



BPH (Male LUTS) Management

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No Disclosures

Objectives

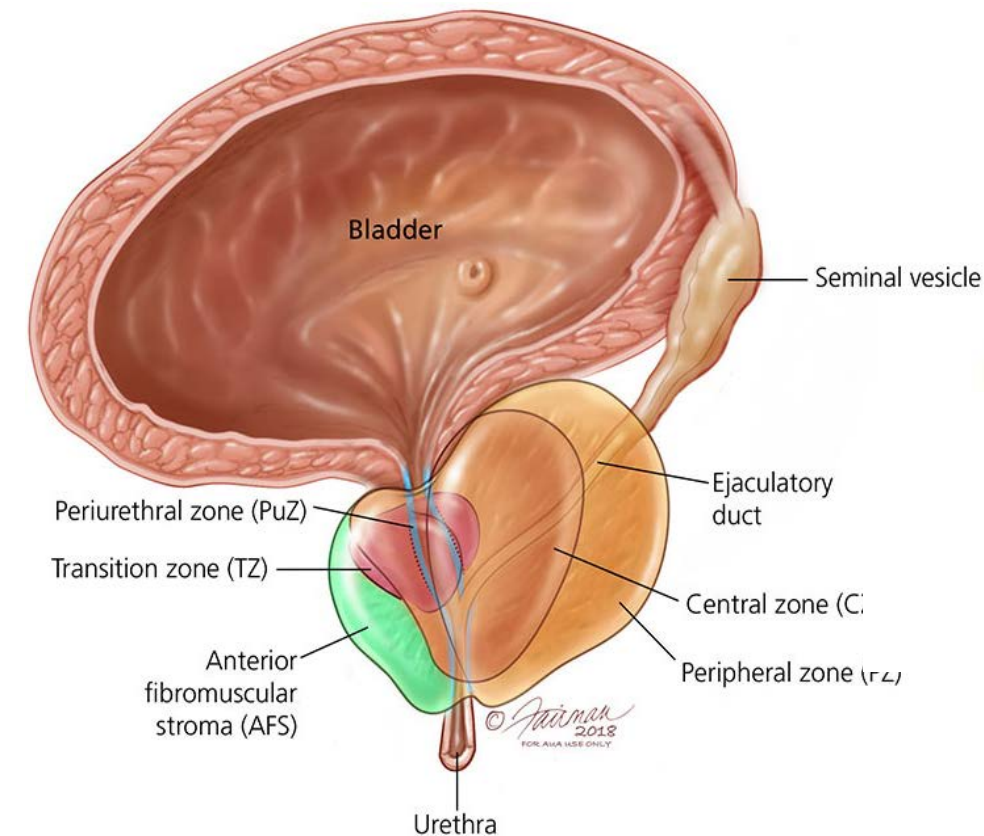
- Differential diagnosis for BPH
- Review of AUA guidelines for diagnosis and treatment of BPH
- Understand the benefits and shortcomings of medical management for BPH
- Review traditional therapies for treating BPH
- Current practice with minimally invasive therapies for BPH
- What's on the Horizon
- When to refer to Urology

About Me

- Born in Canton, OH
- Went to Ohio State for undergraduate and medical school
- Residency at Georgetown University in Washington, DC
- Private practice in 2 years in Baltimore, MD
- Joined faculty at Ohio State in September 2020

The Prostate

- Secretes fluid components of ejaculate
- Transition zone
 - 5-10% of glands
 - BPH
- Peripheral zone
 - 70% of glands
 - 70% of prostate cancer
- Smooth Muscle: 20% of prostate cells
- Facilitate propulsion of ejaculate
- Stimulation increases urethral resistance

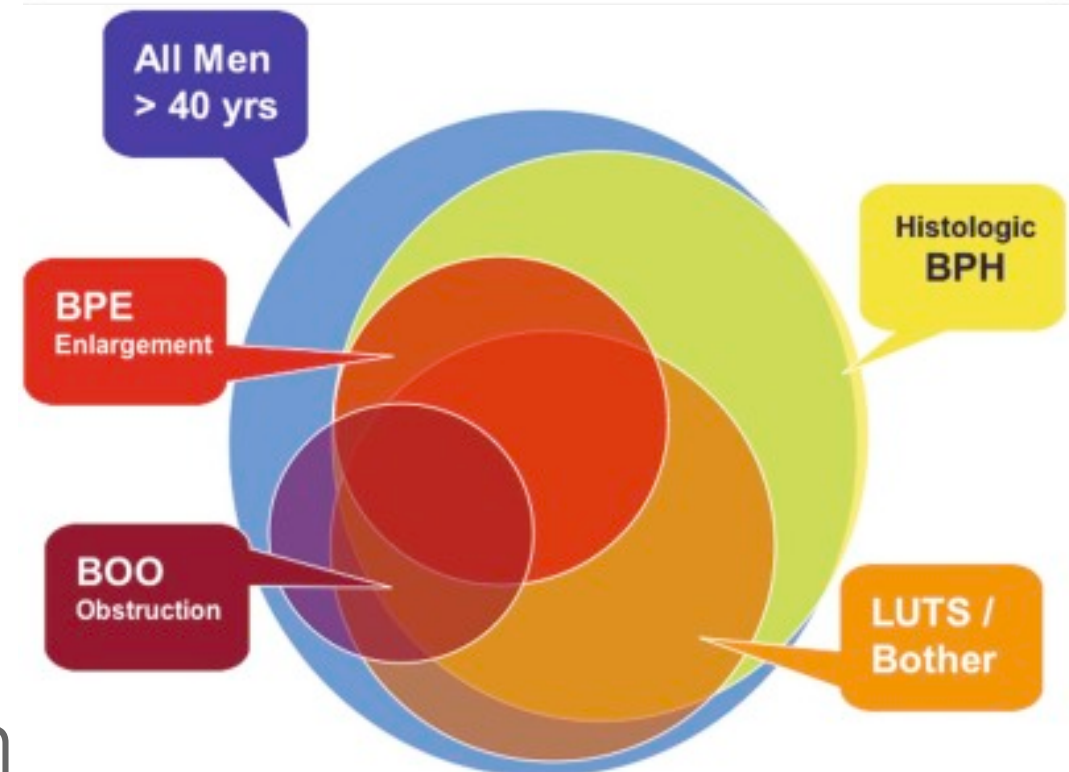
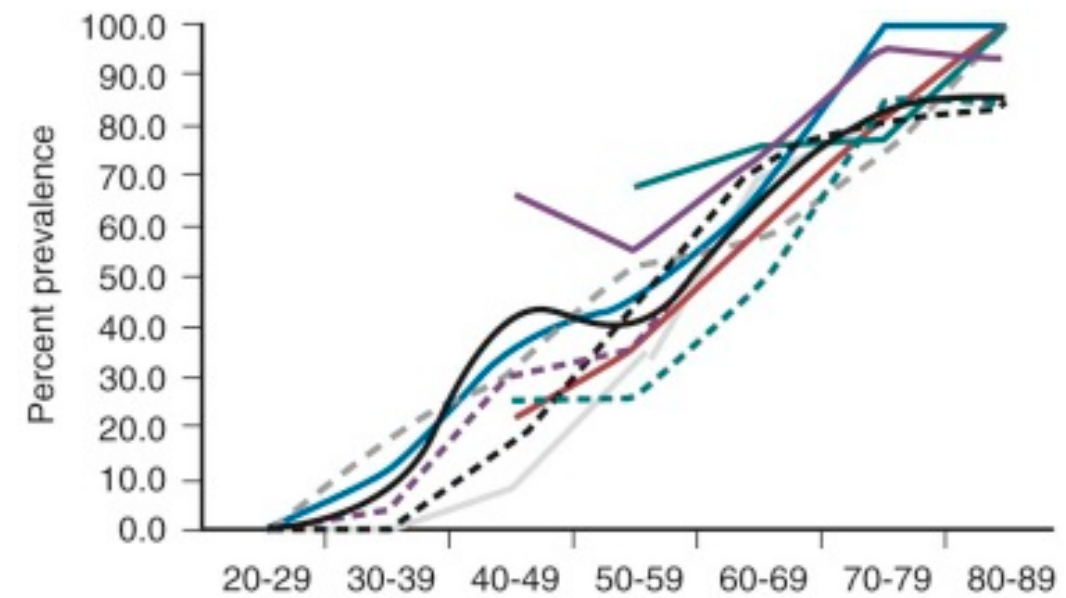


Benign Prostatic Hyperplasia (BPH):

- Increased proliferation of glandular cells causes compression of the urethral canal
→ urinary obstruction
- Result: Lower Urinary Tract Symptoms (LUTS)
 - Weak urinary stream
 - Frequency
 - Urgency
 - Nocturia
 - Incomplete emptying
 - Urinary retention
- Differential considerations
 - Overactive bladder
 - Prostatitis (UTI, CP/CPPS)
 - Bladder cancer
 - Urethral stricture

BPH \approx LUTS

- BPH prevalence (Autopsy)
 - Rare under 30
 - 88% of men in their 80s
 - Similar across racial/ethnic groups
- LUTS prevalence:
 - 25-40% in 40s-50s
 - 50-75% in 70s-80s
- Key points:
 - Not all men with BPH/prostate enlargement develop symptoms
 - Men without enlarged prostates can have symptoms



International Prostate Symptoms Score (IPSS)

Over the past month, how often have you:
0 (not at all) – 5 (almost always)

- | | | | | | | |
|--|---|---|---|---|---|---|
| ■ Incomplete emptying | 0 | 1 | 2 | 3 | 4 | 5 |
| ■ Frequent urination every 2h or less | 0 | 1 | 2 | 3 | 4 | 5 |
| ■ Intermittent stream (stop and start) | 0 | 1 | 2 | 3 | 4 | 5 |
| ■ Urgent urination (difficult to postpone) | 0 | 1 | 2 | 3 | 4 | 5 |
| ■ Weak urinary stream | 0 | 1 | 2 | 3 | 4 | 5 |
| ■ Strain to urinate | 0 | 1 | 2 | 3 | 4 | 5 |
| ■ # nocturia episodes nightly | 0 | 1 | 2 | 3 | 4 | 5 |

Score:

1-7 Mild 8-19 Moderate 20-35 Severe

- Quality of life: 0 (delighted) – 6 (Terrible)

Treatment options

- Behavioral Interventions
 - Limiting excessive fluid intake, especially prior to bedtime
 - Limiting bladder irritants (caffeine, alcohol, etc.)
- Medical Management
 - α -blockers
 - 5 α -reductase inhibitors
 - PDE-5 inhibitors
- Surgical management
 - Endoscopic
 - Open/robotic
- Intermittent or indwelling catheter/suprapubic tube
- Management of comorbidities (DM, OSA, etc.)

BPH treatment is not just about managing lower urinary tract symptoms, It is about preserving the bladder's ability to function normally.

