Canadian Urological Association
The Voice of Urology in Canada

Association des Urologues du Canada
La voix de l'urologie au Canada

Diagnosis and management of BPH

Speaker

Naeem Bhojani

Professor

University of Montreal

Speaker Disclosures | Naeem Bhojani

Relationships with financial sponsors:

Speaker	Advisory Boards	Speaker's Bureau	Payment/ Honoraria	Grants/ Research Support	Clinical Trials	Investments	Patents
Naeem Bhojani	Boston Scientific Olympus Procept J and J	----------	----------	Boston Scientific	Procept Boston Scientific	----------	----------

Disclosure of Financial Support

Potential for conflict(s) of interest:

- Members of the SPC committee (Alan Bell, Peter Lin, and Arthur Kushner) received honorarium from the Canadian Urological Association.
- Naeem Bhojani received honorarium from the Canadian Urological Association.

Mitigating Potential Bias

The scientific planning committee of this program have complete control over the content of this program.

There has been no influence from the sponsors on the content.

Learning Objectives

Upon completion of this program, participants will be able to:

- Interpret the work up for a patient suffering from BPH
- Determine best management for patients suffering from BPH
- Elucidate novel surgical management options for BPH patients

Male LUTS is a growing international burden

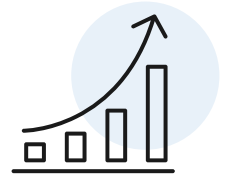
- *These data represent prompted self-reported LUTS in men. LUTS, lower urinary tract symptoms.
  Irwin DE, *et al*. *BJU Int*. 2011;108:1132–1139.

45%

of adult men have reported experiencing LUTS

930 million

men worldwide were estimated to be suffering from LUTS in 2008



1.1 billion

men, at least, were expected to experience LUTS by 2018 (10-year growth)

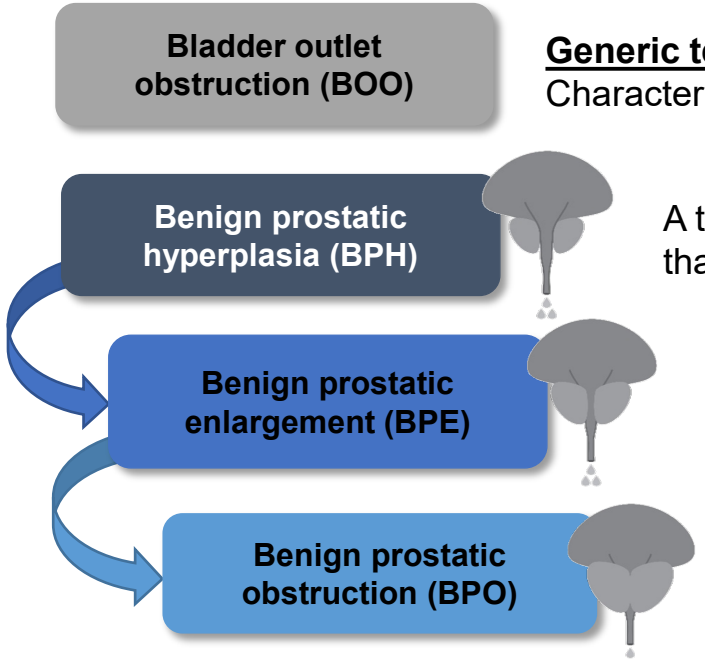
Lower urinary tract symptoms

- D'Ancona C, *et al*. *Neurourol Urodyn*. 2019;38:433–477.

STORAGE	VOIDING	POST-VOIDING
Frequency **Urgency** Urgency incontinence Nocturia	Hesitancy Intermittency Slow stream Splitting/spraying Straining Terminal dribble	Sensation of incomplete bladder emptying Double-voiding Post-voiding incontinence Post-micturition urgency

OAB symptoms

What effect can the prostate have?



Generic term for obstruction during voiding
Characterised by increased detrusor pressure and reduced urine flow rate.

A term used (and reserved for) the typical histological pattern that defines the disease.

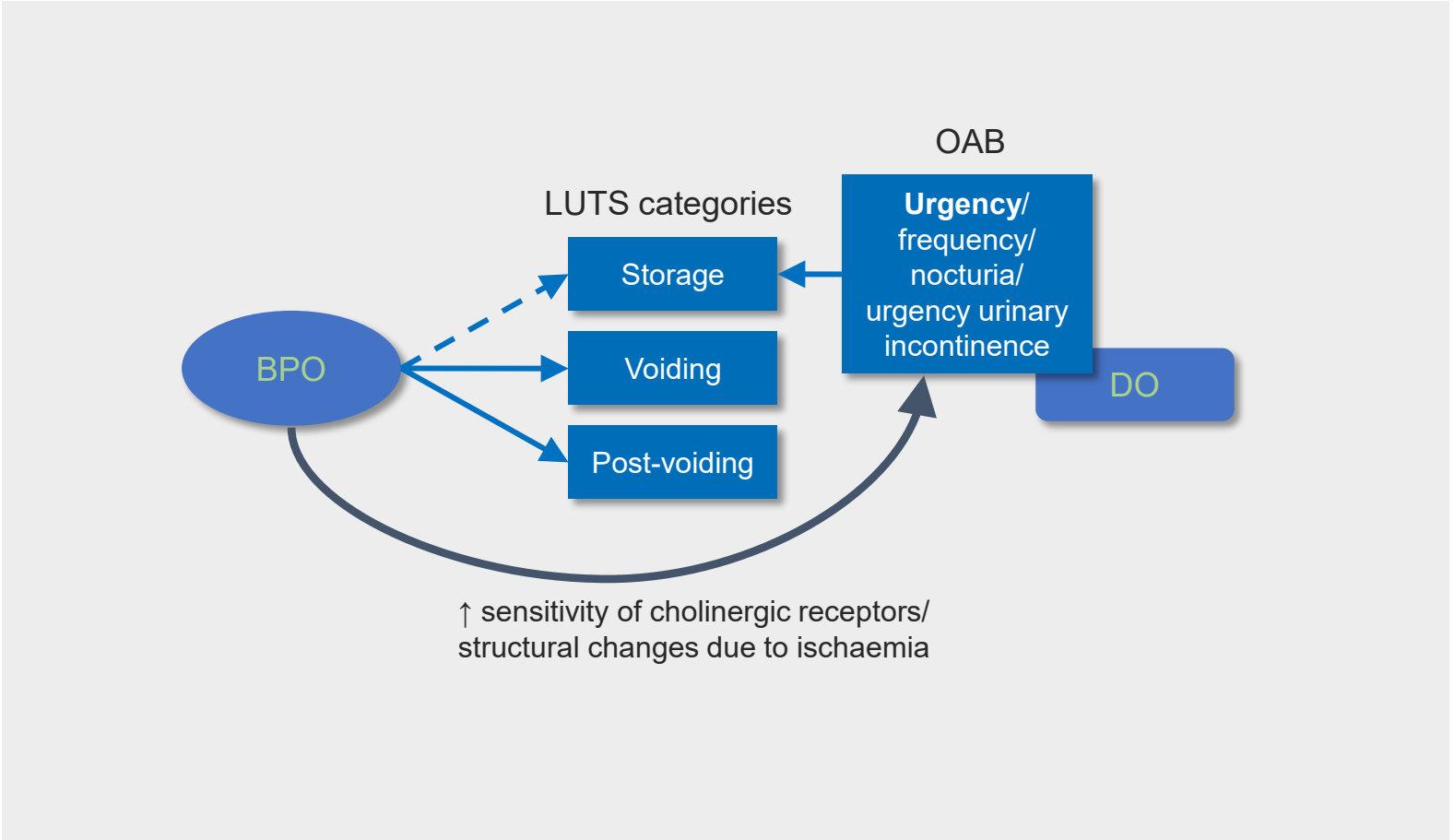
Prostatic enlargement due to histologic BPH.

