NEW GUIDELINES FOR 2018!

• Erectile Dysfunction
• Evaluation and Management of Testosterone Deficiency
• Surgical Management of Lower Urinary Tract Symptoms Attributed to BPH
DEAR READER,

This Guidelines-At-A-Glance pocket guide contains essential summarized information from a number of AUA Guidelines Department documents. The evidence-based guidelines and best practice statements from which this information is derived were developed by multidisciplinary panels of leading physicians and other health experts and underwent extensive peer review prior to publication. The content of these guidelines and best practice statements is reviewed every 12 to 36 months to ensure timeliness and accuracy. This ready reference tool will provide up-to-date, evidence-based statements, expert clinical opinion, and pertinent information to help practicing urologists and other clinicians provide optimal patient care.

Sincerely,

Peter E. Clark, MD
Chair, AUA Practice Guidelines Committee

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May 1, 2018

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Guidelines Disclaimer
Funding of the panel was provided by the AUA. Panel members received no remuneration for their work. Each member of the panel provides an ongoing conflict of interest disclosure to the AUA.

While these guidelines do not necessarily establish the standard of care, AUA seeks to recommend and to encourage compliance by practitioners with current best practices related to the condition being treated. As medical knowledge expands and technology advances, the guidelines will change. Today these evidence-based guidelines statements represent not absolute mandates but provisional proposals for treatment under the specific conditions described in each document. For all these reasons, the guidelines do not pre-empt physician judgment in individual cases.

Treating physicians must take into account variations in resources, and patient tolerances, needs, and preferences. Conformance with any clinical guideline does not guarantee a successful outcome. The guideline text may include information or recommendations about certain drug uses (‘off label’) that are not approved by the Food and Drug Administration (FDA), or about medications or substances not subject to the FDA approval process. AUA urges strict compliance with all government regulations and protocols for prescription and use of these substances. The physician is encouraged to carefully follow all available prescribing information about indications, contraindications, precautions and warnings. These guidelines and best practice statements are not intended to provide legal advice about use and misuse of these substances.

Although guidelines are intended to encourage best practices and potentially encompass available technologies with sufficient data at the close of the literature review, they are necessarily time-limited. Guidelines cannot include evaluation of all data on emerging technologies or management, including those that are FDA-approved, which may immediately come to represent accepted clinical practices.

For this reason, the AUA does not regard technologies or management that are too new to be addressed by this guideline as necessarily experimental or investigational.

Each topic in this pocket guide was developed as a summary of the full AUA guideline or best practice statement for that particular subject. The full AUA guideline or best practice statement on each topic should be consulted as the final authority.
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Efforts currently are centered on improving patient safety and reducing costs by standardizing antimicrobial prophylaxis and encouraging proper application including timing of administration and duration of prophylaxis. The following recommendations should help initiate the decisions regarding use of antimicrobial prophylaxis in urologic surgery, the selection of agent, and determination of appropriate dosing while considering the patient’s specific circumstances.

Principles of Surgical Antimicrobial Prophylaxis

- Surgical antimicrobial prophylaxis is the periprocedural systemic administration of an antimicrobial agent intended to reduce the risk of postprocedural local and systemic infections.

- The potential benefit of surgical antimicrobial prophylaxis is based on:
  - Patient-related factors (ability of the host to respond to bacterial invasion) (Table 1). These factors can be additive, compounding their impact.
  - Procedural factors (likelihood of bacterial invasion at the operative site) (Table 2). Urinary procedures are considered “clean-contaminated.”
  - The potential morbidity of infection.

- Surgical antimicrobial prophylaxis is recommended only when the potential benefit exceeds the risks and anticipated costs.
• The antimicrobial agent used for prophylaxis should be effective against the disease-relevant bacterial flora characteristic of the operative site. Cost, conveniences and safety of the agent also should be considered.