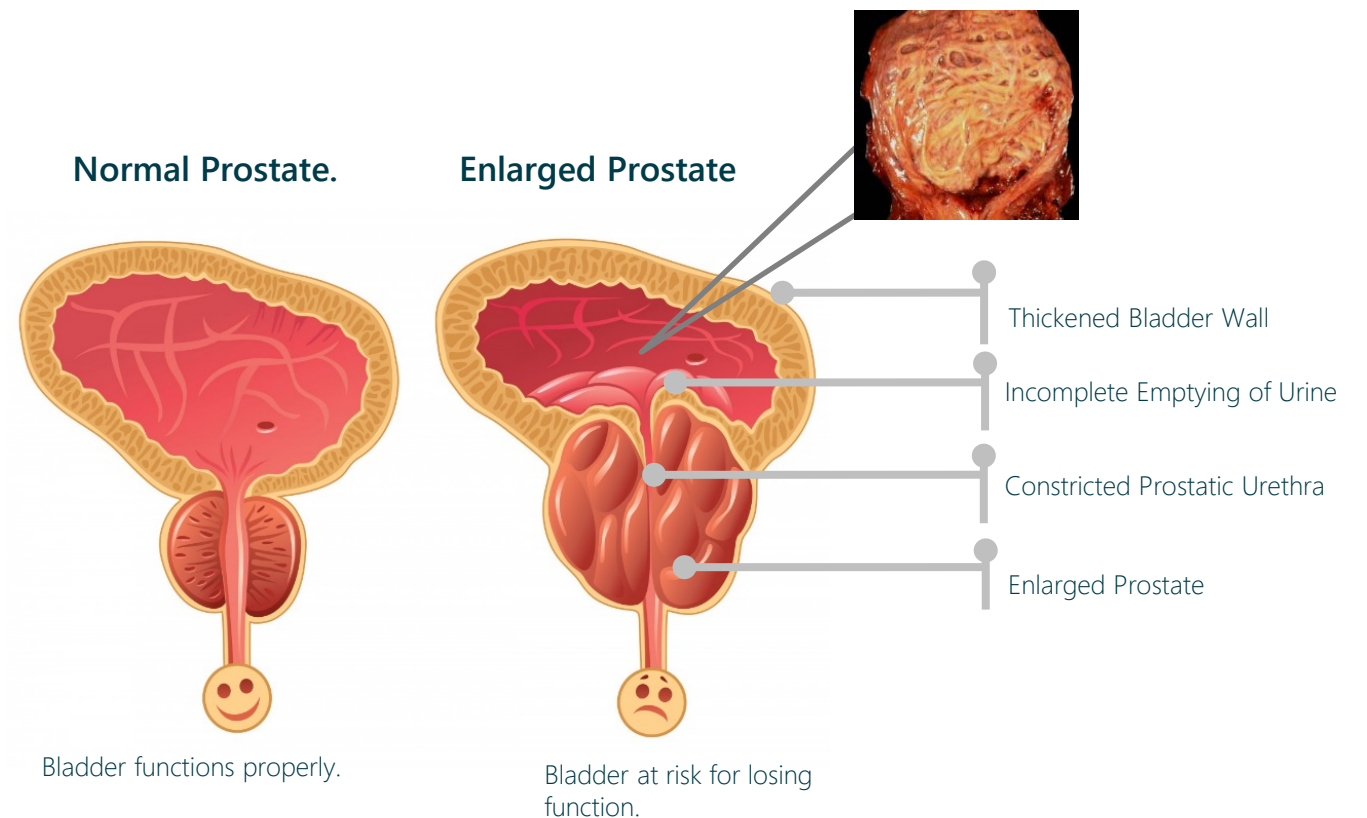
Two important functions of a functioning bladder.

Filling

Bladder needs to accommodate and store urine by **stretching to a reasonable capacity**.

Emptying


Bladder needs to **contract** (pressure) when expelling urine out of the body.



American Urologic Association Guidelines

- 2018/2019 Guidelines

Evaluation and Preoperative Testing

- 
1. Clinicians should take a medical history and utilize the AUA-Symptom Index (AUA-SI) and urinalysis in the initial evaluation of patients presenting with bothersome LUTS possibly attributed to BPH; select patients may also require post-void residual (PVR), uroflowmetry, or pressure flow studies. (Clinical Principle)
 2. Clinicians should consider assessment of prostate size and shape via abdominal or transrectal ultrasound, or cystoscopy, or by preexisting cross-sectional imaging (i.e. magnetic resonance imaging [MRI]/ computed tomography [CT]) prior to surgical intervention for LUTS attributed to BPH. (Clinical Principle)
 3. Clinicians should perform a PVR assessment prior to surgical intervention for LUTS attributed to BPH. (Clinical Principle)
 4. Clinicians should consider uroflowmetry prior to surgical intervention for LUTS attributed to BPH. (Clinical Principle)
 5. Clinicians should consider pressure flow studies prior to surgical intervention for LUTS attributed to BPH when diagnostic uncertainty exists. (Expert Opinion)

Flow studies

Uroflow is an important adjunct in evaluation of BPH
(Clinical principle)

- If the flow is $< 10\text{mLs/sec}$, specificity for obstruction is $\sim 70\%$
- If the flow rate is $> 10\text{mLs/sec}$, surgical treatment may result in failure and patients should be counseled accordingly

Urodynamic testing is the Gold Standard, but often is not necessary and very invasive for the vast majority of BPH patients

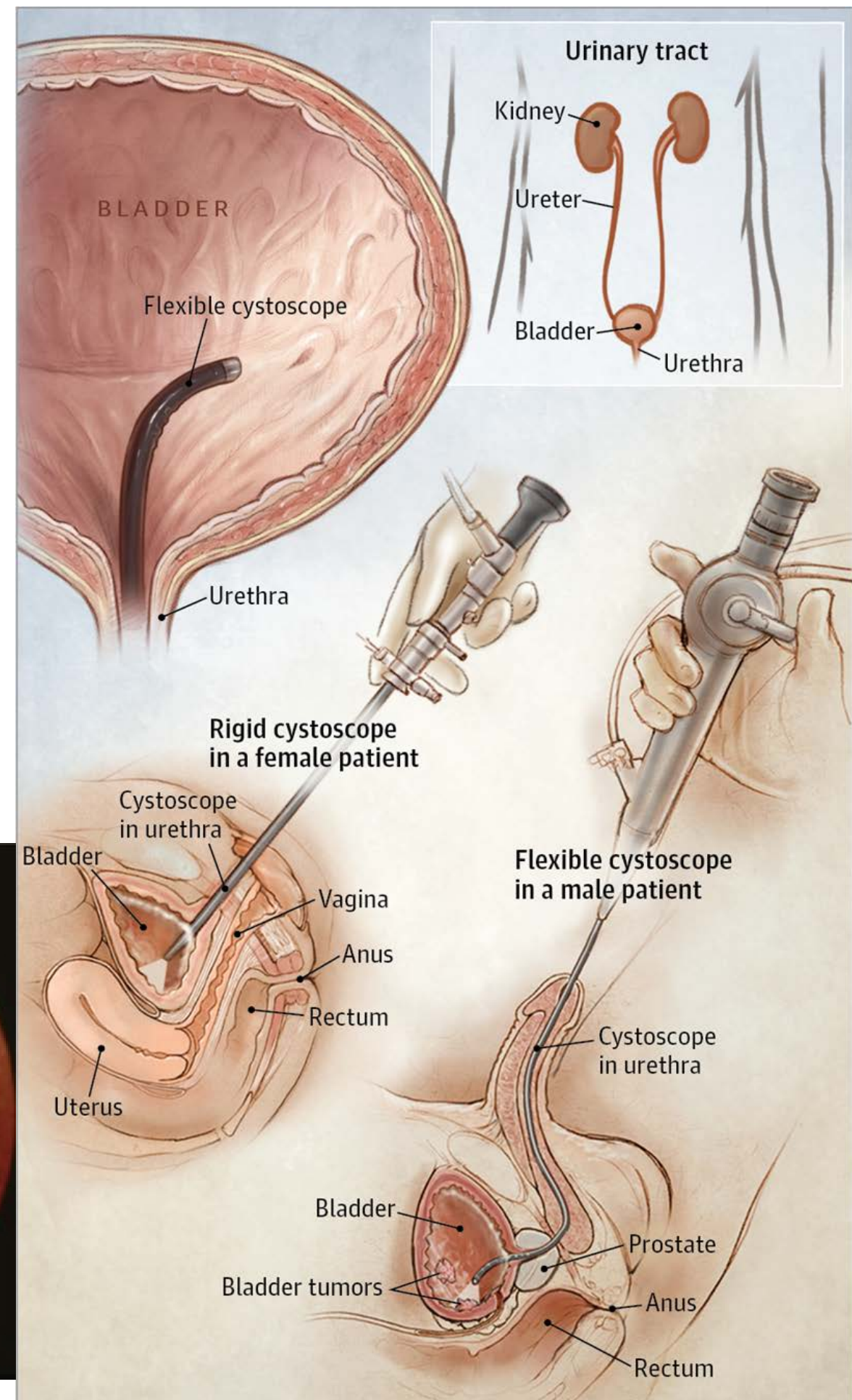
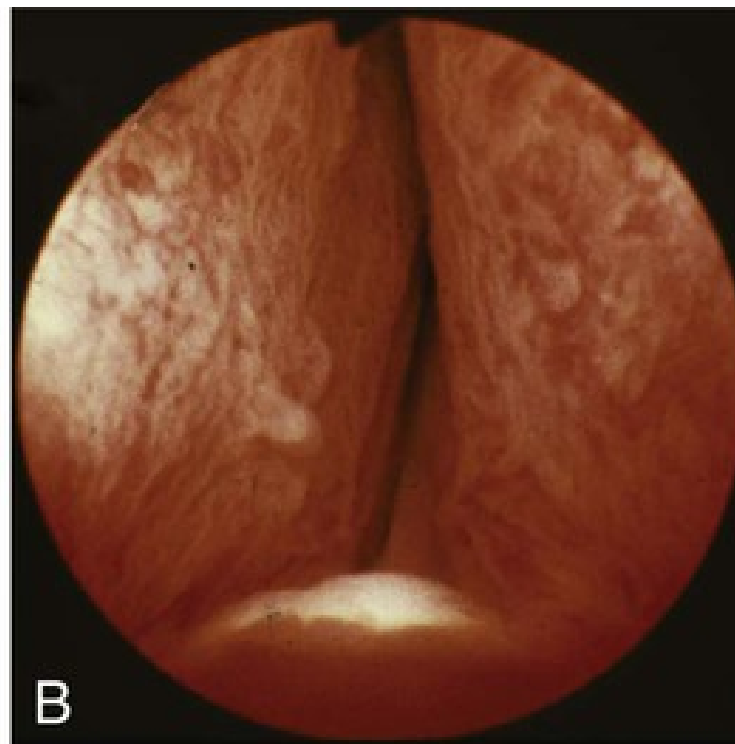
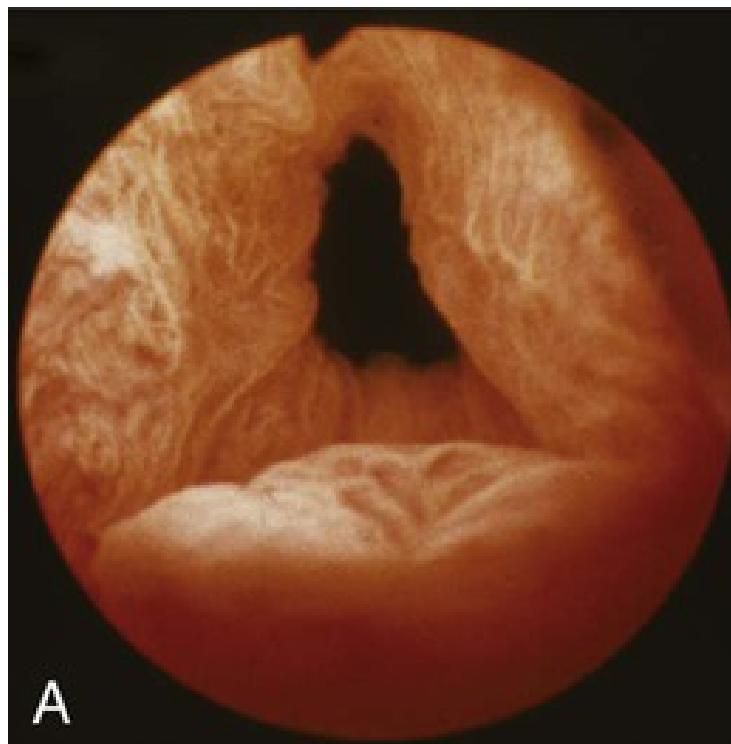


My Practice

- In addition to flow studies for patients who are interested in surgery:
- Cystoscopy
- Prostate sizing (usually transrectal ultrasound at the time of cystoscopy)