Term used when there is evidence from digital rectal examination or ultrasound.

Diagnosed when there is proven outlet obstruction (associated with BPE) from urodynamics.
A form of BOO.

Abrams P, *et al*. *Urology.* 2003;61:37–49.

The relationships between BPO, OAB and male LUTS



- BPH, benign prostatic hyperplasia; BPO, benign prostatic obstruction; DO, detrusor overactivity; LUTS, lower urinary tract symptoms.
  Adapted from Athanasopoulos A, *et al. Eur Urol.* 2011;60:94–105.

CUA Guideline

CUA GUIDELINE

UPDATE – Canadian Urological Association guideline: Male lower urinary tract symptoms/ benign prostatic hyperplasia

UROpedia CANADA

Dean Elterman[1], Mélanie Aubé-Peterkin[2], Howard Evans[3], Hazem Elmansy[4], Malek Meskawi[5], Kevin C. Zorn[5], Naeem Bhojani[5]

[1]Division of Urology, University of Toronto, Toronto, ON, Canada; [2]Division of Urology, McGill University, Montreal, QC, Canada; [3]Division of Urology, University of Alberta, Edmonton, AB, Canada; [4]Division of Urology, Northern Ontario School of Medicine, Thunder Bay, ON, Canada; [5]Division of Urology, Université de Montréal, Montreal, QC, Canada

CUA guidelines

- Initial evaluation
  - History
  - Physical examination
  - Urinalysis
- Recommended
  - Symptom inventory
    - IPSS (International prostate symptom score)
  - PSA
    - Should be offered to patients who have at least a 10-year life expectancy and for whom knowledge of the presence of prostate cancer would change management.
    - PSA may also be used as a surrogate marker of prostate volume/size
- Optional
  - Serum creatinine
  - Urine cytology
  - Uroflow
  - Post void residual volume
  - Voiding diary

CUA guidelines

- Initial evaluation
  - History
  - Physical examination
  - Urinalysis
- Recommended
  - Symptom inventory
    - IPSS (International prostate symptom score)
  - PSA
    - Should be offered to patients who have at least a 10-year life expectancy and for whom knowledge of the presence of prostate cancer would change management.
    - PSA may also be used as a surrogate marker of prostate volume/size
- Optional
  - Serum creatinine
  - Urine cytology
  - Uroflow
  - Post void residual volume
  - Voiding diary

International Prostate Symptom Score (I-PSS)

Patient Name: _____ **Date of birth:** _____ **Date completed** _____

In the past month:	Not at All	Less than 1 in 5 Times	Less than Half the Time	About Half the Time	More than Half the Time	Almost Always	Your score
1. Incomplete Emptying How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. Frequency How often have you had to urinate less than every two hours?	0	1	2	3	4	5	
3. Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to strain to start urination?	0	1	2	3	4	5	
	None	**1 Time**	**2 Times**	**3 Times**	**4 Times**	**5 Times**	
7. Nocturia How many times did you typically get up at night to urinate?	0	1	2	3	4	5	
Total I-PSS Score							

Score: 1-7: *Mild* 8-19: *Moderate* 20-35: *Severe*

Quality of Life Due to Urinary Symptoms	Delighted	Pleased	Mostly Satisfied	Mixed	Mostly Dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	**0**	**1**	**2**	**3**	**4**	**5**	**6**

CUA guidelines

- Initial evaluation
  - History
  - Physical examination
  - Urinalysis
- Recommended
  - Symptom inventory
    - IPSS (International prostate symptom score)
  - PSA
    - Should be offered to patients who have at least a 10-year life expectancy and for whom knowledge of the presence of prostate cancer would change management.
    - PSA may also be used as a surrogate marker of prostate volume/size
- Optional
  - Serum creatinine
  - Urine cytology
  - Uroflow
  - Post void residual volume
  - Voiding diary

CUA guidelines

- Initial evaluation
  - History
  - Physical examination
  - Urinalysis
- Recommended
  - Symptom inventory
    - IPSS (International prostate symptom score)
  - PSA
    - Should be offered to patients who have at least a 10-year life expectancy and for whom knowledge of the presence of prostate cancer would change management.
    - PSA may also be used as a surrogate marker of prostate volume/size
- Optional
  - Serum creatinine
  - Urine cytology
  - Uroflow
  - Post void residual volume
  - Voiding diary

