEP in patients with very large prostates, aiming to reduce prostate size and vascularity to facilitate surgery. HoLEP was performed 3 months later, with no major complications and good functional outcomes.¹²⁰ HoLEP as a salvage procedure following PAE in patients with persistent or recurrent LUTS was investigated by Parmar *et al.*¹²¹ Despite initial concerns that PAE might alter the enucleation plane, intraoperative findings confirmed the plane remained intact, supporting the safety and feasibility of salvage HoLEP after PAE.¹²¹

Conclusion

Treatment of complications and persistence of LUTS after surgery for BPO may be challenging, especially in an era when new treatments—proposed as minimally invasive and allowing for a rapid recovery—are emerging.³ It is important to consider not only the preoperative conditions of the lower urinary tract but also the general health status of the patient. Furthermore, it is fundamental to consider the patient's needs and expectations before selecting a treatment. Complications or unsatisfactory results may be due not only to technical issues but also to an incorrect preoperative evaluation or incomplete patient counseling.^{9,122} A proper pretreatment patient assessment—including a thorough understanding of the patients' needs—is just as important as selecting the most appropriate surgical treatment and, obviously, perfectly executing the procedure.^{104,113}

TABLE 5 Surgical Management of Persisting or Recurrent LUTS After BPO Surgery

Topic	Recommendation	LoE	GoR
Evaluation of persistent LUTS after BPO	Perform PVR and cystourethroscopy to identify anatomic abnormalities (strictures, bladder neck contracture, residual tissue).	II	B
Incomplete resection	Schedule repeat endoscopic surgery if residual adenoma is detected.	III	C
	HoLEP shows lower retreatment rates compared to TURP and PVP.	Ib	A
Urethral stricture or bladder neck contracture	The incidence of bladder neck stricture/contracture post-BPO is ~5% after TURP and ~2% after HoLEP.	IIa	B
	Use endoscopic incision or resection as first-line treatment for bladder neck stenosis or contracture.	IIa	B
	Use steroids or paclitaxel-coated balloons in case of recurrent bladder neck stenosis or contracture.	Ib	A
	In case of urethral stricture < 2–3 cm, perform dilation, DVIU, or paclitaxel-coated balloons as first-line treatment.	II	B
	In cases of urethral stricture >2–3 cm or previous failed endoscopic treatment, refer the patient for urethroplasty.	II	B
Repeat surgery for regrowth	In cases of prostatic regrowth, TURP, HoLEP, or ThuLEP is a feasible option for retreatment.	II	B
	When choosing the technique for the treatment of prostate regrowth, consider prostate anatomy and surgeon expertise.	II	C
	Salvage HoLEP after previous surgery is considered safe and effective for residual or recurrent adenoma.	IIa	B
	HoLEP after previous TURP should be considered technically feasible and safe.	IIa	B
	HoLEP after prior laser therapy appears feasible; however, data are limited.	III	C
	HoLEP after previous PUL should be considered technically feasible and safe; however, it must be taken into account that implants may affect morcellation.	IIa	B
	HoLEP after PAE is safe and effective, with the enucleation plane preserved.	II	C
	PAE as salvage therapy after failed MISTs should be considered an effective option, with good outcomes and a low complication rate.	IIa	B
	Rezūm after prior surgery should be considered a safe treatment option associated with symptom improvement.	III	C
	When performing Rezūm as salvage therapy, it is crucial to adhere to the original injection protocol to avoid sphincter injury and potential incontinence.	III	C

Abbreviations: BPO, bladder outlet obstruction; DVIU, direct vision internal urethrotomy; GoR, Grade of Recommendation; HoLEP, holmium laser enucleation of the prostate; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; MISTs, minimally invasive surgical treatments; PAE, prostatic artery embolization; PUL, prostatic urethral lift; PVP, photoselective vaporization of the prostate; PVR, post-void residual; ThuLEP, thulium laser enucleation of the prostate; TURP, transurethral resection of the prostate.

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COMMITTEE

08

**ALGORITHMS FOR THE
MANAGEMENT OF
MALE LUTS**

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Algorithms, or decision trees, are systematic processes consisting of an ordered sequence of steps, with each of them depending on the outcome of the previous one.¹ A Clinical Algorithm is a stepwise procedure for making decisions about the diagnosis and treatment of a clinical problem to improve the delivery of medical care.² The goal is to simplify complex medical guidelines into actionable formats, and an algorithm is usually depicted as a decision tree, which is a diagram in the shape of an upside-down tree that shows the different choices and possible outcomes of a decision. It uses the simple "if/then" approach and categorizes patients into distinct groups. A treatment algorithm can be used to generate a list of potential treatments, to prioritize treatments, or to select the most effective treatment based on the individual patient's profile.