Cystoscopy

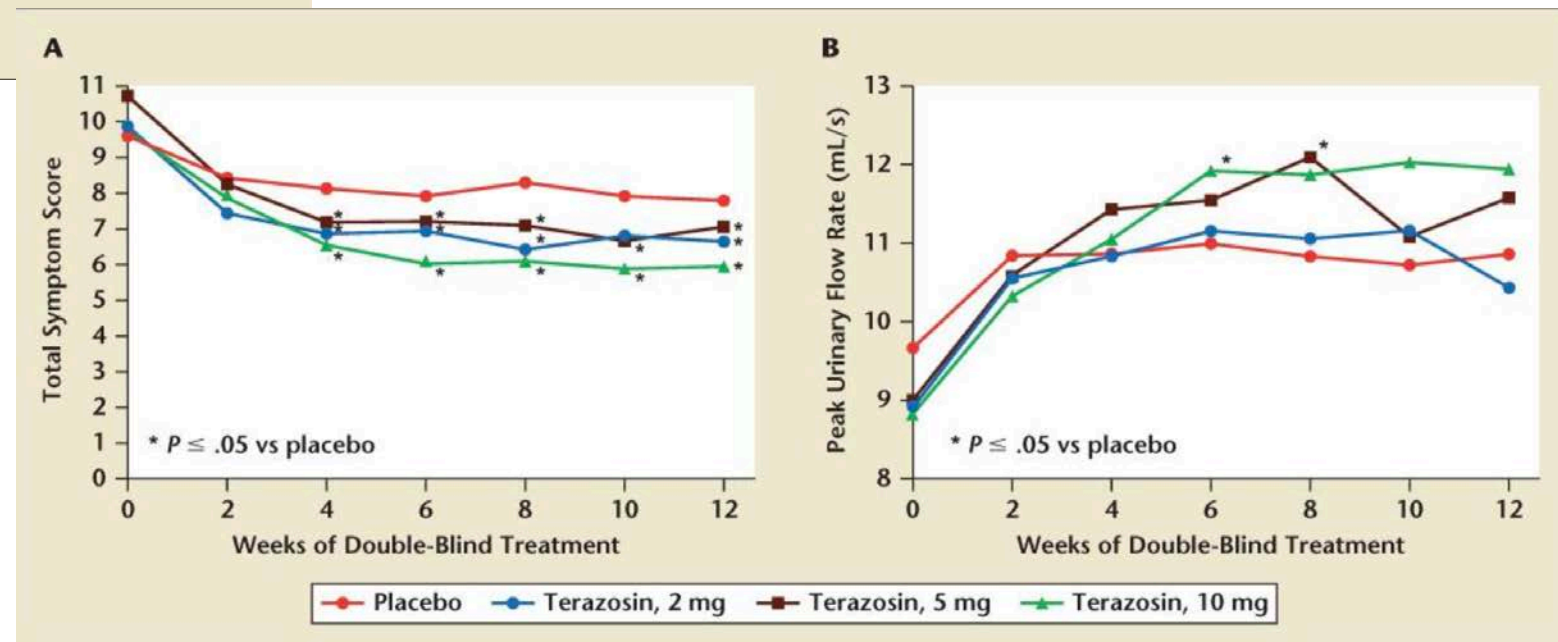
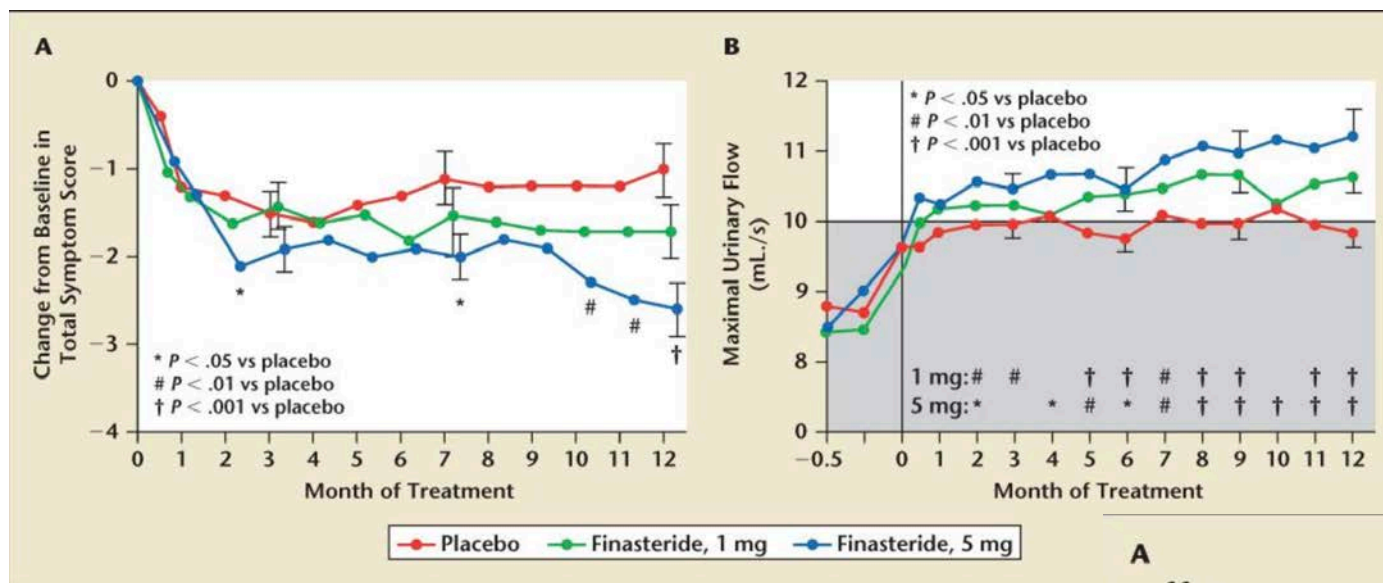
- Direct visualization of urethra and bladder
- Assessment of obstruction



Treatment of BPH

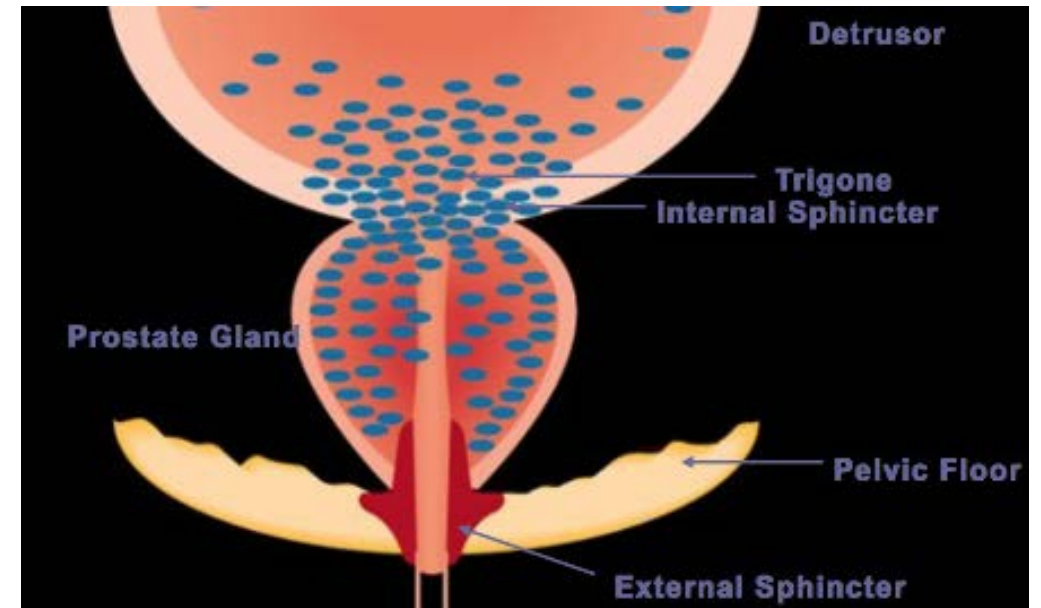
Medical Management

- Randomized, placebo-controlled, double-blinded studies in the early 1990s demonstrated efficacy of alpha blockers and 5-alpha reductase inhibitors



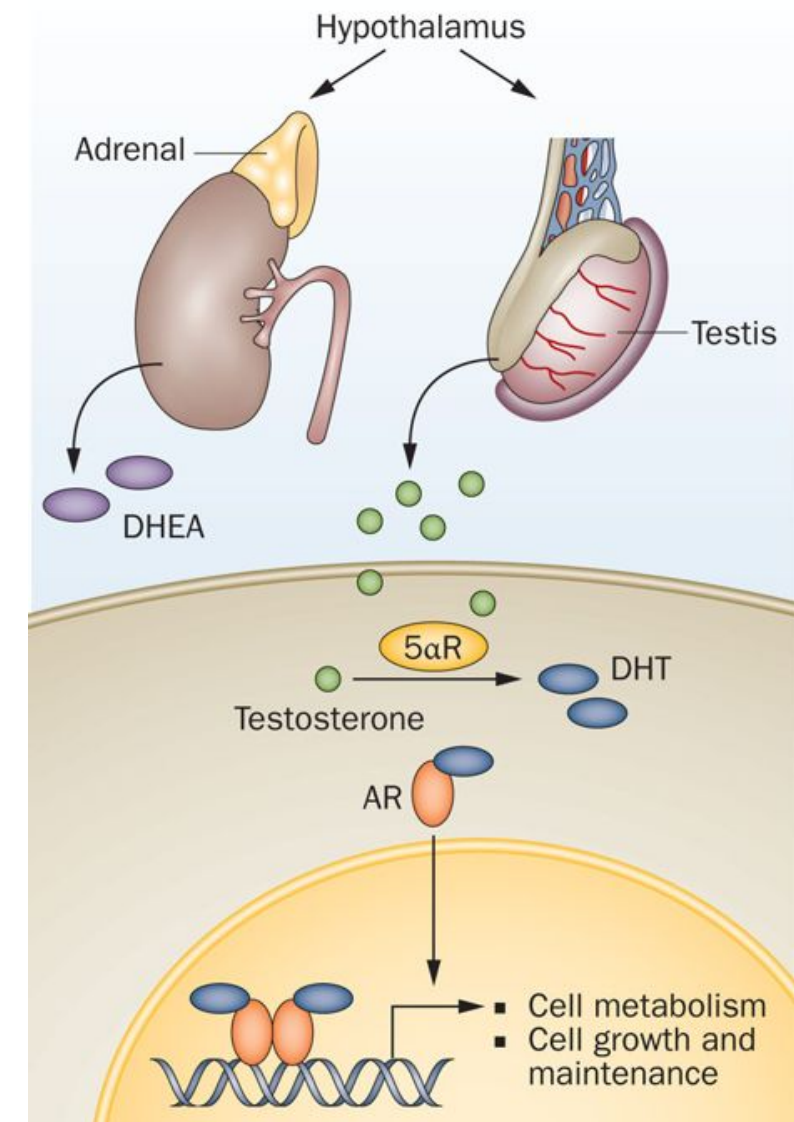
Primary Care Role

- Reasonable to start alpha blocker
- Inhibit smooth muscle contraction
- ~6 point IPSS improvement
- Tamsulosin easily dosed and well tolerated. High rates of retrograde ejaculation.
- Alfuzosin has less chance of retrograde ejaculation
- Silodosin effective, but almost 100% have retrograde ejaculation



Primary Care Role

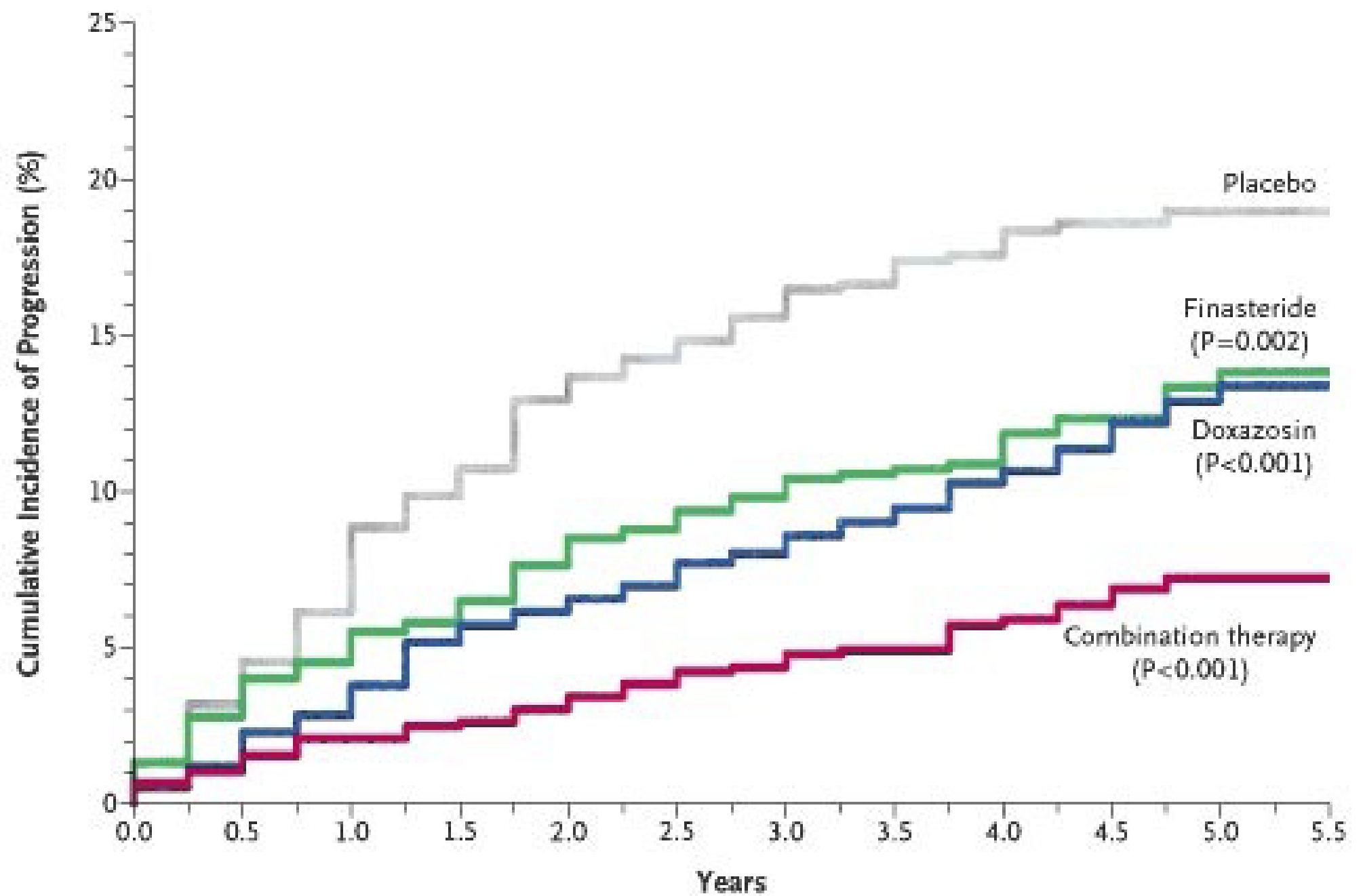
- Can treat 5 alpha reductase
- Blocks enzyme that converts testosterone to DHT
- ~5 point IPSS improvement
- Takes 6 months to start working
- Chance of decreased libido/ED issues
- Will decrease PSA
- High risk prostate cancer Black Box warning
 - Decreases low risk prostate cancer - likely selection bias in study



