Most Noteworthy Literature on BPH and Incontinence from 2018-2019

Dr Helen L. Bernie, DO, MPH
Director of Sexual and Reproductive Medicine
Assistant Professor of Urology
Indiana University

Hbernie@IUHealth.org                     @drhelenbernie
Disclosures

- None
"This year, more than 174,000 men will be diagnosed with prostate cancer in the US and many will undergo treatment. Although most patients do very well after prostate treatment, some will have persistent IPT. There are multiple treatments available for these men, including physical therapy, medications and surgery, which is why physicians and patients should engage in a shared decision-making process to select the best option for each individual patient."

Urinary incontinence after prostate treatment (IPT) is one of the few urologic conditions that is iatrogenic, and therefore predictable, and often preventable.

A condition that tends to cause a high degree of patient distress, and it has gained visibility over the past several years due to the use of surgery to treat PCa, as well as the proliferation of men's continence products available to the lay public and newer minimally invasive treatments for BPH.

The purpose of these guidelines are to provide physicians clinical guidance for the evaluation and management of IPT

- Coined the new term “IPT” Incontinence after Prostate Treatment” more inclusive
- Covers the treatment of men who experience incontinence after undergoing radical prostatectomy (RP), radiation treatment (RT) and treatment of benign prostatic hyperplasia (BPH).
- Evaluation of the patient; risk factors for IPT that should be discussed with all men prior to treatment; assessment of the patient prior to intervention; and a stepwise approach to management are covered.
A systematic review performed from the Mayo Clinic Evidence Based Practice Center from 2000-2018

The new clinical guideline makes 36 recommendations in total.
- New guidelines include Counseling patients undergoing RP that incontinence is expected in the short-term and generally improves to near baseline by 12 months after surgery, but may persist and require treatment.
- Possible maneuvers to decrease rates of IPT, with a specific focus on men with stress urinary incontinence (SUI), are also explored.
Guideline Statements

Pre-Treatment

1. Clinicians should inform patients undergoing radical prostatectomy of all known factors that could affect continence. (Moderate Recommendation; Evidence Level: Grade B)

2. Clinicians should counsel patients regarding the risk of sexual arousal incontinence and climacturia following radical prostatectomy. (Strong Recommendation; Evidence Level: Grade B)

3. Clinicians should inform patients undergoing radical prostatectomy that incontinence is expected in the short-term and generally improves to near baseline by 12 months after surgery but may persist and require treatment. (Strong Recommendation; Evidence Level: Grade A)

4. Prior to radical prostatectomy, patients may be offered pelvic floor muscle exercises or pelvic floor muscle training. (Conditional Recommendation; Evidence Level: Grade C)

5. Patients undergoing transurethral resection of the prostate after radiation therapy or radical prostatectomy after radiation therapy should be informed of the high rate of urinary incontinence following these procedures. (Moderate Recommendation; Evidence Level: Grade C)

Post-Prostate Treatment

6. In patients who have undergone radical prostatectomy, clinicians should offer pelvic floor muscle exercises or pelvic floor muscle training in the immediate post-operative period. (Moderate Recommendation; Evidence Level: Grade B)

7. In patients with bothersome stress urinary incontinence after prostate treatment, surgery may be considered as early as six months if incontinence is not improving despite conservative therapy. (Conditional Recommendation; Evidence Level: Grade C)

8. In patients with bothersome stress urinary incontinence after prostate treatment, despite conservative therapy, surgical treatment should be offered at one year post-prostate treatment. (Strong Recommendation; Evidence Level: Grade B)
Evaluation of Incontinence after Prostate Treatment

9. Clinicians should evaluate patients with incontinence after prostate treatment with history, physical exam, and appropriate diagnostic modalities to categorize type and severity of incontinence and degree of bother. (Clinical Principle)

10. Patients with urgency urinary incontinence or urgency predominant mixed urinary incontinence should be offered treatment options per the American Urological Association Overactive Bladder guideline. (Clinical Principle)