• The duration of surgical antimicrobial prophylaxis should extend throughout the period in which bacterial invasion is facilitated and/or is likely to establish an infection.
  ✦ Begin infusion of the first dose within 60 minutes of the surgical incision (with the exception of 120 minutes for intravenous fluoroquinolones and vancomycin).
  ✦ Do not extend prophylaxis beyond 24 hours after a procedure except when a prosthetic material is being placed, an external urinary catheter is present prior to or is placed at the time of the procedure in patients with certain risk factors, or with documented bacteriuria.
  ✦ With an existing infection, a therapeutic course of antimicrobials should be administered in an attempt to sterilize the field or at least to suppress the bacterial count. If urine culture shows no growth, prophylaxis can be omitted.

**Antimicrobial Prophylaxis Recommendations**

**Patients Undergoing Urologic Surgery**

• Antimicrobial prophylaxis for genitourinary procedures solely to prevent infectious endocarditis is no longer recommended by the American Heart Association; the risk of adverse events exceeds the benefit.

• The efficacy of oral fluoroquinolones for prophylaxis is unique to urologic surgical procedures.
- Choose an antimicrobial agent that is effective against the disease – relevant bacterial flora characteristic of the operative site. Consider cost, convenience and safety of the agent.

  - Tables 3, 4 and 5 provide specific recommendations for the settings in which antimicrobial prophylaxis is indicated and the agents of choice.
  
  - The agent should achieve serum and tissue levels that exceed the minimum inhibitory concentration of the organism characteristic of the operative site, have a long half-life, and be safe, inexpensive and not likely to promote bacterial resistance. For the urinary tract, the cephalosporins, oral fluoroquinolones and aminoglycosides generally meet these criteria.
  
  - Absence of an agent from the Tables should not preclude its appropriate use, depending on the situations such as: medication intolerance, agent compatibility, prior infection and community resistance patterns.
  
  - In some cases, prophylaxis should be limited to patients with specific risk factors.
  
  - For surgical prophylaxis, all antimicrobials should be administered IV except for the oral administration for fluoroquinolones, trimethoprim-sulfamethoxazole, bowel preparation agents and some agents given at catheter removal; in addition, intramuscular administration for antimicrobials for transrectal prostate biopsy is acceptable.

- Table 6 presents standard dosing regimens; however, more frequent dosing may be needed. Adjust some drug doses to the patient’s body weight (or corrected dosing weight) or body mass index. Additional doses are required intraoperatively if the procedure extends beyond two half-lives of the initial dose.
Patients with Orthopedic Considerations

- Use antimicrobial prophylaxis to reduce risk of the following:
  - Hematogenous total joint infection in patients who meet both sets of criteria in Table 7.
  - Other infections in some patients who do not meet both sets of criteria in Table 7.

- Do not use antimicrobial prophylaxis:
  - On the basis of orthopedic pins, plates and screws.
  - For total joint replacement on that basis alone.

- The recommended antimicrobial regimen:
  - A single systemic level dose of a fluoroquinolone orally one to two hours preoperatively.
  - Ampicillin 2 g IV (or vancomycin 1 g IV in penicillin allergic patients, over one to two hours) plus gentamicin 1.5 mg/kg IV 30 to 60 minutes preoperatively.
  - Consider additional or alternative agents against specific organisms and/or other infections.
<table>
<thead>
<tr>
<th>Factor</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Impair natural defense mechanisms</strong></td>
<td></td>
</tr>
<tr>
<td>Advanced age</td>
<td>↓ natural defense mechanisms of the urinary tract and immune system</td>
</tr>
<tr>
<td>Anatomic anomalies of the urinary tract</td>
<td></td>
</tr>
<tr>
<td>Poor nutritional status</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>Chronic corticosteroid use</td>
<td></td>
</tr>
<tr>
<td>Immunodeficiency</td>
<td></td>
</tr>
<tr>
<td><strong>Increase local bacterial concentration and/or spectrum of flora</strong></td>
<td></td>
</tr>
<tr>
<td>Externalized catheters</td>
<td>↓ local bacterial concentration and/or spectrum</td>
</tr>
<tr>
<td>Colonized endogenous/exogenous material</td>
<td></td>
</tr>
<tr>
<td>Distant coexistent infection</td>
<td></td>
</tr>
<tr>
<td>Prolonged hospitalization</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 2.**