- In the Medical Therapy of Prostate Symptoms study, combination alpha blocker and 5-alpha reductase inhibitor therapy resulted in a 7.4 point reduction in AUA Symptom Score/IPSS at 4 years¹.
- However, placebo resulted in 4.9 point decrease in symptom score in control arm¹.
- Studies show an almost 50% rate of discontinuation of medical therapy at 6 months, with only ~30% of patients adhering to medication at 1 year².
- Patients who discontinued medical therapy 2.8 times more likely to be hospitalized for BPH-related surgery²

1. McConnell JD, Roehrborn CG, Bautista OM, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. N Engl J Med 2003;349:2387–98.

2. Nichol MB, Knight TK, Wu J, Barron R, Penson DF. Evaluating use patterns of and adherence to medications for benign prostatic hyperplasia. J Urol 2009;181:2214–21.



No. at Risk

Placebo	737	712	670	631	612	588	575	555	492	337	218	84
Doxazosin	756	735	715	698	675	660	641	627	565	387	259	98
Finasteride	768	737	699	675	659	634	617	599	530	379	257	105
Combination therapy	786	762	747	733	726	715	697	683	599	426	280	112

Primary Care Role

- Can trial Tadalafil 5mg
- ?smooth muscle relaxation/increased perfusion
- ~3-5 point IPSS improvement
 - Headaches, GI upset, muscle aches
- Do not recommend combining with α -blockers (for LUTS management)

When should we intervene?

Guideline Statement 6

6. Surgery is recommended for patients who have renal insufficiency secondary to BPH, refractory urinary retention secondary to BPH, recurrent urinary tract infections (UTIs), recurrent bladder stones or gross hematuria due to BPH, and/or with LUTS attributed to BPH refractory to and/or unwilling to use other therapies. (Clinical Principle)

Surgical Therapy for BPH

- Multiple transurethral options available for treating BPH
 - Monopolar TURP
 - Considered the Gold Standard for surgical therapy of BPH
 - Bipolar TURP
 - Laser Therapy
 - Minimally Invasive Therapy (MIT)
- Simple Prostatectomy

TURP

- Simple goal: resect obstructing portion of prostate (transition zone)
- Limited to relatively smaller sized prostates.
- ~13 point IPSS improvement
- Typically want to spend less than 90 min resection due to TUR syndrome risk¹ (monopolar)

Guideline Statement 8

Transurethral Resection of the Prostate (TURP)

8. TURP should be offered as a treatment option for men with LUTS attributed to BPH. (Moderate Recommendation; Evidence Level: Grade B)

1. Mebust, W.K., Holtgrewe, H.L., et. al.: Transurethral prostatectomy: Immediate and Postoperative complications. A cooperative study of 13 participating institutions evaluating 3,885 patients. J Urol, 141: 243, 1989

- Very good outcomes by 3 months
- Some delayed improvement in patients with acontractile or under-active bladder.
- Risks of hematuria, retention, erectile dysfunction, retrograde ejaculation (RE).
- Re-operation rate 2-3%
- Variable reports of ED and RE - often reported at ~10% and 20% respectively¹.
 - I tell patients they will have 100% risk of retrograde ejaculation
- TUIP used for small glands with lower rates of ejaculatory dysfunction

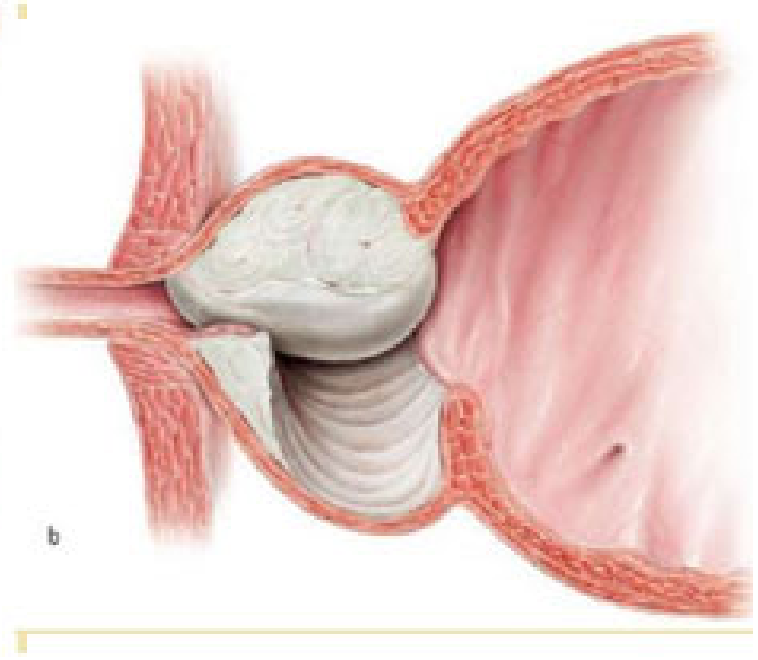
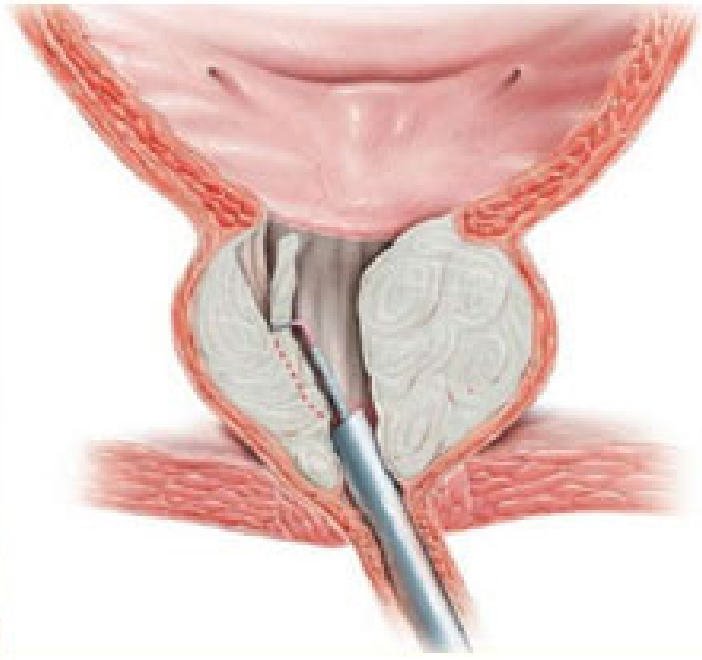
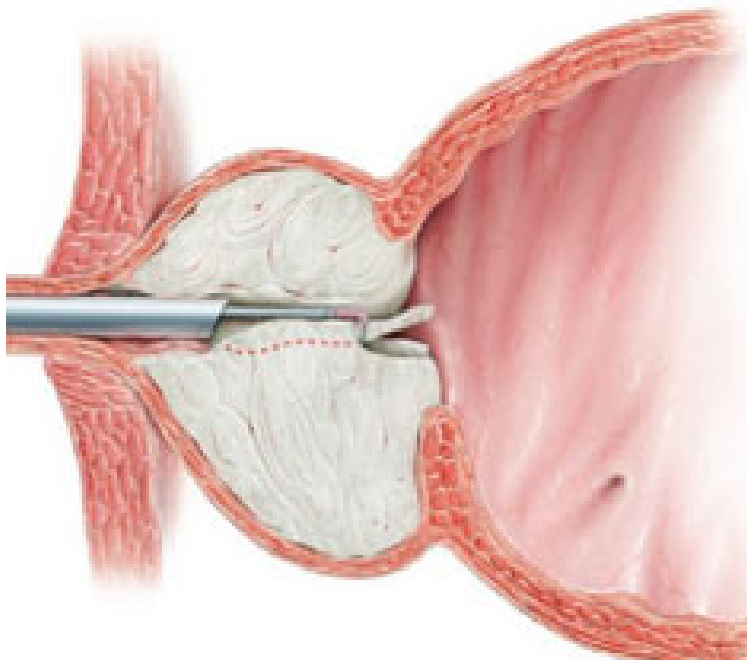
Guideline Statement 11

Transurethral Incision of the Prostate (TUIP)

11. TUIP should be offered as an option for patients with prostates ≤ 30 g for the surgical treatment of LUTS attributed to BPH. (Moderate Recommendation; Evidence Level: Grade B)

1. Gratzke C, Barber N, Speakman MJ, et al. Prostatic urethral lift vs transurethral resection of the prostate: 2-year results of the BPH6 prospective, multicentre, randomized study. BJU Int 2017;119:767-75.

TURP



Decline in TURP

- Study at Queen's University in Canada found a 60% decline in number of TURPs in the decade following introduction of medical management for BPH.
- TURP now most commonly done for “failure” of medical management
- Medical management failure was at least a contributing factor in 87% of TURPs performed in 2008
- There have been limited change in the complications, patient age, and medical co-morbidities of patients, despite delay in TURP

Laser Prostatectomy (Greenlight, Holmium, Diode, Nd:YAG, Thulium)

- Vaporization or Enucleation of prostate tissue
- Lower risk of bleeding, erectile dysfunction, retrograde ejaculation, and fluid absorption than standard TURP
- Can be done in patients on systemic anticoagulation

Medically Complicated Patients

Guideline Statement 23

23. HoLEP, PVP, and ThuLEP should be considered in patients who are at higher risk of bleeding, such as those on anti-coagulation drugs. (Expert Opinion)

Lasers

- Beam of single wavelength of light with all electromagnetic waves in phase
- Specific wavelength determines interaction with tissue
- Tissue heated rapidly¹
 - $>60^{\circ}\text{C}$ protein denatured and tissue coagulated
 - Deep coagulation associated with sloughing and dysuria
 - $>100^{\circ}\text{C}$ vaporization occurs
 - $>150^{\circ}\text{C}$ carbonization occurs

1. Te, A.E.: The next Generation in Laser Treatments and the Role of the GreenLight High-Performance System Laser. Review Urology, 8 Supplemental 3: S24, 2006.