11. Prior to surgical intervention for stress urinary incontinence, stress urinary incontinence should be confirmed by history, physical exam, or ancillary testing. (Clinical Principle)

12. Patients with incontinence after prostate treatment should be informed of management options for their incontinence, including surgical and non-surgical options. (Clinical Principle)

13. In patients with incontinence after prostate treatment, physicians should discuss risk, benefits, and expectations of different treatments using the shared decision-making model. (Clinical Principle)

14. Prior to surgical intervention for stress urinary incontinence, cystourethroscopy should be performed to assess for urethral and bladder pathology that may affect outcomes of surgery. (Expert Opinion)

15. Clinicians may perform urodynamic testing in a patient prior to surgical intervention for stress urinary incontinence in cases where it may facilitate diagnosis or counseling. (Conditional Recommendation; Evidence Level: Grade C)

Treatment Options

16. In patients seeking treatment for incontinence after radical prostatectomy, pelvic floor muscle exercises or pelvic floor muscle training should be offered. (Moderate Recommendation; Evidence Level: Grade B)

17. Artificial urinary sphincter should be considered for patients with bothersome stress urinary incontinence after prostate treatment. (Strong Recommendation; Evidence Level: Grade B)

18. Prior to implantation of artificial urinary sphincter, clinicians should ensure that patients have adequate physical and cognitive abilities to operate the device. (Clinical Principle)

19. In the patient who selects artificial urinary sphincter, a single cuff perineal approach is preferred. (Moderate Recommendation; Evidence Level: Grade C)

20. Male slings should be considered as treatment options for mild to moderate stress urinary incontinence after prostate treatment. (Moderate Recommendation; Evidence Level: Grade B)

21. Male slings should not be routinely performed in patients with severe stress incontinence. (Moderate Recommendation; Evidence Level: Grade C)

22. Adjustable balloon devices may be offered to patients with mild stress urinary incontinence after prostate treatment. (Moderate Recommendation; Evidence Level: Grade B)

23. Surgical management of stress urinary incontinence after treatment of benign prostatic hyperplasia is the same as that for patients after radical prostatectomy. (Moderate Recommendation; Evidence Level: Grade C)

24. In men with stress urinary incontinence after primary, adjuvant, or salvage radiotherapy who are seeking surgical management, artificial urinary sphincter is preferred over male slings or adjustable balloons. (Moderate Recommendation; Evidence Level: Grade C)

25. Patients with incontinence after prostate treatment should be counseled that efficacy is low and cure is rare with urethral bulking agents. (Strong Recommendation; Evidence Level: Grade B)

26. Other potential treatments for incontinence after prostate treatment should be considered investigational, and patients should be counseled accordingly. (Expert Opinion)
Special Situations

31. In a patient presenting with infection or erosion of an artificial urinary sphincter or sling, explantation should be performed and reimplantation should be delayed. (Clinical Principle)

32. A urinary diversion can be considered in patients who are unable to obtain long-term quality of life after incontinence after prostate treatment and who are appropriately motivated and counseled. (Expert Opinion)

33. In a patient with bothersome climacturia, treatment may be offered. (Conditional Recommendation; Evidence Level: Grade C)

34. Patients with stress urinary incontinence following urethral reconstructive surgery may be offered artificial urinary sphincter and should be counseled that complications rates are higher. (Conditional Recommendation; Evidence Level: Grade C)

35. In patients with incontinence after prostate treatment and erectile dysfunction, a concomitant or staged procedure may be offered. (Conditional Recommendation; Evidence Level: Grade C)

36. Patients with symptomatic vesicourethral anastomotic stenosis or bladder neck contracture should be treated prior to surgery for incontinence after prostate treatment. (Clinical Principle)
Retrospective review of all men with PCa who underwent AUS placement and RT between 1987-2016 from 5 institutions with high-volume implanters.