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**Surgical Wound Classification**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean</td>
<td>Uninfected operative site, with primary skin closure</td>
</tr>
<tr>
<td>Clean-contaminated</td>
<td>Entry into respiratory, alimentary, genital or urinary tracts</td>
</tr>
<tr>
<td>Contaminated</td>
<td>Fresh accidental wounds, major break in sterile technique, gross spillage from gastrointestinal tract or presence of acute but nonpurulent inflammation at the operative site.</td>
</tr>
<tr>
<td>Dirty-infected</td>
<td>Old accidental wound with devitalized tissue or presence of clinical infection or perforated viscera at the operative site. This definition implies that organisms that might cause postoperative infection were present at the operative site before surgery.</td>
</tr>
</tbody>
</table>

# TABLE 3.

## Prophylaxis for Lower Tract Instrumentation

<table>
<thead>
<tr>
<th>Procedure (organisms)</th>
<th>Prophylaxis Indicated</th>
<th>Antimicrobial(s) of Choice</th>
<th>Alternative Antimicrobial(s)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Removal of external urinary catheter,³⁴ (GU tract)</td>
<td>Patients with risk factors³</td>
<td>Fluoroquinolone, Trimethoprim-sulfamethoxazole</td>
<td>Aminoglycoside ± Ampicillin 1st/2nd gen. Cephalosporin Amoxicillin/Clavulanate</td>
</tr>
<tr>
<td>Cystography, urodynamic study or simple cystourethroscopy (GU tract)</td>
<td>Patients with risk factors³</td>
<td>Fluoroquinolone, Trimethoprim-sulfamethoxazole</td>
<td>Aminoglycoside ± Ampicillin 1st/2nd gen. Cephalosporin Amoxicillin/Clavulanate</td>
</tr>
<tr>
<td>Cystourethroscopy with manipulation⁶ (GU tract)</td>
<td>All patients</td>
<td>Fluoroquinolone, Trimethoprim-sulfamethoxazole</td>
<td>Aminoglycoside ± Ampicillin 1st/2nd gen. Cephalosporin Amoxicillin/Clavulanate</td>
</tr>
<tr>
<td>Prostate brachytherapy or cryotherapy (Skin)</td>
<td>Uncertain</td>
<td>1st gen. Cephalosporin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Transrectal prostate biopsy (Intestine)</td>
<td>All patients</td>
<td>Fluoroquinolone, 1st/2nd/3rd gen. Cephalosporin</td>
<td>Aminoglycoside + Metronidazole or Clindamycin</td>
</tr>
</tbody>
</table>

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1 Organisms common to the GU tract — *E. coli*, Proteus sp., Klebsiella sp., Enterococcus; Intestine — *E. coli*, Klebsiella sp., Enterobacter, Serratia sp., Proteus sp., Enterococcus, and Anaerobes; Skin — *S. aureus*, coagulase negative Staph. sp., Group A Strep. sp.

2 Order of agents is not indicative of preference.

3 If urine culture shows no growth prior to procedure, antimicrobial prophylaxis is not necessary.

4 Or full course of culture-directed antimicrobials for documented infection (treatment not prophylaxis).

5 Risk factors—see Table 1.

6 Includes transurethral resection of bladder tumor and prostate, and any biopsy, resection, fulguration, foreign body removal, urethral dilation or urethrotomy, or ureteral instrumentation including catheterization or stent placement/ removal.

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Key: gen., generation; GU, genitourinary.