Greenlight

Guideline Statement 13

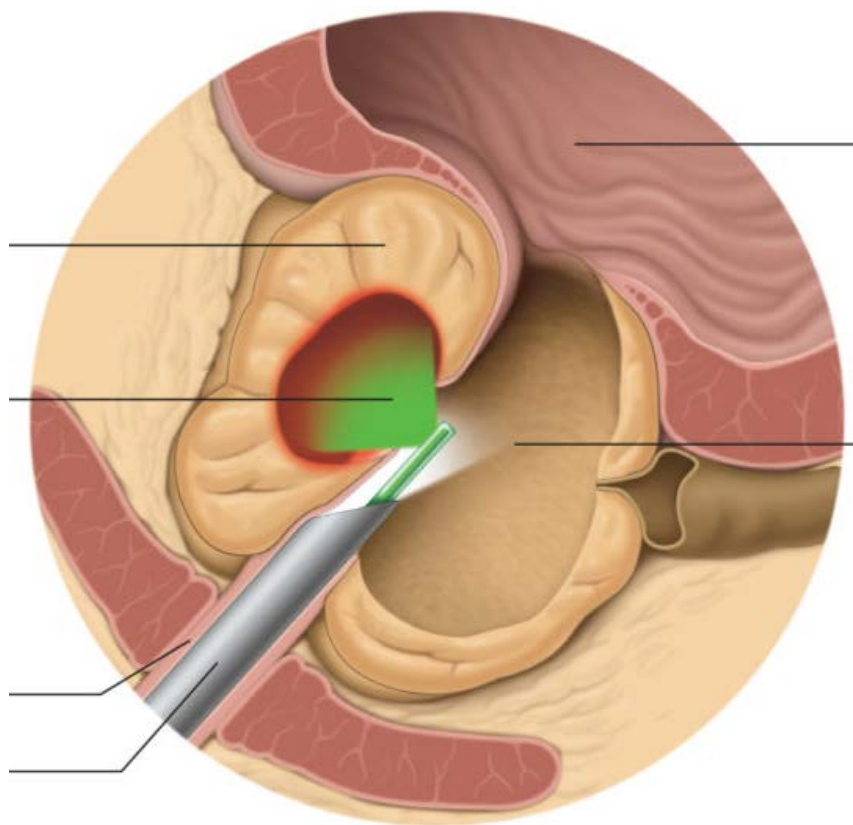
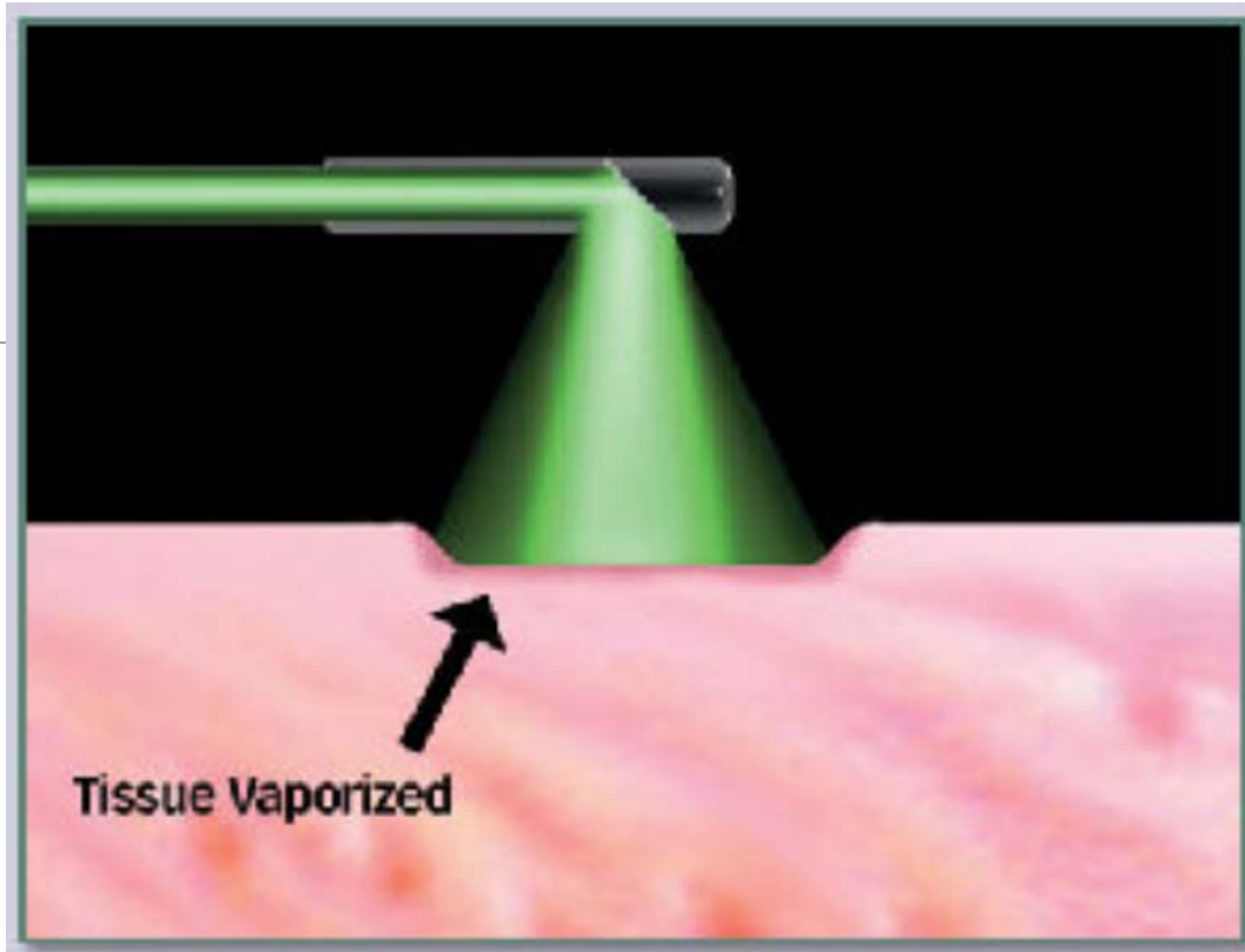
Photoselective Vaporization of the Prostate (PVP)

13. Clinicians should consider PVP as an option using 120W or 180W platforms for patients for the treatment of LUTS attributed to BPH. (Moderate Recommendation; Evidence Level: Grade B)

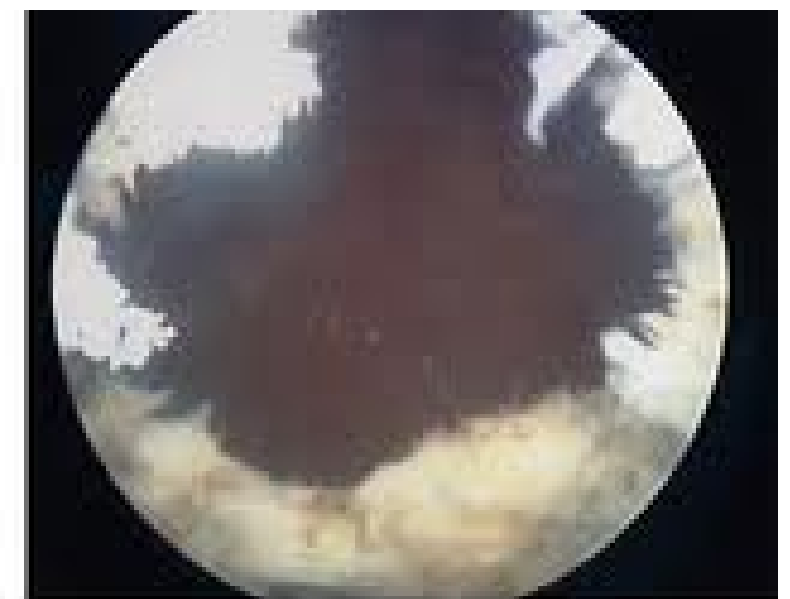
- GOLIATH trial compared latest XPS 180 watt laser with TURP¹
- Shorter length of stay and catheterization time of laser compared to TURP (about 2 days each)
- Non-inferiority on IPSS and Qmax evaluation (~13 points)
- Favorable cost compared to TURP²
 - More expense for laser, but lower complications and length of stay

1. Thomas, J.A., et al. A Multicenter Randomized Noninferiority Trial Comparing GreenLight-XPS Laser Vaporization of the Prostate and Transurethral Resection of the Prostate for the Treatment of Benign Prostatic Obstruction: Two-yr Outcomes of the GOLIATH Study. *European Urology*, Volume 69, Issue 1, 94 - 102

2. Stovsky, M.D., et. al. A clinical outcomes and cost analysis comparing photo selective vaporization of the prostate to alternative minimally invasive therapies and transurethral prostate resection for the treatment of benign prostatic hyperplasia. *Journal of Urology*, 176: 1500, 2006.



Before



After

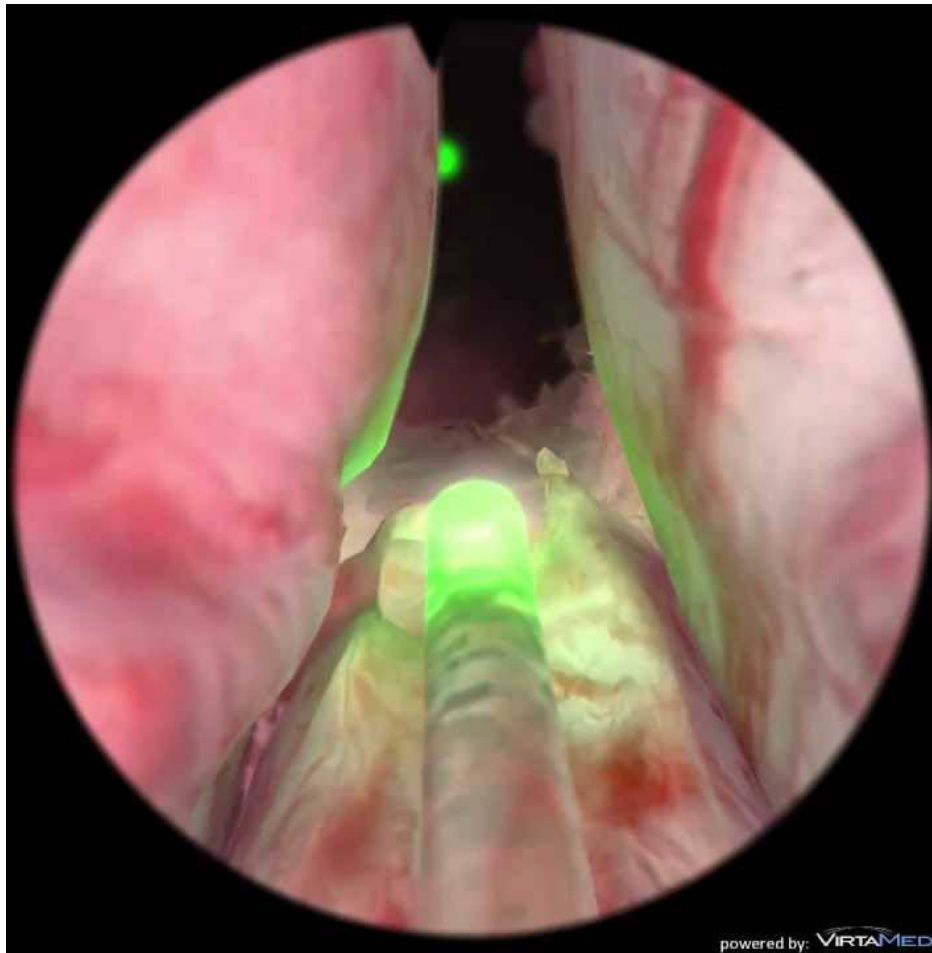
Laser Enucleation

20. Clinicians should consider holmium laser enucleation of the prostate (HoLEP) or thulium laser enucleation of the prostate (ThuLEP), depending on their expertise with either technique, as prostate size-independent suitable options for the treatment of LUTS attributed to BPH. (Moderate Recommendation; Evidence Level: Grade B)

- Most commonly with Holmium or Thulium
 - Rapid vaporization of prostate with minimal depth of penetration.
 - Excellent coagulation
- Multiple studies showing equivalence or superiority to TURP in Qmax, IPSS, and QOL¹
- Size-independent procedure
- Similar complications except for blood transfusion, which was significantly lower in enucleation group²

1. Foster HE, Barry MJ, Gandhi MC, et al. *American Urological Association Guideline: Management of Benign Prostatic Hyperplasia (BPH)*. Linthicum, MD: American Urological Association; 2019:1-33, www.auanet.org/education/guidelines/benign-prostatic-hyperplasia.cfm. Accessed 11/20/2019

2. Fayad AS, Elsheikh MG, Zakaria T et al: Holmium laser enucleation of the prostate versus bipolar resection of the prostate: a prospective randomized study. "pros and cons". *Urology* 2015; 86: 1037.