CUA BPH Guidelines

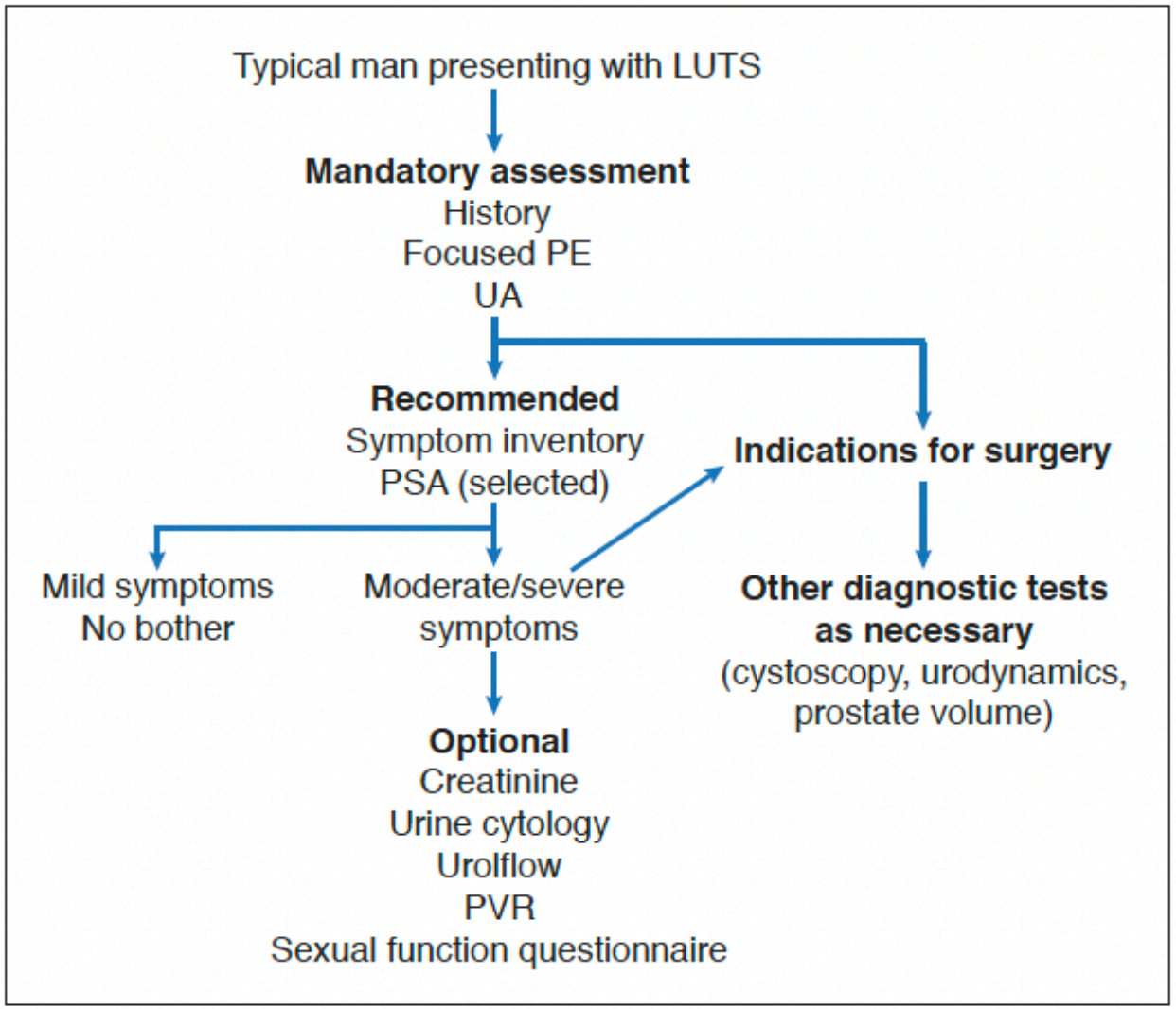


Figure 1. Algorithm of appropriate diagnostic steps in the workup of a typical patient with male lower urinary tract symptoms/benign prostatic hyperplasia (LUTS/BPH). PE: physical exam; PSA: prostate-specific antigen; PVR: postvoid residual; U/A: urinalysis.

Elterman, D. ., Aubé-Peterkin, M., Evans, H. ., Elmansy, H. ., Meskawi, M. ., Zorn, K. C. ., & Bhojani, N. (2022). UPDATE – 2022 Canadian Urological Association guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH). *Canadian Urological Association Journal*, *16*(8), 245–56. https://doi.org/10.5489/cuaj.7906

Principals of Treatment

Principles of treatment

- Guided by
  - Severity of symptoms
  - Degree of bother
  - Patient preference

Lifestyle changes

- Fluid restriction
  - Especially prior to bedtime
- Avoidance of caffeinated beverages, alcohol, and spicy foods
- Avoidance/monitoring of some drugs
  - Diuretics, decongestants, antihistamines, antidepressants
- Timed or organized voiding (bladder retraining)
- Avoidance or treatment of constipation
- Weight loss and prevention or treatment of conditions associated with metabolic syndrome
- Pelvic floor physical therapy in cases of suspected non-relaxing pelvic floor dysfunction or overactive bladder and/or urinary incontinence

Medical therapy

Medical therapy

- Alpha blocker
- 5-alpha reductase inhibitor (5-ARI)
- Combination therapy (alpha blocker and 5-ARI)
- Antimuscarinic/beta 3 agonist
- Combination therapy (antimuscarinic or beta 3 agonist with alpha blockers
- Phosphodiesterase type 5 inhibitors (PDE5 inhibitors)
- Desmopressin

CUA BPH Guidelines

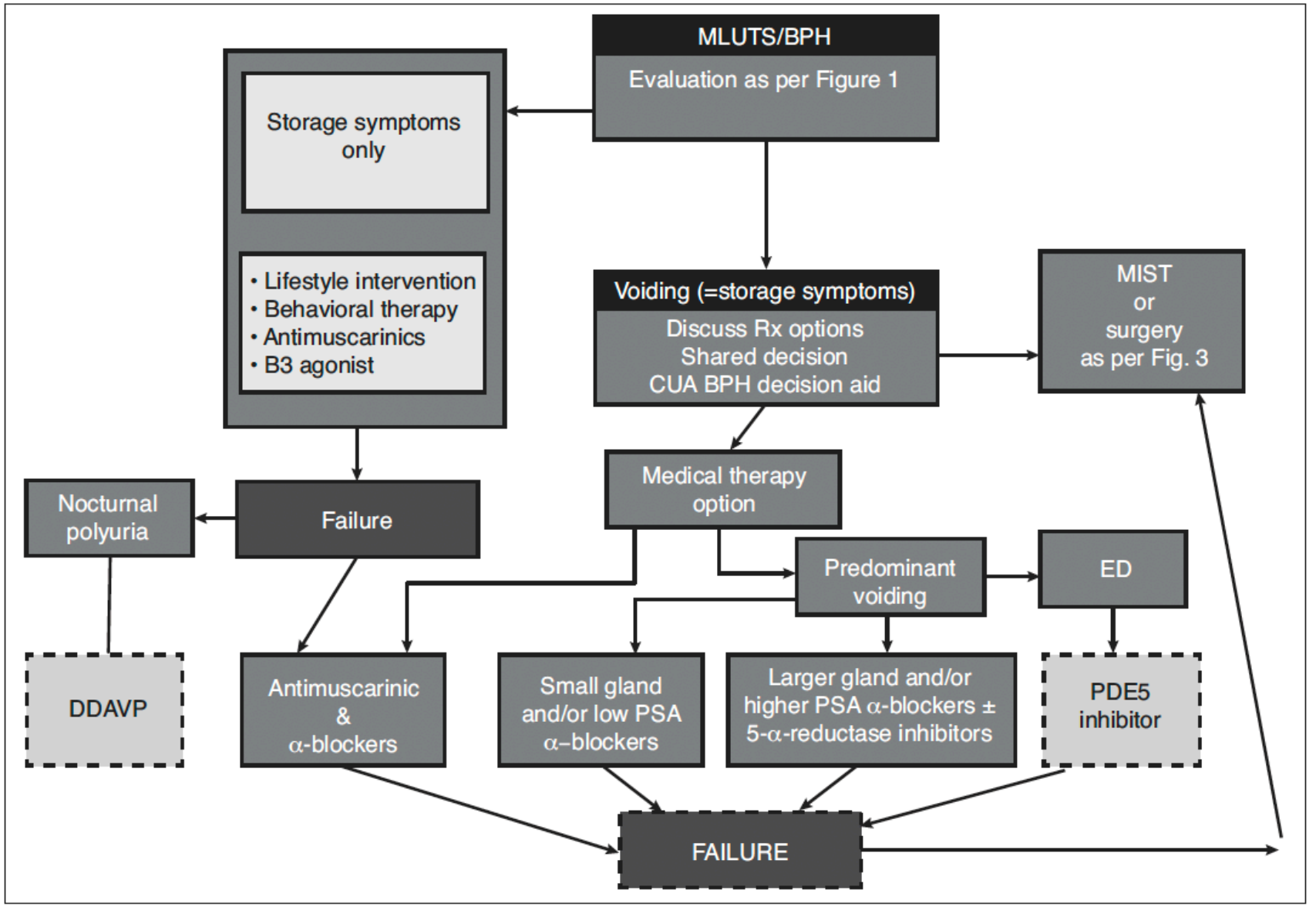


Figure 2. Male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH) management algorithm. ED: erectile dysfunction; PDE5: phosphodiesterase type 5; PSA: prostate-specific antigen.