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### TABLE 4. Prophylaxis for Upper Tract Instrumentation

<table>
<thead>
<tr>
<th>Procedure (organisms)¹</th>
<th>Prophylaxis Indicated</th>
<th>Antimicrobial(s) of Choice²</th>
<th>Alternative Antimicrobial(s)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shock-wave lithotripsy (GU tract)</td>
<td>If risk factors</td>
<td>Fluoroquinolone, trimethoprim-sulfamethoxazole</td>
<td>Aminoglycoside ± Ampicillin 1st/2nd gen. Cephalosporin Amoxicillin/Clavulanate</td>
</tr>
<tr>
<td>Percutaneous renal surgery (GU tract and skin)</td>
<td>All patients</td>
<td>1st/2nd gen. Cephalosporin, Aminoglycoside + Metronidazole or Clindamycin</td>
<td>Aminoglycoside/ Sulbactam Fluoroquinolone</td>
</tr>
<tr>
<td>Ureteroscopy (GU tract)</td>
<td>All patients</td>
<td>Fluoroquinolone, trimethoprim-sulfamethoxazole</td>
<td>Aminoglycoside ± Ampicillin 1st/2nd gen. Cephalosporin Amoxicillin/Clavulanate</td>
</tr>
</tbody>
</table>

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Key: gen., generation; GU, genitourinary.

1 Organisms common to the GU tract – *E. coli, Proteus sp.*, *Klebsiella sp.*, *Enterococcus;* Skin – *S. aureus*, coagulase negative *Staph. sp.*, *Group A Strep. sp.*

2 Order of agents is not indicative of preference.
# TABLE 5.

**Prophylaxis for Open or Laparoscopic Surgery**

<table>
<thead>
<tr>
<th>Procedure (organisms)¹</th>
<th>Prophylaxis Indicated</th>
<th>Antimicrobial(s) of Choice²</th>
<th>Alternative Antimicrobial(s)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal surgery (GU tract, skin and Group B Strep.)</td>
<td>All patients</td>
<td>1st/2nd gen. Cephalosporin Aminoglycoside + Metronidazole or Clindamycin</td>
<td>Ampicillin/Sulbactam Fluoroquinolone</td>
</tr>
<tr>
<td>Involving entry into the urinary tract (GU tract and skin)</td>
<td>All patients</td>
<td>1st/2nd gen. Cephalosporin Aminoglycoside + Metronidazole or Clindamycin</td>
<td>Ampicillin/Sulbactam Fluoroquinolone</td>
</tr>
<tr>
<td>Without entering urinary tract (skin)</td>
<td>Patients with risk factors³</td>
<td>1st gen. Cephalosporin (single dose)</td>
<td>Clindamycin (single dose)</td>
</tr>
<tr>
<td>Involving intestine⁴ (GU tract, skin, and intestine)</td>
<td>All patients</td>
<td>2nd/3rd gen. Cephalosporin, Aminoglycoside + Metronidazole or Clindamycin</td>
<td>Ampicillin/Sulbactam Ticarcillin/Clavulanate Pipercillin/Tazobactam Fluoroquinolone</td>
</tr>
<tr>
<td>Involving implanted prosthesis (GU tract and skin)</td>
<td>All patients</td>
<td>Aminoglycoside + 1st/2nd gen. Cephalosporin or Vancomycin</td>
<td>Ampicillin/Sulbactam Ticarcillin/Clavulanate Pipercillin/Tazobactam</td>
</tr>
</tbody>
</table>

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Key: gen., generation; GU, genitourinary.

1 Organisms common to the GU tract – *E. coli, Proteus sp., Klebsiella sp., Enterococcus;* Intestine – *E. coli, Klebsiella sp., Enterobacter, Serratia sp., Proteus sp., Enterococcus,* and Anaerobes; Skin – *S. aureus, coagulase negative Staph. sp.,* Group A *Strep. sp.*

2 Order of agents is not indicative of preference.

3 Risk factors - see Table 1.

4 For surgery involving colon, bowel preparation with oral neomycin plus either erythromycin base or metronidazole can be added to or substituted for systemic agents.
# TABLE 6.