Goal: To determine if the timing of RT on artificial urinary sphincter (AUS) impacts complication rates, revision rates, and number of pads per day after placement.

METHODS: Demographic data, comorbidities, BMI, DOS, +/- radiotherapy, type of radiation, pre/post-operative pads per day, surgical approach, cuff size, previous incontinence treatments, postop complications, duration of follow-up, and need for revision surgery were included.

- Primary outcome measures: complications, revision rates, and # of pads per day before and after AUS.
  - Other postop characteristics: infection, erosion, sub-cuff atrophy, persistent incontinence, and mechanical failure.

- The # of pts from each institution: 17, 27, 64, 65, and 135. *With the exception of the institution that performed 135 AUS procedures, all other institutions had only 1 surgeon contribute to the data.

- Patients were stratified into 2 groups whether they received adjuvant radiation therapy for their prostate cancer before (group 1) or after AUS placement (group 2).
The Infection rate, sub-cuff atrophy, persistent incontinence, mechanical failure, and revision rates were NOT sig diff bw groups.
CONCLUSIONS:

- The timing of RT does not appear to significantly affect complication rates or urinary continence, as measured in pads used after AUS placement.
- This multi-institutional retrospective analysis showed similar erosion and revision rates when radiation occurred after AUS placement and demonstrates preliminary safety and feasibility of the administration of radiation after AUS placement.

LIMITATIONS: Retrospective review, Very small number of patients in group 2 (After RT group) and the institution contributing the largest number of patients had multiple surgeons

Further research should be performed to guide evidence-based clinical decision-making, as there is a potential benefit to placing an AUS before radiotherapy.
BACKGROUND: A variety of new minimally invasive surgical approaches are available as an alternative to TURP for the management of LUTS in men with BPH.

OBJECTIVE: To assess the effects of PUL for the treatment of LUTS in men with BPH as compared with TURP.

METHOD: We performed a comprehensive search of multiple databases (the Cochrane Library, MEDLINE, Embase, LILACS, Scopus, Web of Science, and Google Scholar), trials registries, other sources of grey literature, through January 2019

- Included parallel group randomized controlled trials (RCTs).
  - Two review authors independently screened the literature, extracted data, and assessed risk of bias.
  - Planned subgroup analyses by age, prostate volume, and severity of baseline symptoms
  - Used the GRADE approach to rate the certainty of the evidence.
RESULTS: Two RCTs with 297 pts comparing PUL to sham surgery or TURP.

- mean age was 65.6 years
- mean IPSS score was 22.7.
- mean prostate volume was 42.2 mL.

Outcomes measured up to and including 12 months after randomization were considered short-term, and later than 12 months as long-term.

For patient-reported outcomes: lower scores indicated more urological symptom improvement and higher quality of life. In contrast, higher scores referred to better erectile and ejaculatory function.
RESULTS: 1 RCT study of 91 pts, w/ long term follow-up (up to 24 months)

PUL may result in a “substantially lesser improvement” in urological symptom score and result in little worse to no difference in quality of life. The study did not report on major adverse events. The authors were “very uncertain” whether PUL increases retreatment (very low-certainty evidence). PUL likely results in “little to no difference” in erectile function (MD 1.60, 95% CI –0.80 to 4.00; moderate-certainty evidence), but may result in substantially better ejaculatory function (MD 4.30, 95% CI 2.17 to 6.43; low-certainty evidence).
Conclusions: PUL appears less effective than TURP in improving urological symptoms both short-term and long term, while quality of life outcomes may be similar.

- The effect on erectile function appears similar but ejaculatory function may be better.
- The authors were “very uncertain” about retreatment rates both short-term and long-term, and were unable to assess the effects of PUL in subgroups based on age, prostate size, or symptom severity and also could not assess how PUL compared to other surgical management approaches.

Given the large numbers of alternative treatment modalities to treat men with LUTS secondary to BPH, this represents important information that should be shared with men considering surgical treatment.