Elterman, D. ., Aubé-Peterkin, M., Evans, H. ., Elmansy, H. ., Meskawi, M. ., Zorn, K. C. ., & Bhojani, N. (2022). UPDATE – 2022 Canadian Urological Association guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH). *Canadian Urological Association Journal*, *16*(8), 245–56. https://doi.org/10.5489/cuaj.7906

Medical Treatment for BPH-LUTS

- *Alpha Blockers*
  - Do not alter the natural progression of the disease
  - Most common adverse effect is dizziness (2–10%)
  - Retrograde ejaculation
    - Most often with tamsulosin and silodosin
  - Alfuzosin (10mg), Tamsulosin 0.4mg), Silodosin (8mg)
  - Guideline: Excellent first-line therapeutic option for men with symptomatic bother due to BPH who desire treatment

Bozlu M, Ulusoy E, Cayan S, et al. A comparison of four different alpha 1-blockers in benign prostatic hyperplasia patients with and without diabetes. *Scand J Urol Nephrol* 2004;38:391-5. https://doi.org/10.1080/00365590410015678

Medical Treatment for BPH-LUTS

- *5 alpha reductase inhibitors*
  - Alter the natural progression of the disease (reduced risk of acute urinary retention & surgery)
  - Efficacy is noted in patients with a prostate volume >30 cc (and/or PSA levels >1.5 ng/ml) →25-30% shrinkage
  - Side effects: erectile dysfunction (9%), decreased libido (6%), ejaculation disorders (2%), and rarely, gynecomastia (2.8%) and post-finasteride syndrome.
  - Guideline: 5-ARI are an appropriate and effective treatment for patients with LUTS associated with demonstrable prostatic enlargement

Trost L, Saitz TR, Hellstrom WJ. Side Effects of 5-Alpha Reductase Inhibitors: A Comprehensive Review. Sex Med Rev. 2013 May;1(1):24-41. doi: 10.1002/smrj.3. Epub 2015 Oct 21. PMID: 27784557.

Medical Treatment for BPH-LUTS

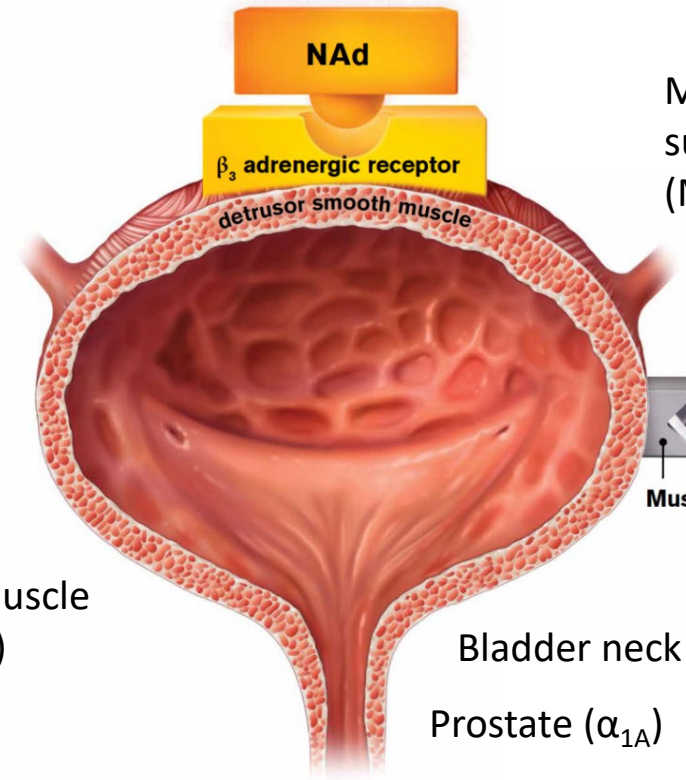
- *Combination (alpha blocker and 5ARI)*
  - Clinical trial results have shown that combination therapy significantly improves symptom score and peak urinary flow compared with either of the monotherapy options.
  - Decreased risk of urinary retention and/or prostate surgery but
    - Additive side effects (ejaculatory disturbances)
  - Guideline: Combination therapy is recommended for men with enlarged prostates
    - Discontinuing the alpha blocker after 6-9 months of combination therapy is appropriate

McConnell JD, Roehrborn CG, Oliver OM, et al for the MTOPS Research Group. The long term effect of doxazosin, finasteride and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med* 2003;349:2385-96. https://doi.org/10.1056/NEJMoa030656

Bladder Functioning Involves Both The Muscarinic And B-3 Adrenergic Receptors

M = muscarinic
α = α_1 and α_2-adrenergic
β = β_3-adrenergic
NAd = noradrenaline
ACH = acetylcholine

STORAGE PHASE
Sympathetic nerves release NAd, activating **β-adrenoceptors** to **relax** the bladder



Mucosa and submucosa (M_2, M_3)

VOIDING PHASE
Parasympathetic nerves release ACH, activating **M receptors** to **contract** the bladder

Detrusor muscle (M_2, M_3, β_3)

Bladder neck & urethra (α_{1A})

Prostate (α_{1A})

In OAB, the bladder leaves the storage phase by suddenly and involuntarily contracting.

Fowler CJ et al. *Nat Rev Neurosci* 2008;9(6):453-466. François N et al. Chapter 7, In: *Male lower urinary tract symptoms and benign prostatic hyperplasia*, 2014.