Prostate lobes enucleated from capsule into bladder



Simple Prostatectomy

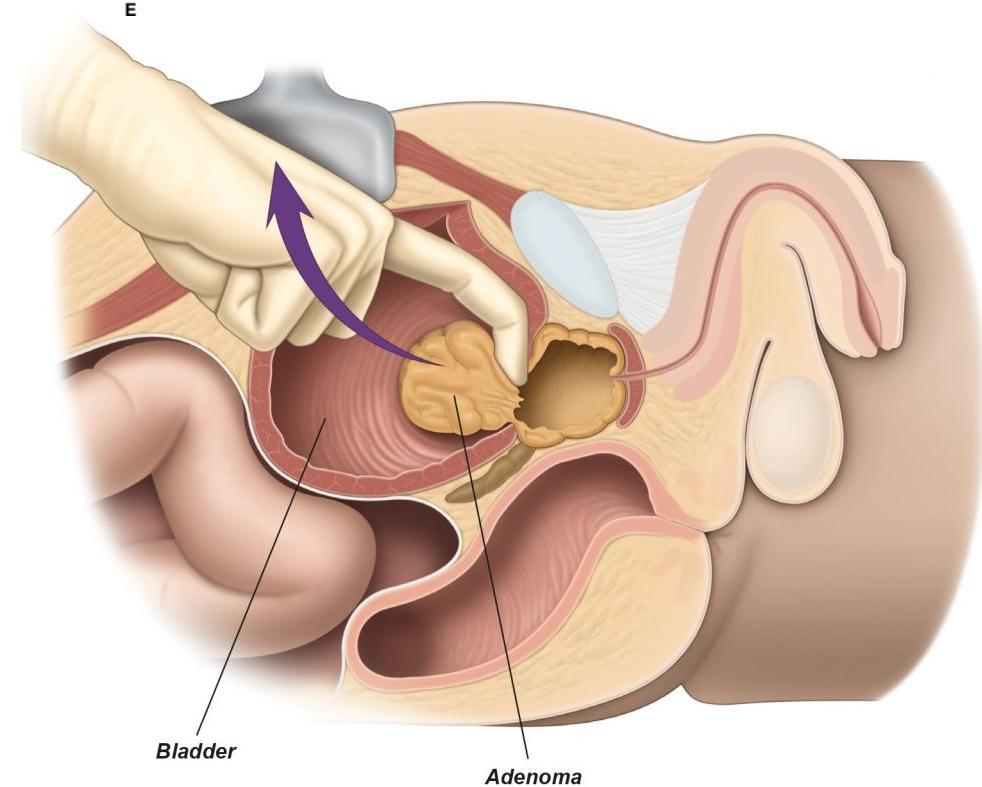
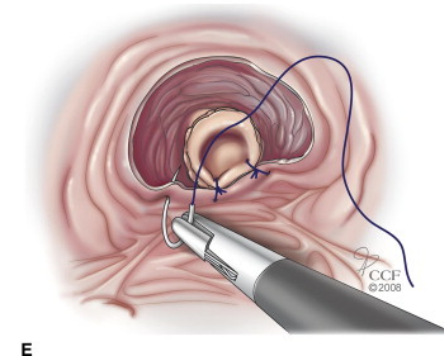
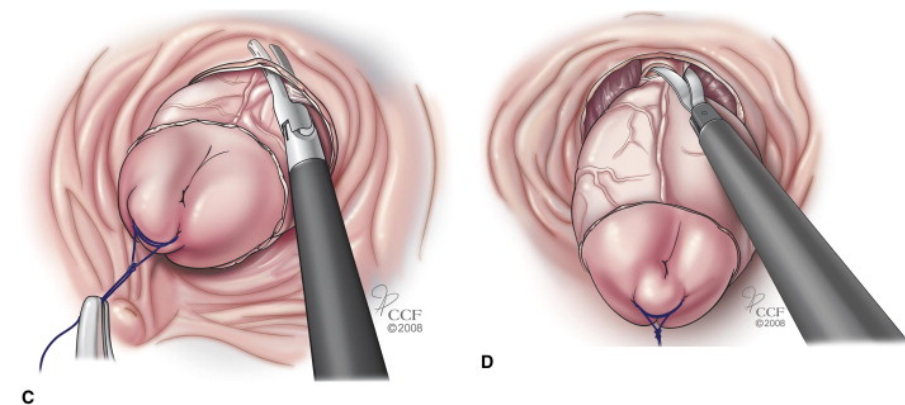
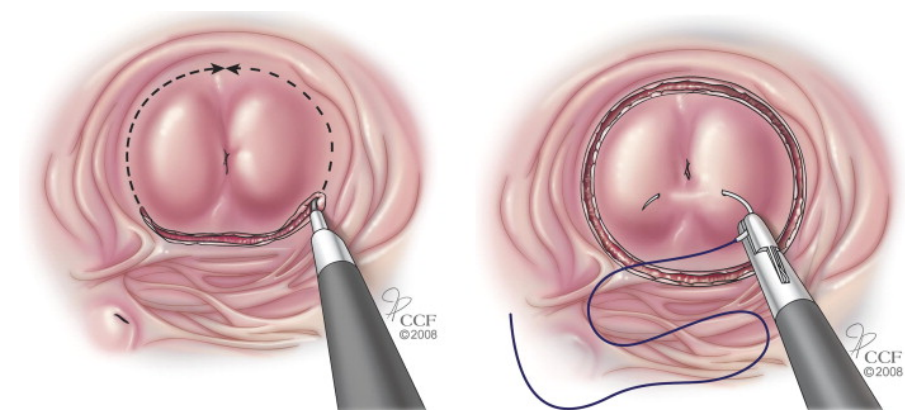
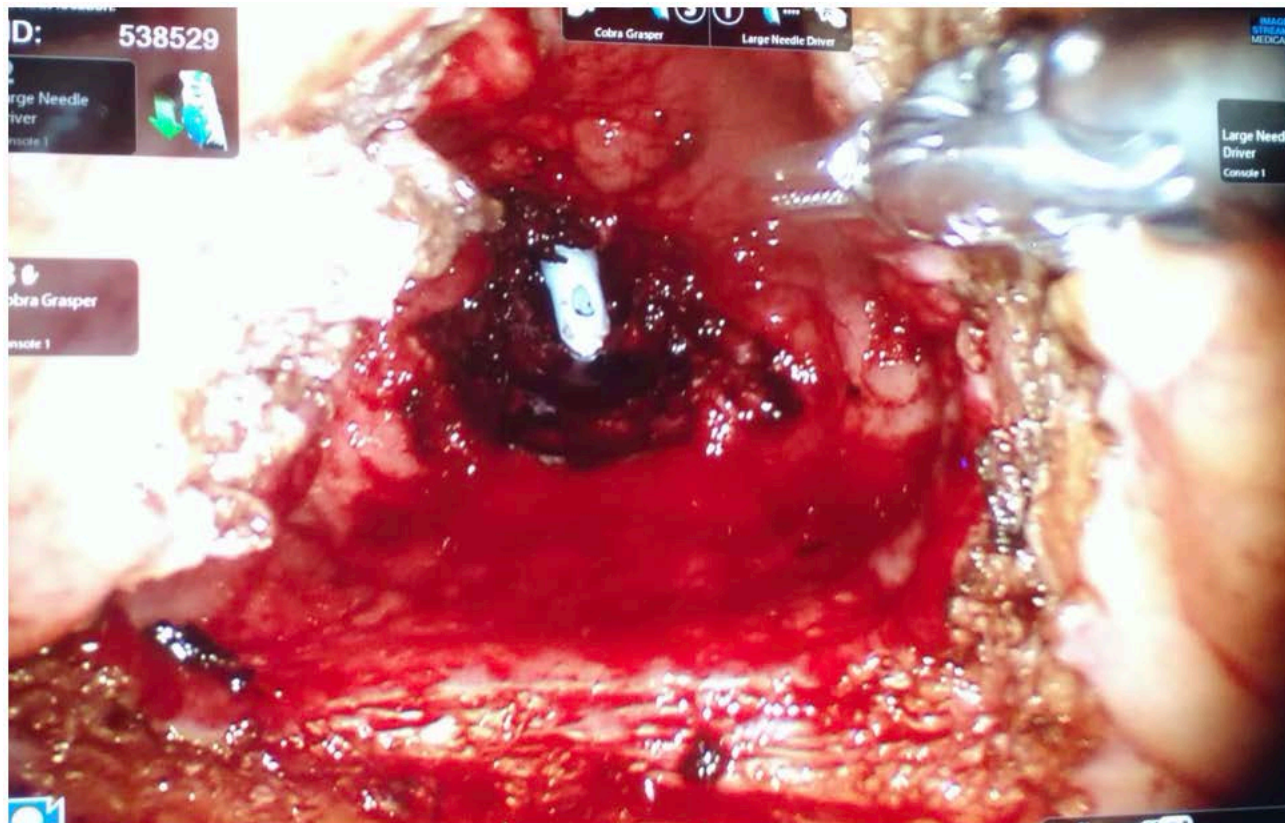
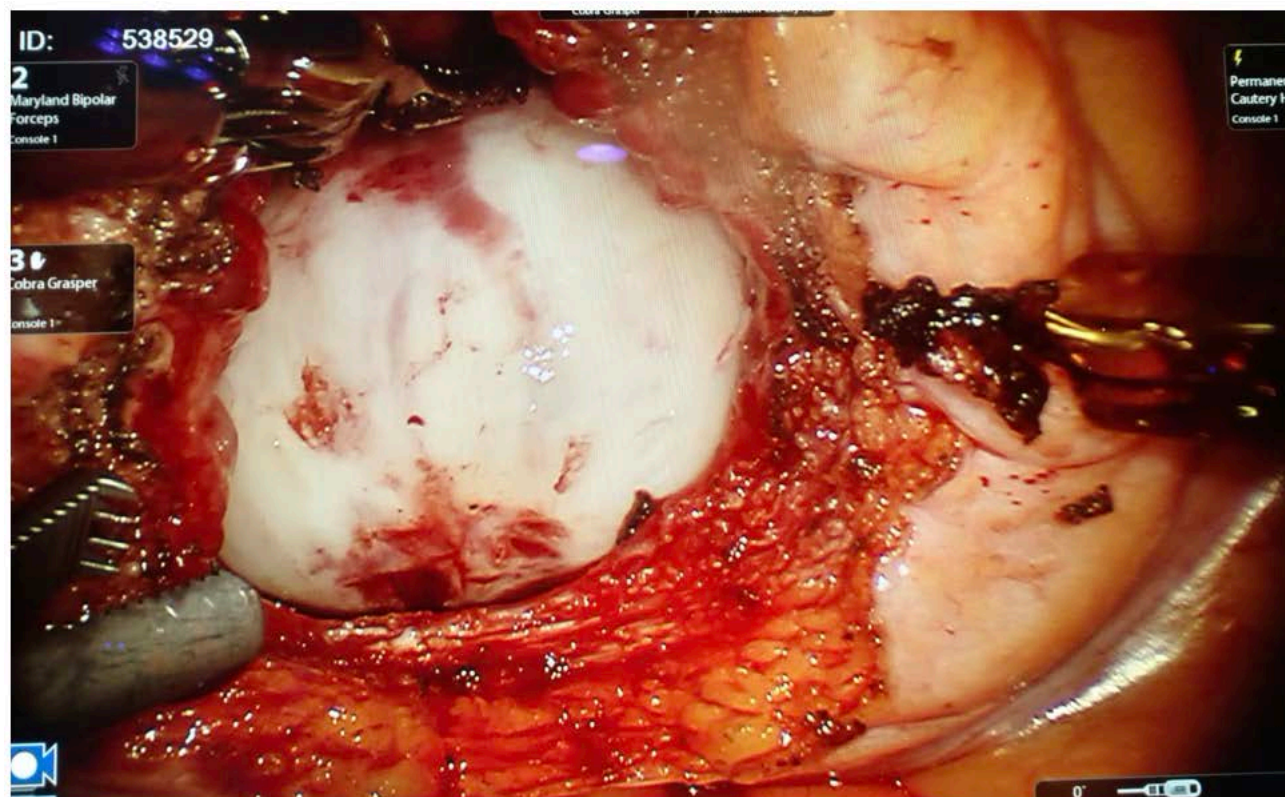
- Alternative for patients who are not candidates for transurethral prostatectomy due to prostate size.
- Generally glands over 100cc (although no particular recommendation exists), associated bladder diverticula, or bladder stones.
- Less morbidity when done using minimally invasive techniques¹

Guideline Statement 10

Simple Prostatectomy

10. Clinicians should consider open, laparoscopic or robotic assisted prostatectomy, depending on their expertise with these techniques, for patients with large prostates. (Moderate Recommendation; Evidence Level: Grade C)

1. Li, J, Cao, D, et. al. Comparison Between Minimally Invasive Simple Prostatectomy and Open Simple Prostatectomy for Large Prostates: A Systematic Review and Meta-Analysis of Comparative Trials. Journal of Endourology. Sep 2019.767-776.