However, there are several barriers to the adoption of treatment algorithms in daily practice including complexity and lack of practicality, uncertainty about their capabilities, difficulty in understanding the thinking process, and lack of access to the proposed therapies in different countries and healthcare systems. In addition, algorithms should be regularly updated to ensure that the guidance provided is aligned with the current best practices and the most recently published studies.

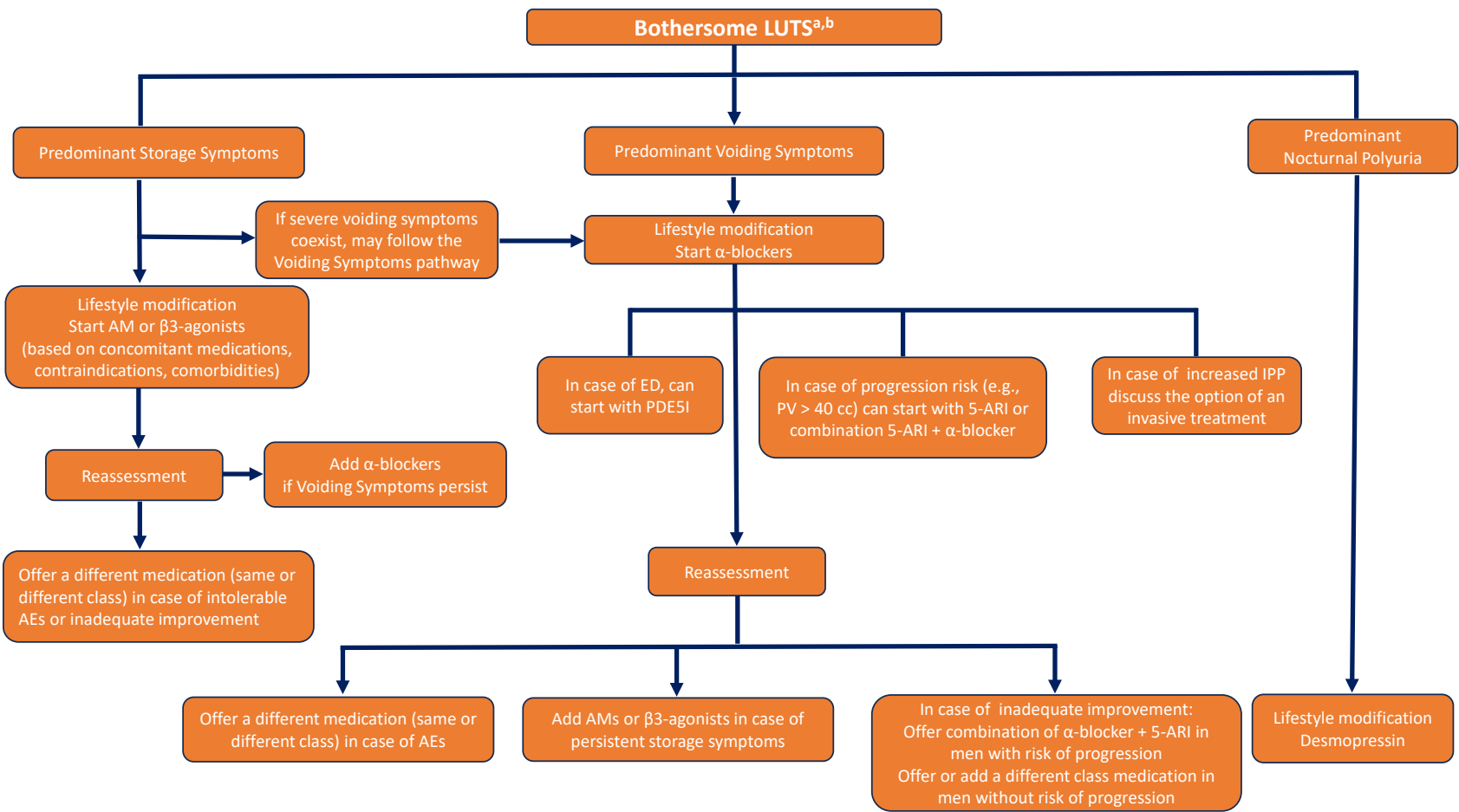
The present SIU-ICUD Consultation has developed and presents two new algorithms for the medical and surgical management of male lower urinary tract symptoms (LUTS). After several discussions, the Committee reached to a consensus regarding which decision points should be included in the Algorithms:

- a) The Medical Algorithm has the following decision points: Type of symptoms, risk of progression, intravesical prostatic protrusion, and presence of erectile dysfunction at baseline, and inadequate improvement of symptoms, and occurrence of adverse events (**FIGURE 1**).
- b) The Surgical Algorithm includes the ability to receive anesthesia, prostate volume, presence of obstructing middle lobe, and patient's wish for ejaculation preservation (**FIGURE 2**).