Maybe not the best new minimally invasive procedure for Urinary symptom control???
OBJECTIVE: To determine the impact of concurrent IPP and AUS implantation on perioperative complications and long-term device survival, among men with postprostatectomy erectile dysfunction and urinary incontinence.

METHODS: We identified men older than 65 treated with RP in the Surveillance, Epidemiology, and End Results Medicare database between 2002-2016.

- IPP or AUS placement was determined by current procedural terminology (CPT) code, with dual implantation (DI) defined as IPP and AUS placement on the same date.
- Device survival was assessed using CPT codes for device removal, replacement, and/or repair. Complications were assessed within 90 days using ICD-9 codes.
RESULTS:

A total of 37,599 men underwent RP, with AUS placed in 793 (2.1%), IPP placed in 644 (1.7%), and DI in 62 (0.2%).

Relative to AUS placement alone, men undergoing DI were younger (68.8 vs 70.2 years, \( P = 0.03 \)), but had equivalent Charlson comorbidity index, tumor grades, and rates of prior radiotherapy.

Relative to IPP placement alone, men were more likely to undergo DI if treated with adjuvant or salvage radiotherapy.
**RESULTS:** The incidence of complications within 30 and 90 days of prosthetic implantation did not differ between groups.

Long-term device survival on Kaplan-Meier analysis was not impacted by DI relative to single device implantation, median follow-up of 61 months.
CONCLUSION: Combined AUS & IPP placement does not adversely affect perioperative complications or device survival relative to placement of either device alone.

LIMITATIONS: Possible coding errors, data are lacking on factors that could influence outcomes such as surgeon volume, operative time, or antibiotic selection (Selection bias with more experienced surgeons opting to perform DI, improved outcomes), No details on surgical approach, and the use of a Medicare linked dataset limits our analysis to patients over the age of 65, unable to comment on utilization of DI in a younger group.
The Role of PSA Monitoring after Holmium Laser Enucleation of the Prostate (HoLEP).

Abedali ZA\textsuperscript{1}, Calaway AC\textsuperscript{1}, Large T\textsuperscript{1}, Lingeman JE\textsuperscript{1}, Mellon MJ\textsuperscript{1}, Boris RS\textsuperscript{1}.

Author information

1 Department of Urology, Indiana University School of Medicine, Indianapolis, Indiana.

\begin{itemize}
\item BACKGROUND: PSA screening for PCa has recently been challenged due to poor sensitivity.
\begin{itemize}
\item A number of conditions elevate PSA besides PCa with benign prostatic hypertrophy (BPH) being most common.
\end{itemize}
\item OBJECTIVE: To assess the positive predictive value (PPV) of PSA and PSA density (PSAD) for PCa risk following Holmium laser enucleation of the prostate (HoLEP).
\end{itemize}

\begin{itemize}
\item METHODS: Retrospective review of a database of HoLEP surgeries performed at Indiana University from 1999-2018.
\begin{itemize}
\item Identified 1147 pts with post-HoLEP PSA data.
\item 55 post-HoLEP biopsies were recorded.
\item Demographics, PSA, prostate volume, and oncologic details were analyzed.
\item The primary outcome was biopsy proven prostate cancer.
\end{itemize}
\end{itemize}
RESULTS: 55 patients underwent "for cause" transrectal ultrasound prostate biopsy following HoLEP.

- Cancer was identified in over 90% of those biopsied.
- Men with PSA above 1 at time of biopsy had a 94% probability of cancer detection and 80% risk of clinically significant disease.
- PSAD above 0.1 was associated with a 95% risk of cancer and 88% risk of clinically significant cancer.
- A PSA greater than 5.8 or PSAD greater than 0.17 was universally associated with biopsy proven cancer.
CONCLUSIONS: Post HoLEP PSA and PSAD have high PPV for PCa risk. **Thresholds for biopsy should be lower than for non-HoLEP patients.**

- HoLEP pts with PSA above 1 or PSAD above 0.1 have higher likelihoods of harboring clinically significant disease and should undergo biopsy.