Minimally Invasive Therapy

- Transurethral Needle Ablation of the Prostate (TUNA)
- Transurethral Microwave Thermotherapy of the Prostate (TUMT)
- Prostatic Urethral Lift (Urolift)
- Transurethral Water Vapor Therapy (Rezüm)

TUNA

- Under cystoscopic guidance, needles placed in lateral lobes of the prostate
- Each needle emits radio-frequency energy heating the prostate
- Necrosis of prostate tissue with preservation of urethral mucosa
- Been around since the 1990s
- Initially promising results in reduction of prostate tissue
- Later studies demonstrated prostate architecture replaced by scar, resulting in limited absolute reduction in prostate size.
- Lack of randomized trials meeting AUA guideline panel criteria to recommend to procedure.

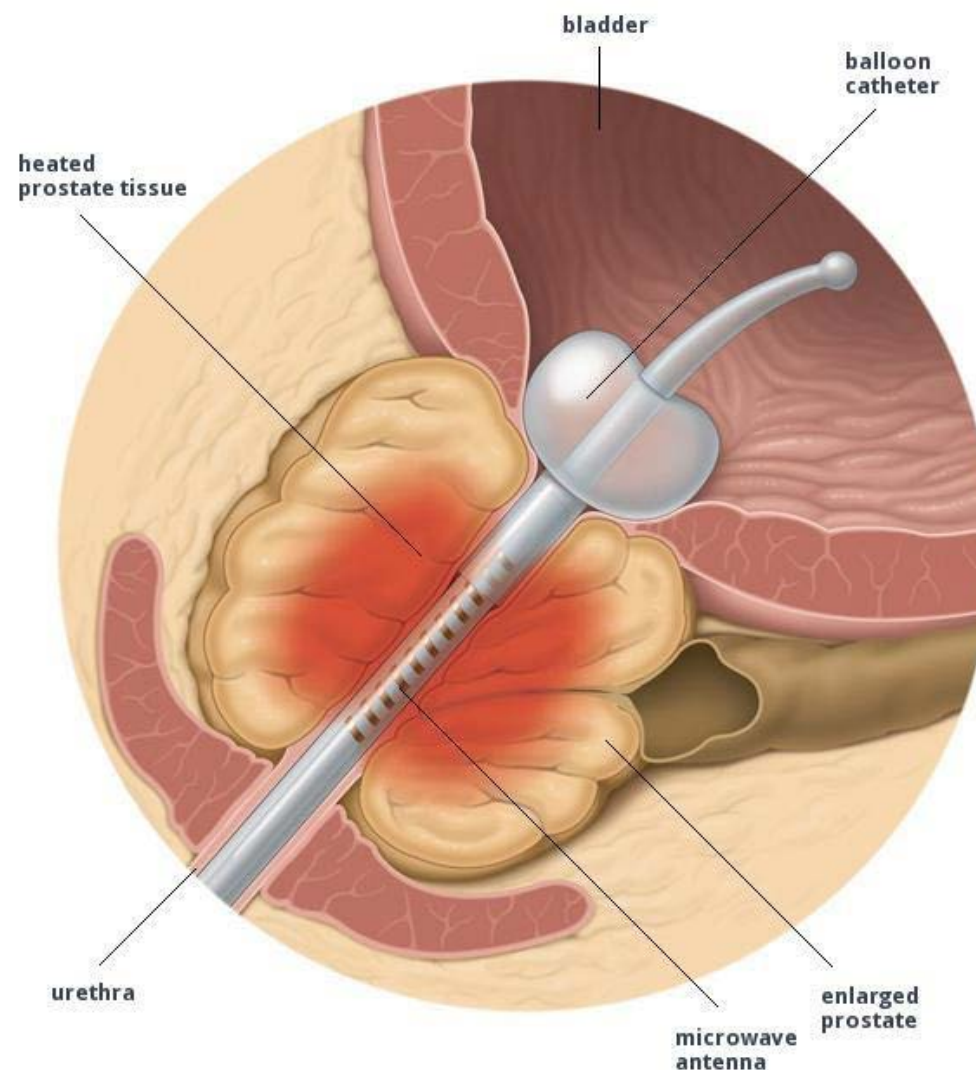
Guideline Statement 19

Transurethral Needle Ablation (TUNA)

19. TUNA is not recommended for the treatment of LUTS attributed to BPH. (Expert Opinion)

TUMT

- Microwave antennae on urethral catheter
- Heating the prostate causing necrosis of prostate tissues



- Has also been around since 1990s.
- Wide variety of manufacturers and devices
- Lack of well-controlled trials
- Studies conflicting in efficacy and durability of treatment¹.
- However, there does seem to be some initial benefit and about 1/2 the rate of ED compared to TURP

Guideline Statement 16

Transurethral Microwave Therapy (TUMT)

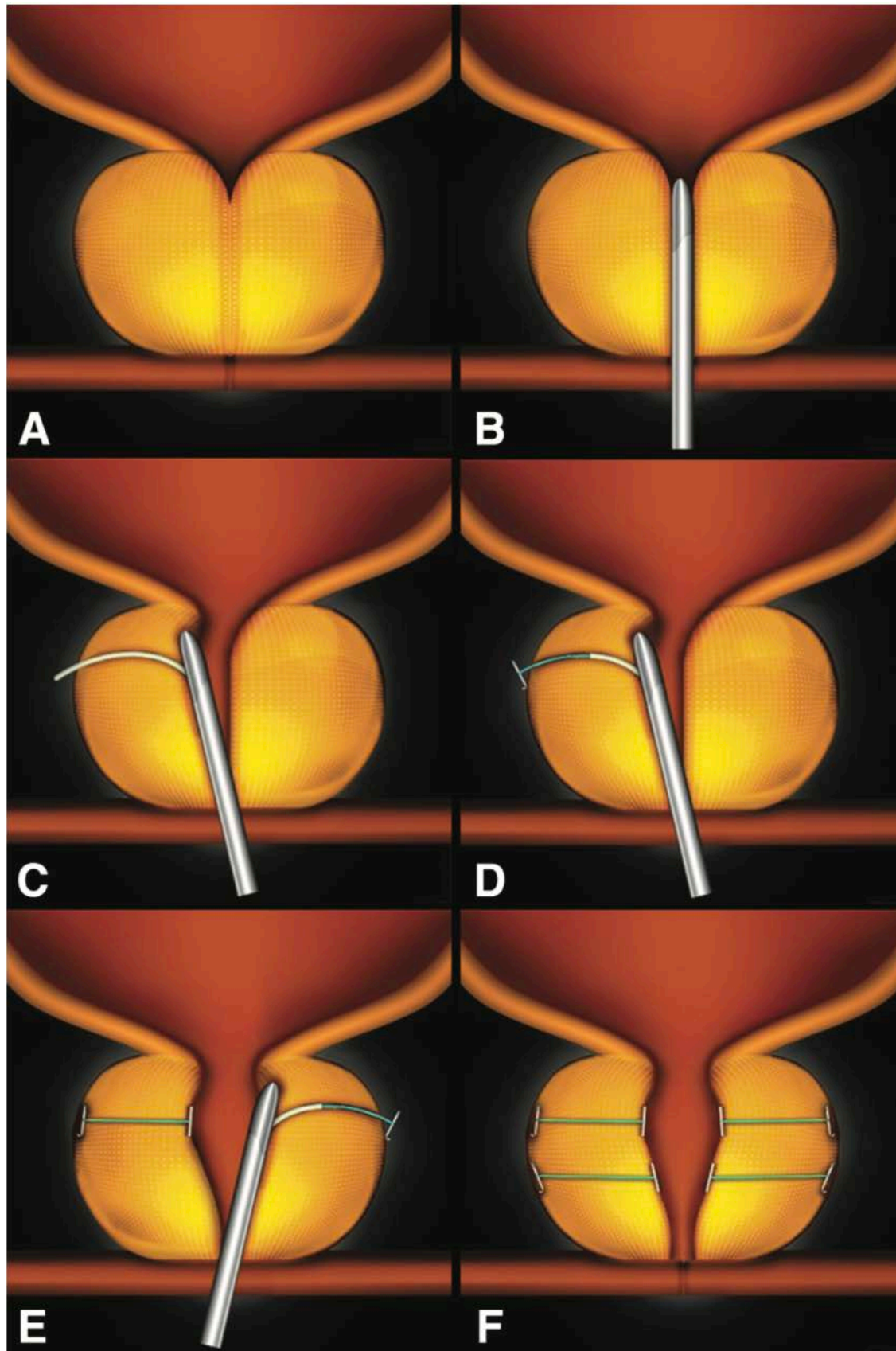
16. TUMT may be offered to patients with LUTS attributed to BPH; however, patients should be informed that surgical retreatment rates are higher compared to TURP. (Conditional Recommendation; Evidence Level: Grade C)

1. Brehmer M, Wiskell H, Kinn AC: Sham treatment compared with 30 or 60 min of thermotherapy for benign prostatic hyperplasia: a randomized study. BJU Int 1999; 84: 292.

Prostatic Urethral Lift (Urolift)

- Developed in 2004 to alter prostate anatomy without destroying tissue
- One clip outside the prostate capsule and the other in the urethral lumen.
- The prostate between is tensioned or compressed, opening the prostatic fossa.
- NO changes in erectile function with no ejaculatory dysfunction
- Unlike prior urethral “stents” there is no encrustation and the urethral clip epithelializes in under a year¹.

1. Roehrborn CG, Gange SN, Shore ND et al: The prostatic urethral lift for the treatment of lower urinary tract symptoms associated with prostate enlargement due to benign prostatic hyperplasia: the L.I.F.T. Study. J Urol 2013; 190: 2161.



L.I.F.T. Study¹

- 2013 study Comparing Urolift to Sham
- IPSS improved 11 points from baseline
 - This was a 5 point improvement over the Sham control
- ~4-5mL/sec improvement in peak urine flow
- 2 point improvement in QOL scores at 1 month which were sustained at 1 year.

5 years after L.I.F.T.¹

- Qmax maintained at 5 years - about 4mL/sec improvement over baseline (statistically significant).
- IPSS improvement slightly decreased (about 2 points)
- QOL stable after 5 years - 2 point improvement from baseline
- NO change in IIEF-5 at 5 years

BPH6 Study¹

- Compared Urolift to TURP over a 2 year period
- Greater IPSS improvement as well as Qmax improvement with TURP over Urolift
 - IPSS improved by 15 points in TURP group compared to 9 points in Urolift group
 - Qmax improved by ~16mL/sec in TURP group vs. 5 in Urolift
- QOL improvement was not a statistically significant different at 2 years (2.5 vs. 3.3 - $p=0.066$)

1. Gratzke C, Barber N, Speakman M et al: Prostatic urethral lift vs transurethral resection of the prostate: 2-year results of the BPH6 prospective, multicentre, randomized study. BJU Intern

- BPH6 demonstrated an approximately 2 point drop in SHIM score at 2 years after TURP this compared to no change in Urolift group. However, this was not statistically significant
- Ejaculatory function essentially unchanged with Urolift. TURP demonstrated a 4 point decrease in MHSQ-EjD
- Urolift only treatment with no de novo ED or ejaculatory dysfunction

Guideline Statement 15

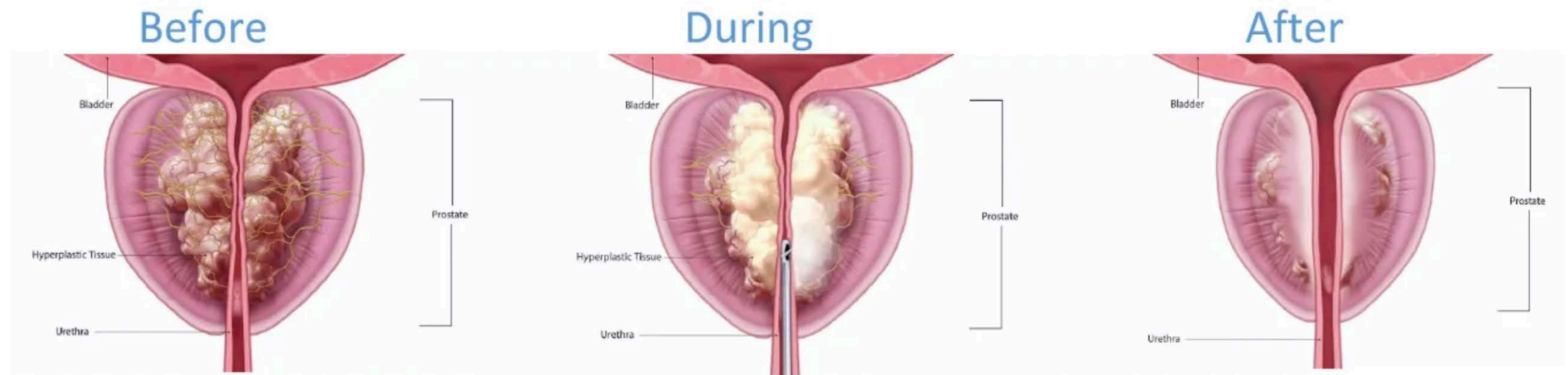
Prostatic Urethral Lift (PUL)

15. PUL may be offered to eligible patients concerned with erectile and ejaculatory function for the treatment of with LUTS attributed to BPH. (Conditional Recommendation; Evidence Level: Grade C)

Transurethral Water Vapor Therapy (Rezum)

- Needle deployed into prostate under cystoscopic guidance
- Water vapor delivered to hyperplastic tissue
- Water vapor travels rapidly through prostate until the prostate capsule
- As the vapor comes into contact with the prostate, it condenses into liquid water and transfers thermal energy to the prostate.