The Algorithms were developed by using the recommendations of the different Committees and supporting evidence that apply to each decision point and the corresponding subgroup of patients. Therapies with Recommendation Grade 4 due to low Level of Evidence (Experts' Opinion) were not included in the Algorithms.

Both the European Association of Urology (EAU) and the American Urological Association (AUA) have developed treatment algorithms for the management of male LUTS/BPO.^{3,4} Our Algorithms reflect the latest advancements in medical and surgical management of patients and for the first time, the preferences of patients, the presence of obstructing middle lobe, the sexual function, and the occurrence of adverse events have been included as decision points.

FIGURE 1 Medical Algorithm for the individualized management of male LUTS.

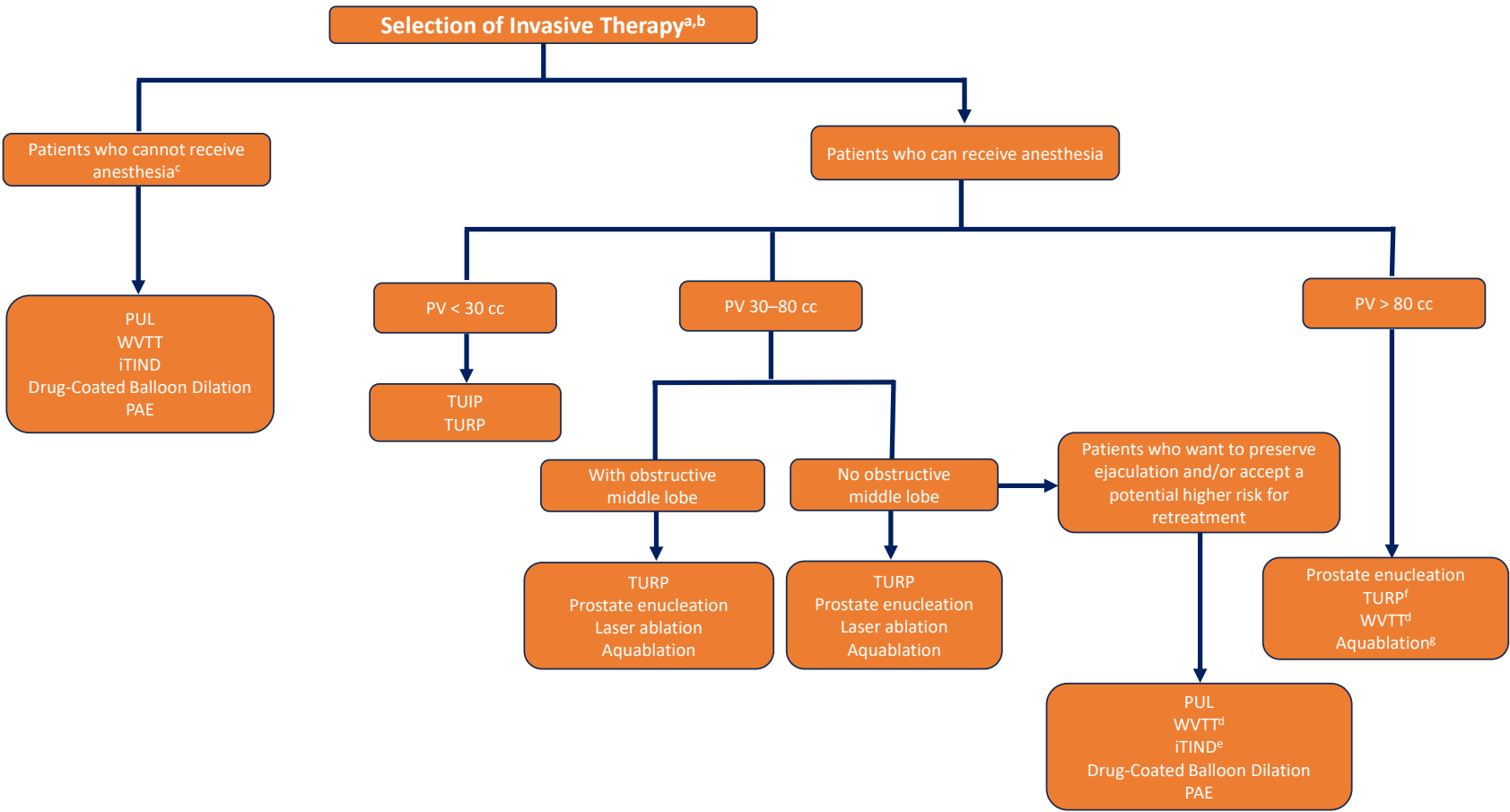


Abbreviations: 5-ARI, 5 α -reductase inhibitor; AEs, adverse events; AMs, antimuscarinics; ED, erectile dysfunction; IPP, intravesical prostatic protrusion; LoE, Level of Evidence; LUTS, lower urinary tract symptoms; PDE5I, phosphodiesterase type 5 inhibitor; PV prostate volume.

^a Please read the full Consultation for the detailed position of each therapy.

^b The LoE varies for the different therapies.

FIGURE 2 Surgical Algorithm for the individualized management of male LUTS.