Medical Treatment for BPH-LUTS

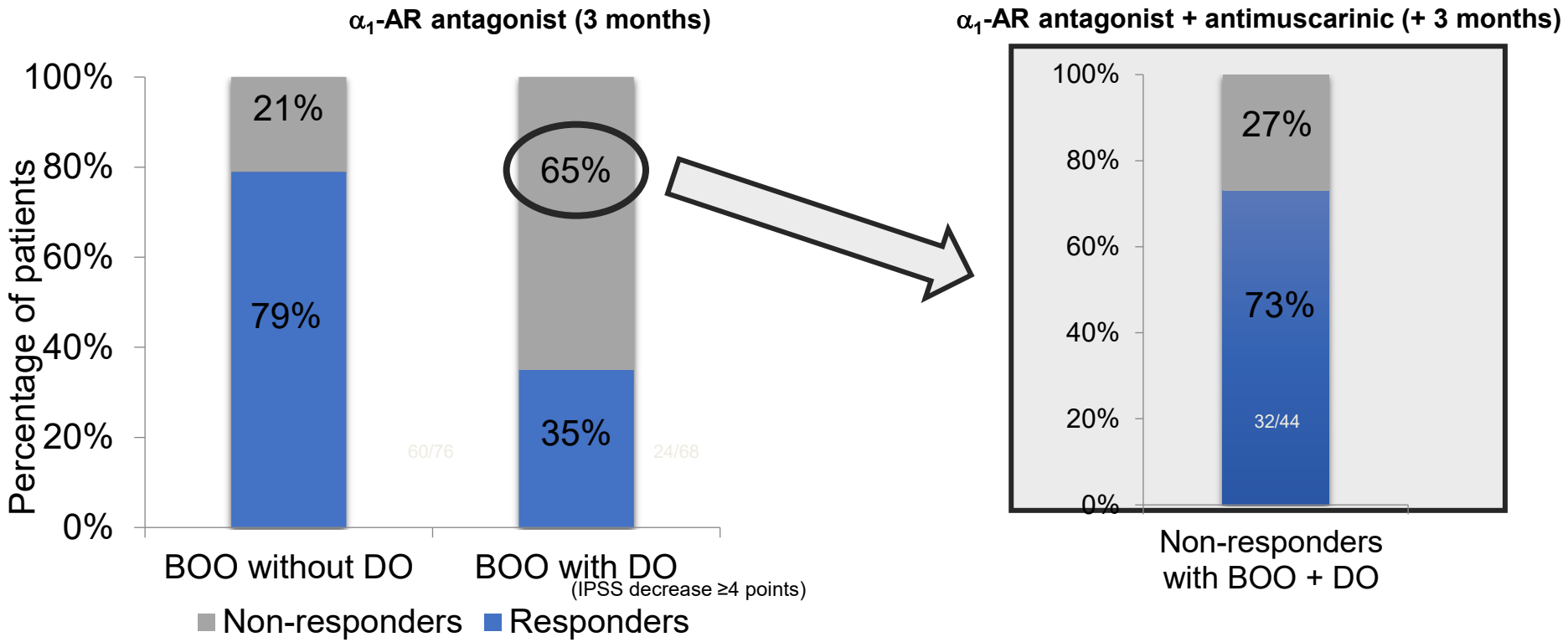
- *Antimuscarinic and Beta-3 Agonist*
  - Storage symptoms (urgency, frequency, nocturia) are a bothersome component of MLUTS
  - Low rates of urinary retention
  - Caution used in elderly men and bladder outlet obstruction (BOO) (with post void residual >250–300 cc
  - Guideline: Suggest AM or B-3 useful therapies in MLUTS with caution in those with significant BOO and/or PVR

Tubaro A, Batista JE, Nitti VW, et al. Efficacy and safety of daily mirabegron 50 mg in male patients with overactive bladder: A critical analysis of five phase 3 studies. *Ther Adv Urol* 2017;10;9:137-54. https://doi.org/10.1177/1756287217702797

Kaplan SA, Herschorn S, McVary KT, et al. Efficacy and Safety of Mirabegron versus Placebo Add-On Therapy in Men with Overactive Bladder Symptoms Receiving Tamsulosin for Underlying Benign Prostatic Hyperplasia: A Randomized, Phase 4 Study (PLUS). *J Urol* 2020 Jun; 203(6):1163-1171. https://doi: 10.1097/JU.0000000000000738

Chapple C, Herschorn S, Abrams P, et al. Tolterodine treatment improves storage symptoms suggestive of overactive bladder in men treated with alpha-blockers. Eur Urol 2009 Sep;56(3):534-41. https:// doi: 10.1016/j.eururo.2008.11.026

a1-adrenergic receptor antagonist monotherapy is not sufficient in all men with LUTS



- AR, adrenergic receptor; BOO, bladder outlet obstruction; DO, detrusor overactivity; IPSS, International Prostate Symptom Score.
Lee JY, *et al*. *BJU Int.* 2004;94:817–820.

Medical Treatment for BPH-LUTS

- *Combination (Antimuscarinic or beta 3 agonists in combination with alpha blockers)*
  - Mixed LUTS (storage and voiding symptoms) can be managed safely with alpha-blockers in combination with antimuscarinics or beta 3 agonists.
  - Clinical trials studied:
    - Tamsulosin 0.4mg plus solifenacin 5mg
    - Tamsulosin plus tolterodine ER 4mg
    - Tamsulosin 0.4mg plus mirabegron 50mg
  - Evidence showed that combination therapies provide significant improvement in storage symptoms without clinical or statistical evidence of decreased maximum flow rate or increased risk of retention

    *Patient with high PVR >200ml or previous history of retention were excluded

Medical Treatment for BPH-LUTS

- *PDE5 inhibitors*
  - Tadalafil 5 mg daily, due to its longer half-life, is approved for male LUTS.
  - Studies have shown improvements in IPSS, storage and voiding symptoms, and quality of life
  - Recommend long-acting PDE5Is particularly men with both MLUTS and erectile dysfunction

Gacci M, Corona G, Salvi M, et al. A systematic review and meta-analysis on the use of phosphodiesterase 5 inhibitors alone or in combination with α-blockers for lower urinary tract symptoms due to benign prostatic hyperplasia. Eur Urol 2012 May;61(5):994-1003. https:// doi: 10.1016/j.eururo.2012.02.033

Medical Treatment for BPH-LUTS

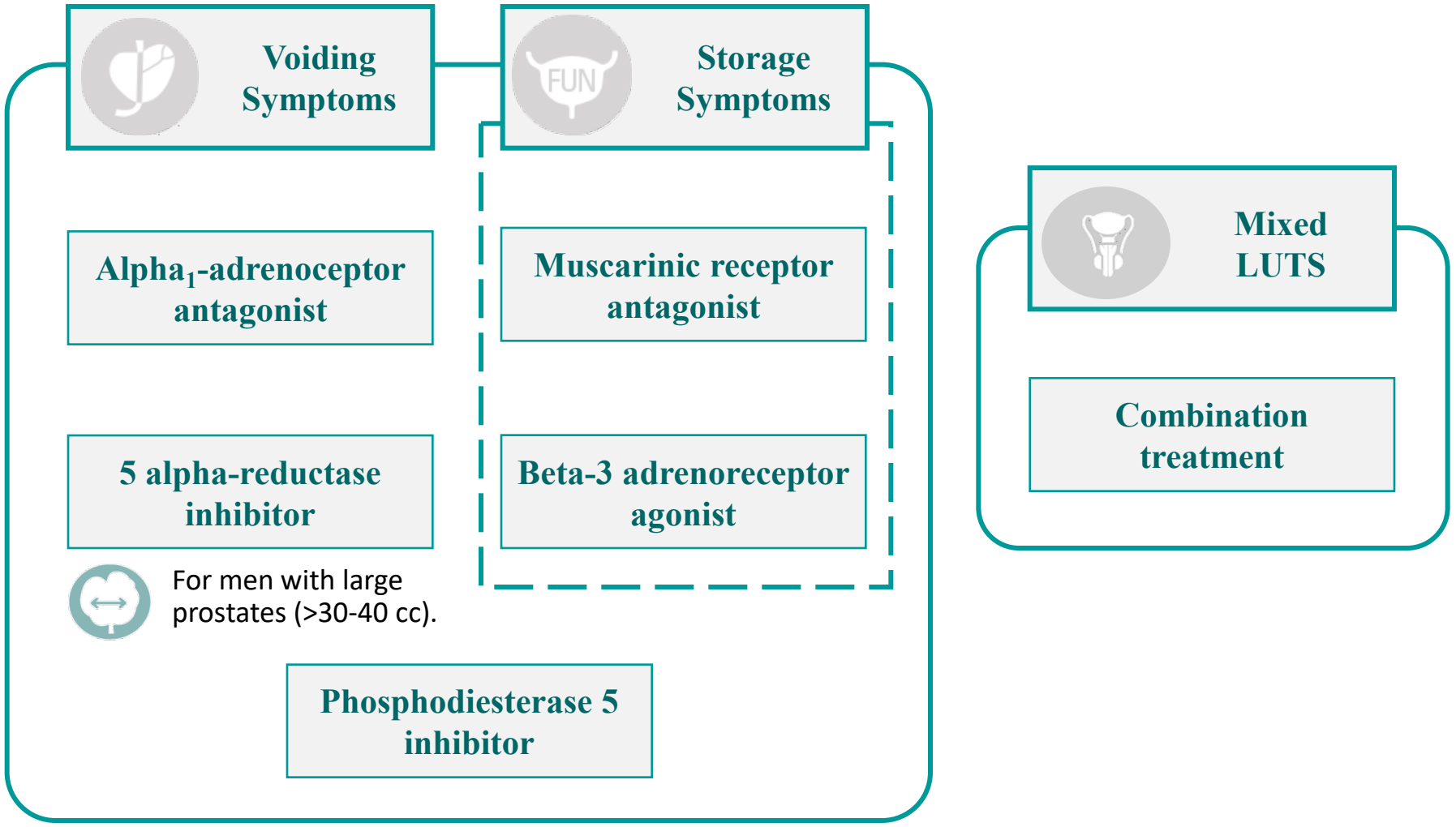
- *Nocturnal polyuria*
  - Often coexists with male LUTS and BPH but may not respond to typical BPH pharmacotherapies
  - Major contributing factor of nocturia and is defined as
    - Abnormally large volume of urine during sleep
      - 33% of the total daily urine volume occurs at night