Rezum



Initial Rezum study

- 2015 study comparing Rezum to sham
- AUA-SS improved 7 points over sham treatment (about 11 points from baseline)
- ~5.5mL/sec improvement in peak urine flow (at 3 months)
- 2 point improvement in QOL scores at 1 month which were sustained at 1 year.
- No limitation for median lobe/median bar

4 Years after - WAVE Study

- 47% improvement in baseline IPSS (~10 point improvement)
- 40% improvement in QOL (about 2 points)
- 50% improvement in Qmax (about 4.2mL/sec)
- IIEF - 2 point decrease in erectile quality (statistically significant $P=0.033$)
- However no change in MSHQ bother score

- No head to head trials with TURP
- Relatively high rate of UTIs - risk of infection about 17% with Rezum (0-5% with Urolift)
- About 3/4 of patients require catheterization (less than 1/3 of Urolift require catheters)
- Initial study with no ED or ejaculatory effects - follow up with ~3% risk of ED and 5% risk of EJD

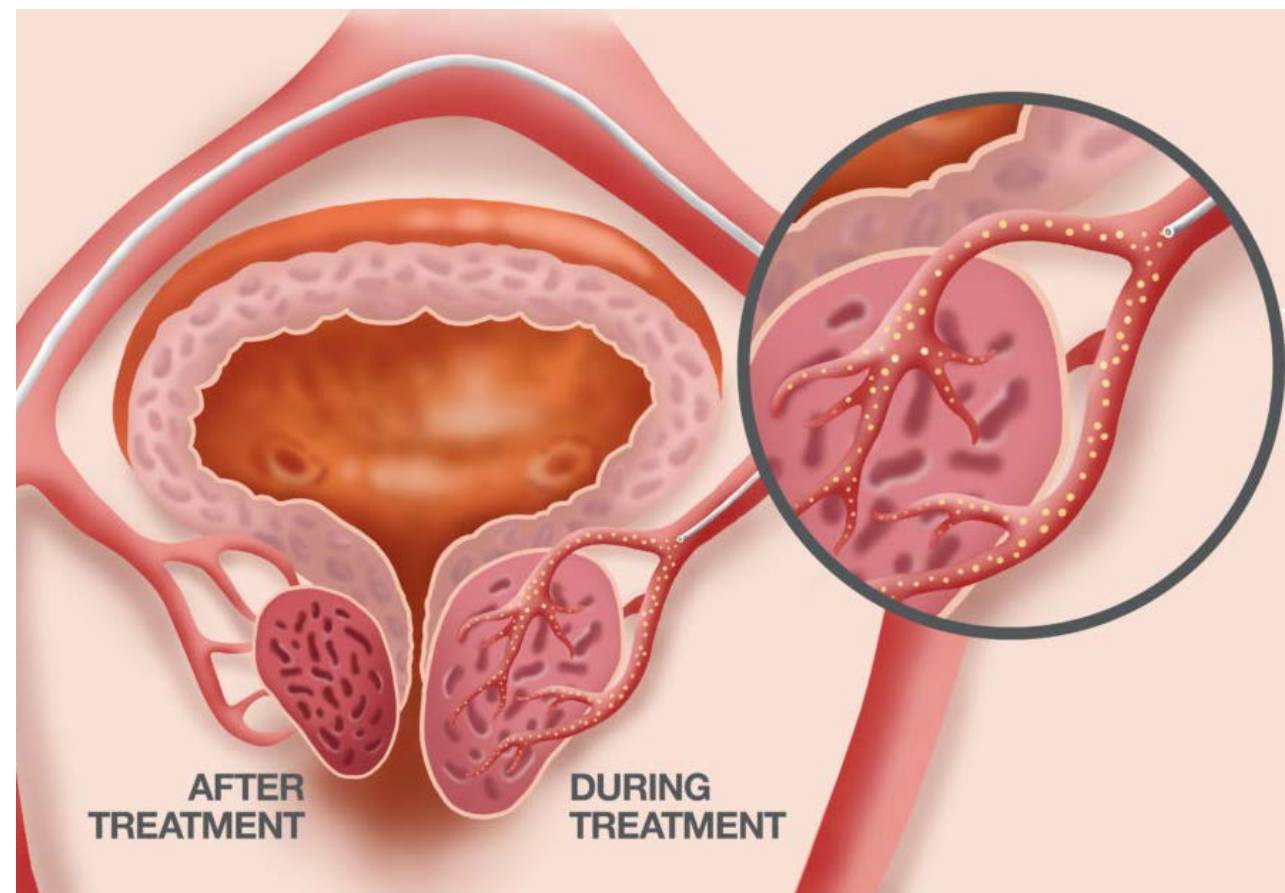
Guideline Statement 17

Water Vapor Thermal Therapy

17. Water vapor thermal therapy may be offered to patients with LUTS attributed to BPH provided prostate volume <80g; however, patients should be counseled regarding efficacy and retreatment rates. (Conditional Recommendation; Evidence Level: Grade C)

Prostate Artery Embolization

- Can be used in medically complex patients (no GA)
- Lacks sufficient evidence of benefit compared to other ablative treatments
- Requires skilled interventional radiologist



What's Next?

- Aquablation
- Intra-prostate injections
- New prostatic stents
- Catheter coated balloons

Aquablation

- Computer controlled high-velocity saline used to ablate prostate tissue through hydrodissection
- Depth of tissue penetration controlled by adjusting the flow rate of saline.
- No thermal energy, so more likely erectile function preserved along with ejaculatory function

Prostate stents

- Well documented issues with Urolume
- Most recent iteration is the Allium stent
- Nitinol stent covered with polymer to prevent encrustation
- Opens to 45Fr
- Short term study with 19 point IPSS improvement and 10mL/sec improvement in Qmax¹
- 51 patients treated - stent only had to be removed in 2 (chronic UTI and hematuria) with no removal issues reported



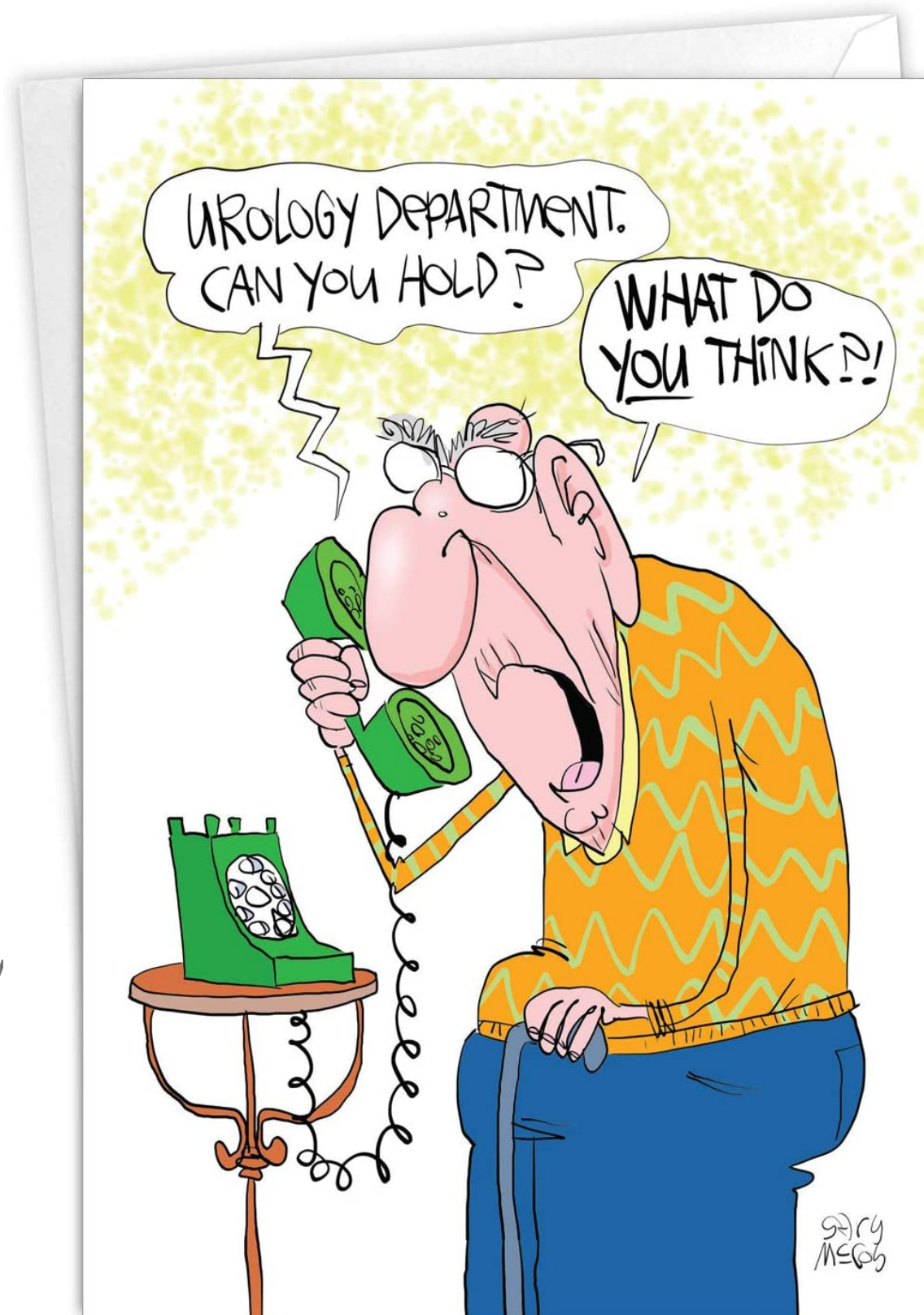
Overactive Bladder

- Urinary urgency, usually accompanied by frequency and nocturia, with or without urge incontinence
- First line: Behavioral
 - Bladder training
 - PFPT
 - Elimination diet
- Second line: Medical
 - Anticholinergics (dry eye, dry mouth, constipation)
 - Oxybutynin, Tolterodien Tropium, Solifenacin
 - Beta-3 Agonists (hypertension)
 - Myrbetriq
- Third line: Advanced therapies
 - Percutaneous Tibial Nerve Stimulation
 - Sacral Nerve Stimulator
 - Botox injections



OAB Take Home Point:

- Both BPH and OAB can cause urgency/frequency
- If LUTS could be due to BPH or OAB → Try a-blocker before anticholinergic
- Risk of urinary retention
- If symptoms are primarily irritative (i.e. frequency/ urgency only) and would like to start anticholinergic → check PVR first



Prostatitis (Chronic Prostatitis/Chronic Pelvic Pain Syndrome)

- Most common urologic diagnosis in men <50 years old
 - Prevalence 3-13%
 - 3rd most common >50 years old (#1 BPH, #2 prostate cancer)
- Management: Phenotype based
 - **Pelvic Floor Physical Therapy**
 - α -blockers
 - Tadalafil
 - NSAIDs
 - Muscle relaxants – Klonopin
 - Nerve modulations – Amitriptyline/Gabapentin
 - Antibiotics (culture-directed if culture positive)
 - Historically – 6 week course of fluoroquinolone



Summary

- BPH (LUTS) can have profound impact on patient's quality of life
 - Management driven by bother (and retention)
- Many benefit from behavioral change
- Most men will want to try medications first
 - α -blockers or PDE-5i
 - Can add 5ARI if prostate enlarged
- Refer to Urology if:
 - No improvement
 - Not interested in long term med(s)
 - Interested in procedural management
 - Sequelae of obstruction (renal failure/kidney obstruction, bladder stones, UTIs, hematuria)
 - Diagnostic uncertainty



Thank you

- Questions?
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