## Antimicrobial Agents and Doses for Periprocedural Use

<table>
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<tr>
<th>Category</th>
<th>Drug/Agent</th>
<th>Dose/Route</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluoroquinolones</strong></td>
<td>Levofloxacin: 500 mg PO single dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin: 500 mg PO [q12h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ofloxacin: 400 mg PO [q12h]</td>
<td></td>
</tr>
<tr>
<td><strong>Aminoglycosides</strong></td>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tobramycin: 5 mg/kg IV single dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Amikacin: 15 mg/kg IV single dose</td>
<td></td>
</tr>
<tr>
<td><strong>1st Generation cephalosporins</strong></td>
<td>Cephalexin: 500 mg PO [q6h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cephradine: 500 mg PO [q6h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefadroxil: 500 mg PO [q12h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefazolin: 1 g IV [q8h]</td>
<td></td>
</tr>
<tr>
<td><strong>2nd Generation cephalosporins</strong></td>
<td>Cefaclor: 500 mg PO [q8h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefprozil: 500 mg PO [q12h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefuroxime: 500 mg PO [q12h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefoxitin: 1 - 2 g IV [q8h]</td>
<td></td>
</tr>
<tr>
<td><strong>3rd Generation cephalosporins</strong> (oral agents not listed)</td>
<td>Ceftizoxime: 1 g IV [q8h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftazidime: 1 g IV [q12h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone: 1 - 2 IV single dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefotaxime: 1 g IV [q8h]</td>
<td></td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td>Amoxicillin/clavulanate: 875 mg PO [q12h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ampicillin: 1 - 2 g IV [q6h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ampicillin/sulbactam: 1.5 - 3 g IV [q6h]</td>
<td></td>
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<tr>
<td></td>
<td>Aztreonam 1 - 2 g IV [q8h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clindamycin: 600 mg IV [q8h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Erythromycin base (for bowel preparation): 1 - 2 g PO [variable]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metronidazole: 1 g IV [q12h]; (for bowel preparation) 1 - 2 g PO [variable]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neomycin(for bowel preparation): 1 - 2 g PO [variable]</td>
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<tr>
<td></td>
<td>Pipercillin/tazobactam: 3.375 g IV [q6h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ticarcillin/clavulanate: 3.1 g IV [q6h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trimethoprim-sulfamethoxazole: 1 double-strength tablet PO [q12h]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vancomycin: 1 g IV [q12h]</td>
<td></td>
</tr>
</tbody>
</table>

Key: g, gram; h, hour; IV, intravenous; kg, kilogram; mg, milligram; PO, orally; q, every.

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### TABLE 7. Criteria for antimicrobial prophylaxis for patients with orthopedic conditions

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Increased risk of hematogenous total joint infection</th>
<th>Increased risk of bacteremia associated with urologic procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased risk of bacteremia associated with urologic procedures</td>
<td>Stone manipulation (includes shock-wave lithotripsy)</td>
<td>Transmural incision into urinary tract (does not include simple ligation with excision or percutaneous drainage procedure)</td>
</tr>
<tr>
<td>Immunocompromise and prosthetic joint replacement</td>
<td>Transmural incision into urinary tract</td>
<td>Endoscopy of upper tract (ureter and kidney)</td>
</tr>
<tr>
<td>• Inflammatory arthropathies (e.g., rheumatoid arthritis, systemic lupus erythematosus)</td>
<td>Procedures including bowel segments</td>
<td>Transrectal prostate biopsy</td>
</tr>
<tr>
<td>• Drug-induced immunosuppression</td>
<td>Stone manipulation (includes shock-wave lithotripsy)</td>
<td>Urinary tract entry (except for urethral catheterization) in individuals with higher risk of bacterial colonization:</td>
</tr>
<tr>
<td>• Radiation-induced immunosuppression</td>
<td>Stone manipulation (includes shock-wave lithotripsy)</td>
<td>• Indwelling catheter or intermittent catheterization</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>Stone manipulation (includes shock-wave lithotripsy)</td>
<td>• Indwelling ureteral stent</td>
</tr>
<tr>
<td>• Previous prosthetic joint infection</td>
<td>Stone manipulation (includes shock-wave lithotripsy)</td>
<td>• Urinary retention</td>
</tr>
<tr>
<td>• Malnourishment</td>
<td>Stone manipulation (includes shock-wave lithotripsy)</td>
<td>• History of recent/recurrent urinary tract infection or prostatitis</td>
</tr>
<tr>
<td>• Hemophilia</td>
<td>Stone manipulation (includes shock-wave lithotripsy)</td>
<td>• Urinary diversion</td>
</tr>
<tr>
<td>• HIV infection</td>
<td>Stone manipulation (includes shock-wave lithotripsy)</td>
<td></td>
</tr>
<tr>
<td>• Diabetes</td>
<td>Stone manipulation (includes shock-wave lithotripsy)</td>
<td></td>
</tr>
<tr>
<td>• Malignancy</td>
<td>Stone manipulation (includes shock-wave lithotripsy)</td>
<td></td>
</tr>
</tbody>
</table>