Gacci M, Corona G, Salvi M, et al. A systematic review and meta-analysis on the use of phosphodiesterase 5 inhibitors alone or in combination with α-blockers for lower urinary tract symptoms due to benign prostatic hyperplasia. Eur Urol 2012 May;61(5):994-1003. https:// doi: 10.1016/j.eururo.2012.02.033

Medical Treatment for BPH-LUTS

- *Desmopressin*
  - Synthetic analogue of the antidiuretic hormone, arginine vasopressin (AVP)
  - Reduces total nocturnal voids
  - Increases hours of undisturbed sleep by reducing urine production in men with nocturnal polyuria
  - Low risk of hyponatremia when baseline sodium is normal
  - Sodium must be checked at baseline, at 4-8 days and at 30 days after initiation of treatment
  - Guidelines: recommend desmospression as a therapeutic option in men with LUTS/BPH with. Nocturia as a result of nocturnal polyuria

Summary of key treatment recommendations for men



An international consultation on male LUTS. SIU. 2012; Guidelines on the Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO). European Association of Urology. 2014; Nickel JC et al. *Can Urol Assoc J.* 2010;4(5):310-316; Diagnosis and Treatment of Overactive Bladder(Non-Neurogenic) in Adults: AUA/SUFU Guideline. 2014.

Surgical therapy

CUA BPH Guidelines

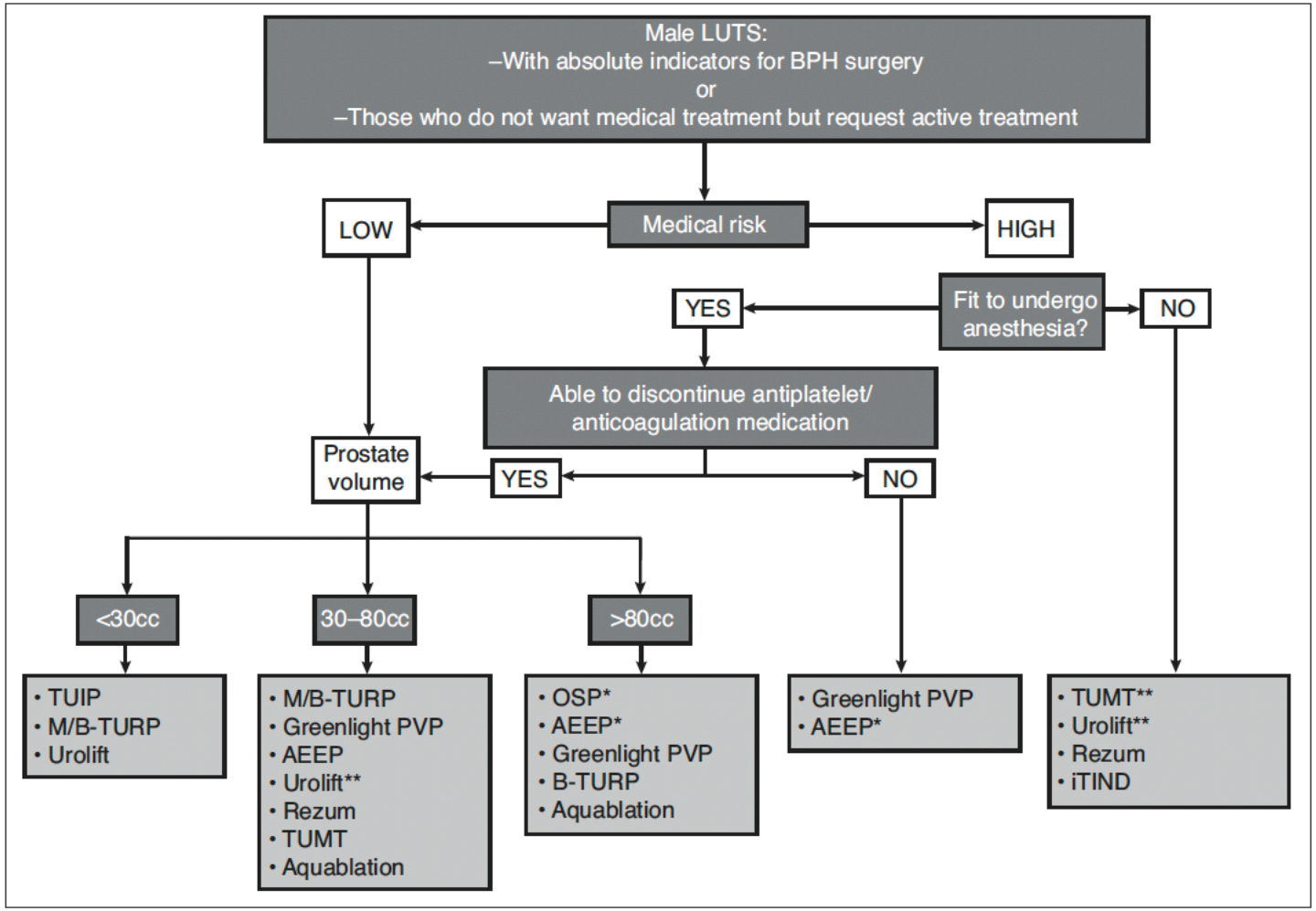


Figure 3. Treatment algorithm of bothersome lower urinary tract symptoms (LUTS) refractory to conservative/medical treatment or in cases of absolute operation indications. The flowchart was stratified by the patient's ability to have anesthesia, cardiovascular risk, and prostate volume. *Current standard/first choice. The alternative treatments are presented in alphabetical order. **Must exclude the presence of a middle lobe. BPH: benign prostatic hyperplasia; B-TURP: bipolar transurethral resection of the prostate; HoLEP: holmium laser enucleation of the prostate; iTIND: temporary implantable nitinol device; M/TURP: monopolar transurethral resection of the prostate; PVP: photoselective vaporization of the prostate; TUIP: transurethral incision of the prostate; TUMT: transurethral microwave therapy.