Abbreviations: iTIND, temporary implantable nitinol device; LoE, Level of Evidence; PAE, prostatic artery embolization; PUL, prostatic urethral lift; PV, prostate volume; TUIP, transurethral incision of the prostate; TURP, transurethral resection of the prostate; WVTT, water vapor thermal therapy.

^a Please read the full Consultation for the detailed position of each therapy.
^b The LoE varies for the different therapies.
^c I.V. sedation may be needed for some therapies.
^d PV up to 150 cc in select cases including those with middle lobe.
^e PV 25–70 cc.
^f Depending on the surgeon experience.
^g Emerging data for larger prostates in select cases depending on the expertise of the surgeons.

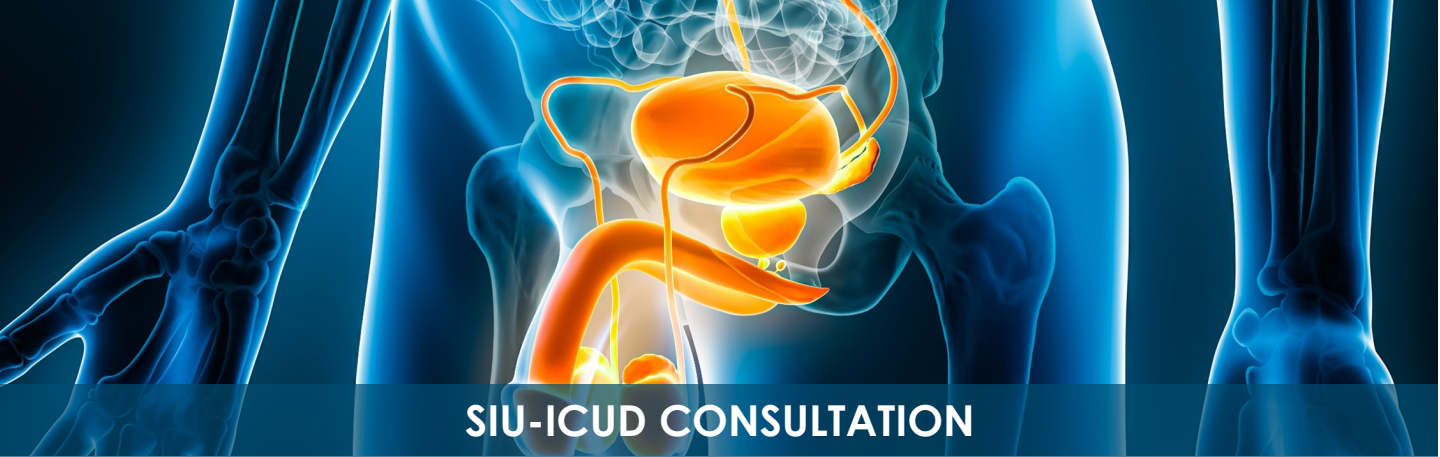
There are some limitations: The proposed algorithms represent a step toward the individualized management of male LUTS since they stratify patients to several subgroups. However, to make the algorithms reasonably concise for clinical usefulness and practicality, it is impossible to include all possible eventualities and clinical scenarios.

The Algorithms provide a list of potential treatments for a specific scenario, but the Level of Evidence that support each therapy may vary significantly. The algorithms may also need adaptation according to local resource availability.

Therefore, the user of the Algorithms must also read the full Consultation for the better understanding of the position of each therapy.

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SIU-ICUD CONSULTATION

INDIVIDUALIZED MANAGEMENT OF MALE LUTS

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