Purpose

Benign prostatic hyperplasia (BPH) is a histologic diagnosis that refers to the proliferation of smooth muscle and epithelial cells within the prostatic transition zone. The prevalence and the severity of lower urinary tract symptoms (LUTS) in the aging male can be progressive and is an important diagnosis in the healthcare of patients and the welfare of society. In the management of bothersome LUTS, it is important that healthcare providers recognize the complex dynamics of the bladder, bladder neck, prostate, and urethra, in addition to the fact that symptoms may result from interactions of these organs as well as with the central nervous system or other systemic diseases (e.g., metabolic syndrome, congestive heart failure). Despite the more prevalent (and often first line) use of medical therapy for men suffering from LUTS attributed to BPH, there still remain clinical scenarios where surgery is indicated as the initial intervention for LUTS/BPH and should be recommended, providing other medical comorbidities do not preclude this approach. It is the hope that this revised guideline will provide a useful reference on the effective evidence-based surgical management of male LUTS secondary to BPH (LUTS/BPH). Please see the accompanying algorithm for a summary of the surgical procedures detailed in the guideline.
AUA Nomenclature

The AUA nomenclature system links statement types to a number of factors including strength of evidence, magnitude of benefit and risks/burdens, and panel judgment. There are three evidence-based statement types: **Strong Recommendations** and **Moderate Recommendations** are directive statements that indicate that there is a net benefit (or harm) associated with a clinical action, while a **Conditional Recommendation** is a non-directive Statement that is used when the clinical action does not have a clear net benefit (or harm).

In addition, there are two statement types that are used when pertinent evidence is not present in the systematic review of literature associated with the guideline: **Expert Opinions** are statements made by panel consensus based on members’ clinical training, experience, knowledge, and judgment, while a **Clinical Principle** is a statement about a component of clinical care that is very widely agreed upon by urologists or other clinicians.

**Evaluation and Preoperative Testing**

• 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)

• Clinicians should consider assessment of prostate size and shape via abdominal or transrectal ultrasound, or cystoscopy, or by preexisting cross-sectional imaging
Benign Prostatic Hyperplasia (i.e. magnetic resonance imaging [MRI]/ computed tomography [CT]) prior to surgical intervention for LUTS attributed to BPH. (Clinical Principle)

- Clinicians should perform a PVR assessment prior to surgical intervention for LUTS attributed to BPH. (Clinical Principle)

- Clinicians should consider uroflowmetry prior to surgical intervention for LUTS attributed to BPH. (Clinical Principle)

- Clinicians should consider pressure flow studies prior to surgical intervention for LUTS attributed to BPH when diagnostic uncertainty exists. (Expert Opinion)

**Surgical Therapy**

- 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)

- Clinicians should not perform surgery solely for the presence of an asymptomatic bladder diverticulum; however, evaluation for the presence of BOO should be considered. (Clinical Principle)

**Transurethral Resection of the Prostate (TURP)**

- TURP should be offered as a treatment option for men with LUTS attributed to BPH. (Moderate Recommendation; Evidence Level: Grade B)
Clinicians may use a monopolar or bipolar approach to TURP, depending on their expertise with these techniques. (Expert Opinion)

**Simple Prostatectomy**

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)

**Transurethral Incision of the Prostate (TUIP)**

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

**Transurethral Vaporization of the Prostate (TUVP)**

Bipolar TUVP may be offered to patients for the treatment of LUTS attributed to BPH. (Conditional Recommendation; Evidence Level: Grade B)