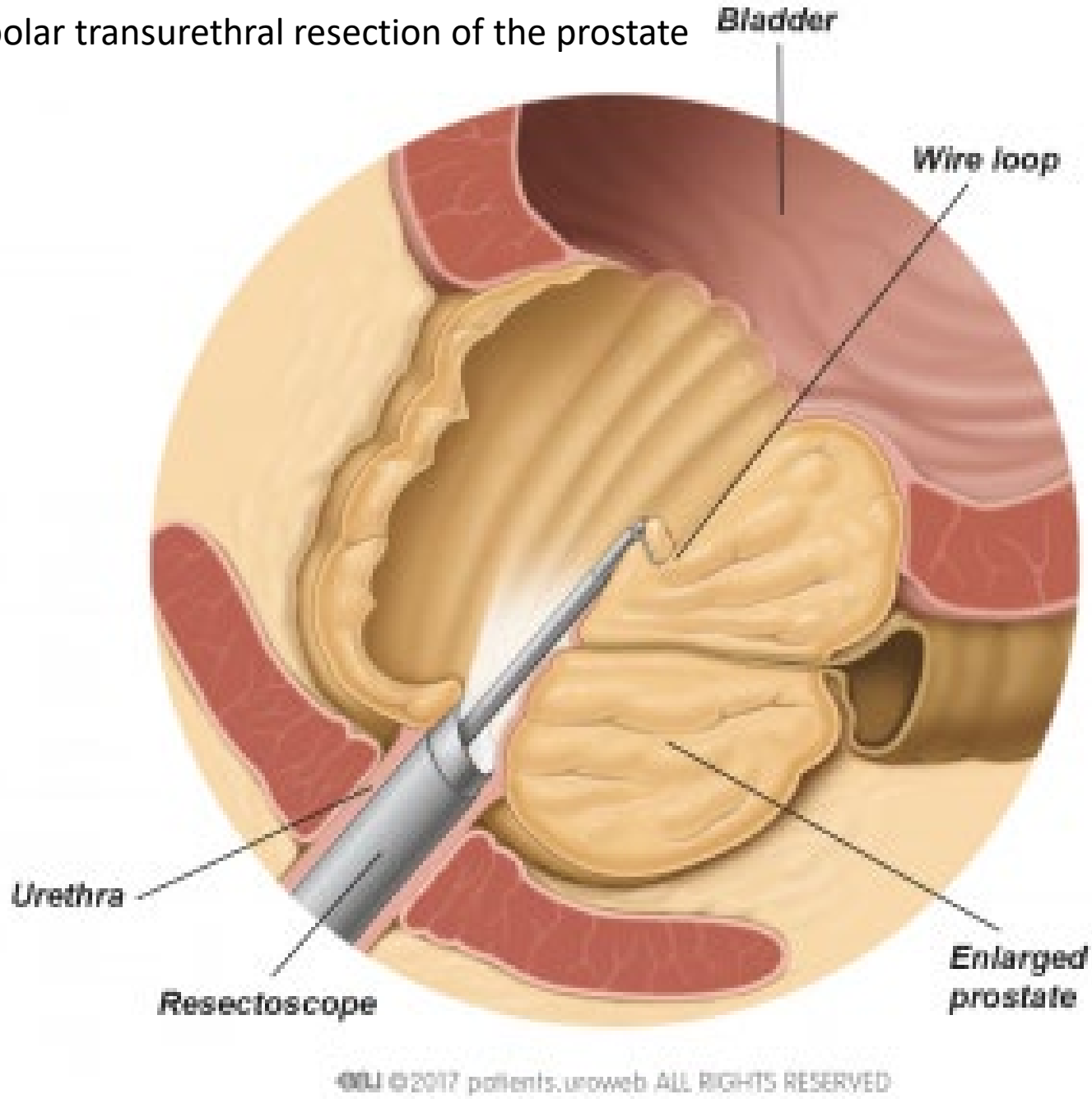
Elterman, D. ., Aubé-Peterkin, M., Evans, H. ., Elmansy, H. ., Meskawi, M. ., Zorn, K. C. ., & Bhojani, N. (2022). UPDATE – 2022 Canadian Urological Association guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH). *Canadian Urological Association Journal*, *16*(8), 245–56. https://doi.org/10.5489/cuaj.7906

Evolution

- Monopolar turp
- Open simple prostatectomy

- MONOPOLAR TURP
- OPEN SIMPLE PROSTATECTOMY
- BIPOLAR TURP
- PROSTATIC URETHRAL LIFT; UROLIFT (MIST)
- CONVECTIVE WATER VAPOR ENERGY ABLATION; REZUM (MIST)
- ANATOMICAL ENDOSCOPIC ENUCLEATION OF THE PROSTATE (AEEP)
- GREENLIGHT VAPORIZATION
- IMAGE-GUIDED ROBOTIC WATERJET ABLATION (AQUABLATION)
- ROBOTIC SIMPLE PROSTATECTOMY

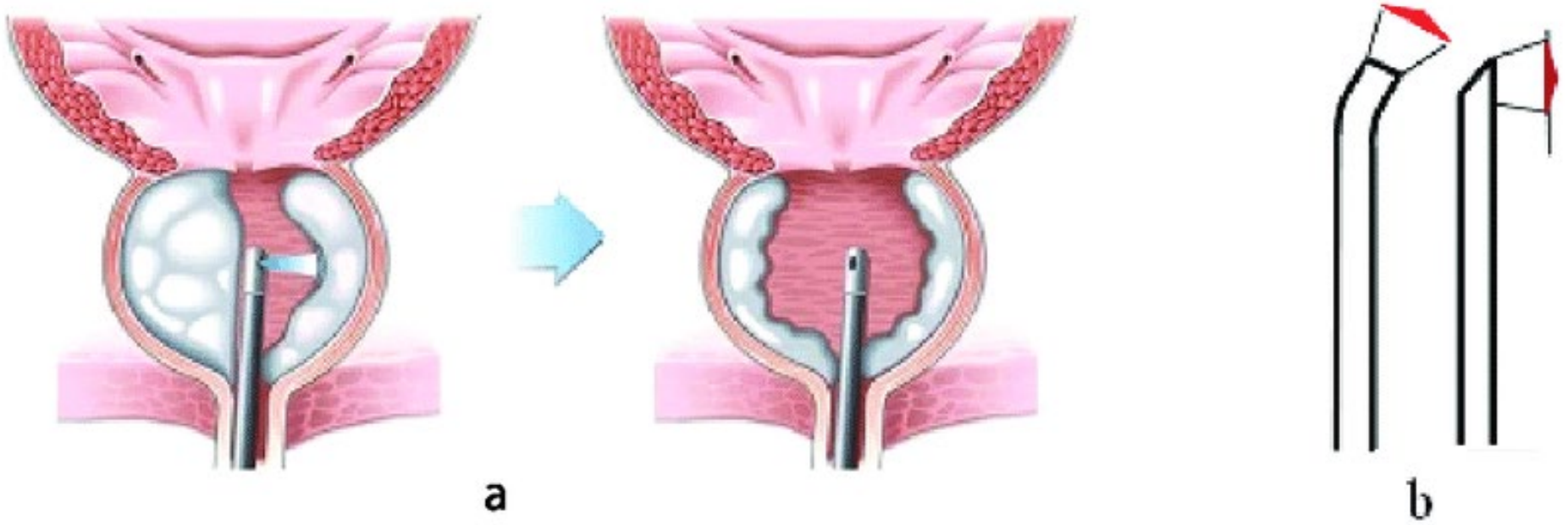
Monopolar transurethral resection of the prostate