Limitations: Restrospective review, only 55 pt with biopsy available however, pretty significant findings and suggest new threshold for biopsy s/p HoLEP.
OBJECTIVE: To determine whether postop oral antibiotics are associated w/ decreased risk of explantation following artificial urinary sphincter (AUS) or inflatable penile prosthesis (IPP) placement.

Although frequently prescribed, the role of postoperative oral antibiotics in preventing AUS or IPP explantation is unknown.

METHODS: Retrospective review using a MarketScan database to identify male patients undergoing AUS or IPP placement between 2003 - 2014.

The primary end point: device explantation within 3 months of placement.

- Multivariate regression analysis controlling for clinical risk factors assessed the impact of postop oral antibiotic admin on explant rates.
RESULTS: 10,847 and 3594 men who underwent IPP and AUS placement, respectively, bw 2003-2014.

Postoperative oral antibiotics were prescribed to 60.6% of patients following IPP placement and 61.1% of patients following AUS placement.

The most frequently prescribed antibiotics:
- fluoroquinolones (35.6%), cephalexin (17.7%), trimethoprim/sulfamethoxazole (7.0%), and amoxicillin-clavulanate (3.2%).
- Explant rates did not differ based upon receipt of oral antibiotics (antibiotics vs no antibiotics: IPP: 2.2% vs 1.9%, P = .18, AUS: 3.9% vs 4.0%, P = .94).
- On multivariate analysis, no individual class of antibiotic was associated with decreased odds of device explantation.

### Table 2

Postoperative oral antibiotic prescription data

<table>
<thead>
<tr>
<th></th>
<th>Artificial Urinary Sphincter</th>
<th>Penile Prosthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients Prescribed, n (%)</td>
<td>Duration prescribed in days, mean (±SD)</td>
</tr>
<tr>
<td>Overall</td>
<td>2304 (64.1)</td>
<td>9.2 (±6.1)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>686 (29.8)</td>
<td>8.8 (±0.2)</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>534 (24.1)</td>
<td>8.9 (±0.18)</td>
</tr>
<tr>
<td>Trimethoprim- Sulfamethoxazole</td>
<td>286 (12.4)</td>
<td>12.3 (±0.7)</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>725 (31.5)</td>
<td>8.7 (±0.2)</td>
</tr>
<tr>
<td>Amoxicillin- Clavulanate</td>
<td>118 (5.1)</td>
<td>8.3 (±0.3)</td>
</tr>
<tr>
<td>Cefepidine</td>
<td>2 (0.1)</td>
<td>8.5 (±1.5)</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>20 (0.9)</td>
<td>18.8 (±4.5)</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>18 (0.8)</td>
<td>9.8 (±1.8)</td>
</tr>
<tr>
<td>Macrolide</td>
<td>6 (0.3)</td>
<td>4.5 (±0.7)</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>24 (1.0)</td>
<td>10.1 (±1.2)</td>
</tr>
<tr>
<td>Pencillin</td>
<td>28 (1.2)</td>
<td>10.5 (±1.5)</td>
</tr>
</tbody>
</table>
CONCLUSION: Postop oral antibiotics are prescribed to nearly two-thirds of patients but are NOT associated with reduced odds of explant following IPP or AUS placement.

Given the risks to individuals associated with use of antibiotics and increasing bacterial resistance, the role of oral antibiotics after prosthetic placement should be reconsidered and further studied in a prospective fashion.

LIMITATIONS: Retrospective Review, further prospective data needed.

Figure 1. Trends in Prescription of Oral Antibiotics Following Device Implantation Over Time
Most Noteworthy Literature on BPH and Incontinence from 2018-2019

Thank you!

Dr Helen L. Bernie, DO, MPH
Director of Sexual and Reproductive Medicine
Assistant Professor of Urology
Indiana University

Hbernie@IUHealth.org @drhelenbernie

Indiana University Health Indiana University School of Medicine