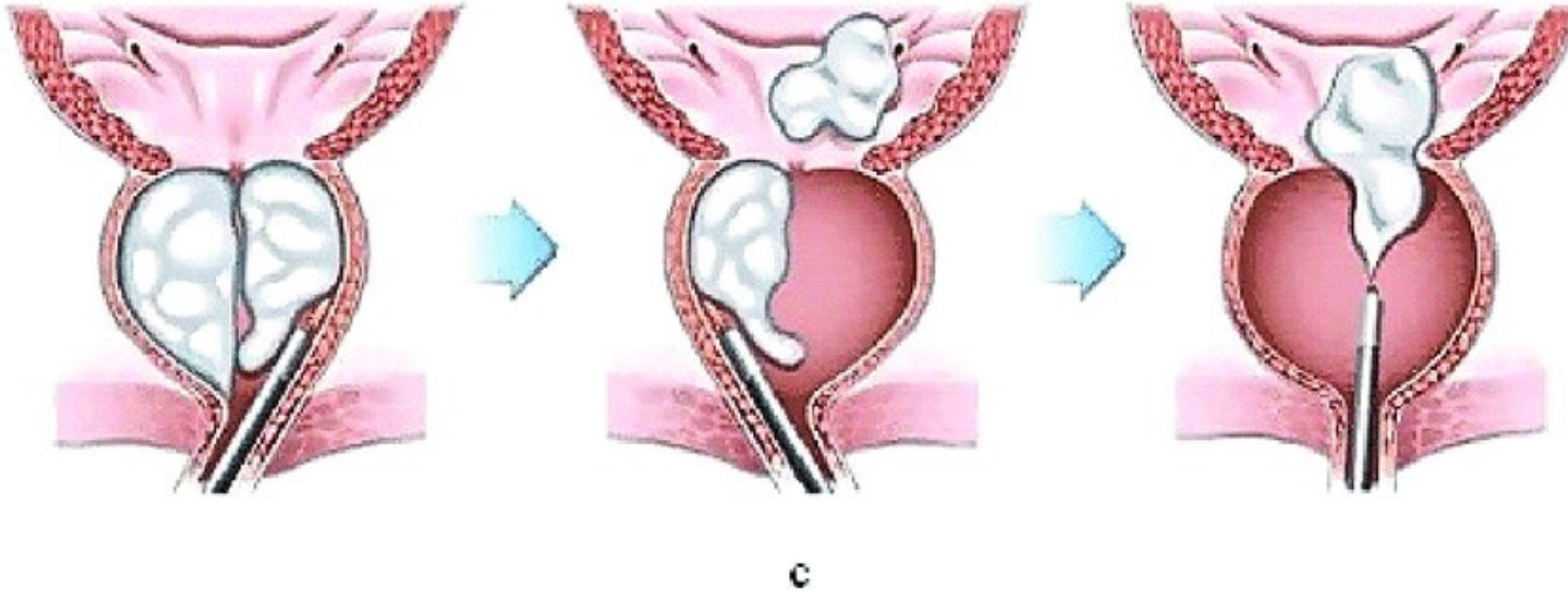
Monopolar transurethral resection of the prostate

- Primary, standard-reference surgical treatment option for moderate to severe LUTS due to BPH with prostate volume 30-80 cc.

Laser Vaporization Guidelines: Recommended as alternative to TURP especially for patients who are anticoagulated

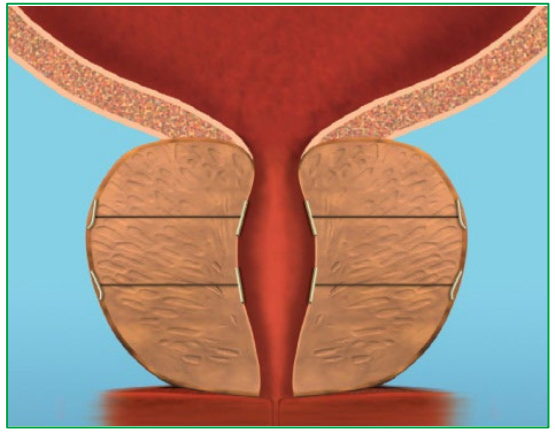


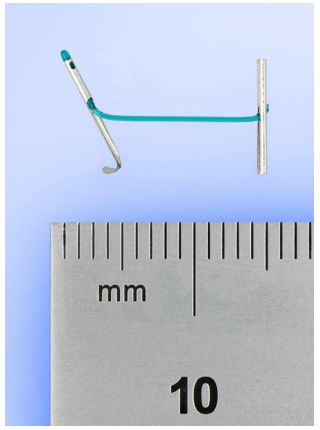
Anatomical Endoscopic Enucleation of the Prostate (AEEP) Guidelines: Recommended as alternative to TURP for any size prostate and in patients who are anticoagulated



Minimally Invasive Surgical Therapies (MIST)

- Prostatic urethral lift





- Convective water vapor energy ablation

- Guidelines: MIST is recommended for patients with prostate glands 30-80cc and patients who want to maintain ejaculatory function

*MIST only available privately in most provinces

IMAGE-GUIDED ROBOTIC WATERJET ABLATION (AQUABLATION)

ONLY IMAGE-GUIDED, HEAT-FREE, AUTOMATED ROBOTIC THERAPY FOR BPH

REAL-TIME IMAGE GUIDANCE

Intraoperative ultrasound imaging combined with cystoscopic visualization provide a multidimensional view of the treatment area

PERSONALIZED TREATMENT PLANNING

Advanced planning software allows the surgeon to map the treatment contour by identifying tissue to preserve and resect

AUTOMATED ROBOTIC EXECUTION

Robotic execution of the waterjet along the treatment plan results in standardized outcomes and operative experience

HEAT-FREE WATERJET RESECTION

Heat-free waterjet precisely removes prostate tissue and minimizes thermal damage to surrounding tissue

AQUABEAM®
ROBOTIC SYSTEM

- Guidelines: Aquablation recommended for patients with prostate glands <150cc and patients who want to maintain ejaculatory function

Summary

- Male LUTS
  - One of the most common age-related disorders afflicting men
- CUA BPH guidelines
  - Storage vs voiding sx based on work up/evaluation
- Medical management still effective
- Significant evolution in the surgical management of BPH
  - Now many more options than ever before
  - Surgery can now be made to measure based on patient characteristics, values and objectives.

Thank you

Canadian Urological Association
The Voice of Urology in Canada

Association des Urologues du Canada
La voix de l'urologie au Canada

Diagnosis and management of BPH

Speaker

Naeem Bhojani

Professor

University of Montreal