**Photoselective Vaporization of the Prostate (PVP)**

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)
Prostatic Urethral Lift (PUL)

- Clinicians should consider PUL as an option for patients with LUTS attributed to BPH provided prostate volume <80g and verified absence of an obstructive middle lobe; however, patients should be informed that symptom reduction and flow rate improvement is less significant compared to TURP. (Moderate Recommendation; Evidence Level: Grade C)

- 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 Microwave Therapy (TUMT)

- 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)

Water Vapor Thermal Therapy

- Water vapor thermal therapy may be offered to patients with LUTS attributed to BPH provided prostate volume <80g; however, patients should be informed that evidence of efficacy, including longer-term retreatment rates, remains limited. (Conditional Recommendation; Evidence Level: Grade C)

- Water vapor thermal therapy may be offered to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C)
Transurethral Needle Ablation (TUNA)

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

Laser Enucleation

- 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)

Prostate Artery Embolization (PAE)

- PAE is not recommended for the treatment of LUTS attributed to BPH outside the context of a clinical trial. (Expert Opinion)

Medically Complicated Patients

- 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)
Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia

**EVALUATION AND PREOPERATIVE TESTING**

**Recommended Evaluation**
- Relevant medical history
- Assessment of LUTS
- Discussion of symptom severity and bother (AUA-SI)
- Physical examination

**Preoperative Testing**
- Assessment of PVR
- Assessment of prostate size and shape

**Additional Considerations**
- Uroflowmetry
- Pressure flow studies

Some individuals found to have catheter-dependent urinary retention may have compromised detrusor function, and some are unlikely to benefit from surgery, though most with retention, CIC, and documented detrusor underactivity can still benefit from an outlet procedure. Those with acute and/or chronic renal insufficiency, refractory urinary retention, recurrent UTIs, bladder stones, or gross hematuria secondary to BPH are more likely to benefit from more aggressive interventional therapy.
Benign Prostatic Hyperplasia

SURGICAL THERAPY

Assessment of Prostate Size

- Simple Prostatectomy
- HoLEP
- ThuLEP

Large Prostate

• HoLEP
• PVP
• PUL
• ThuLEP
• TUMT
• TURP

Size Independent Options

- HoLEP
- ThuLEP

Average Prostate

Small Prostate

- TURP
- TUVP
- Water Vapor Thermal Therapy

MEDICALLY COMPLICATED PATIENTS

In patients who are at higher risk of bleeding, such as those on anticoagulation drugs, therapies with a lower need for blood transfusion, such as HoLEP, PVP and ThuLEP, should be considered. For additional information on the use of anticoagulation and antiplatelet therapy in surgical patients, refer to the ICUD/AUA review on Anticoagulation and Antiplatelet Therapy in Urologic Practice.

1 Eligibility for a PUL procedure is dependent upon absence of obstructing midline prostate tissue and prostate volume <80g

2 Eligibility for a TUIP procedure is dependent upon prostate volume <30g

3 Eligibility for a Water Vapor Thermal Therapy procedure is dependent upon prostate volume <80g
AUA/SUO GUIDELINE – 2016

Purpose

The survival rate for the majority of patients with non-muscle invasive bladder cancer (NMIBC) is favorable; however, the rates of recurrence and progression to muscle-invasive bladder cancer (MIBC) are important surrogate endpoints for overall prognosis, as these are major determinants of long-term outcome. The recurrence and progression probability rates depend on several clinical and pathologic factors. Therefore, the ability to predict risk of recurrence and progression and treat the disease appropriately is important. This guideline provides a risk-stratified clinical framework for the management of NMIBC.

AUA Nomenclature

The AUA nomenclature system links statement types to a number of factors including strength of evidence, magnitude of benefit and risks/burdens, and panel judgment. There are three evidence-based statement types: **Strong Recommendations** and **Moderate Recommendations** are directive statements that indicate that there is a net benefit (or harm) associated with a clinical action, while a **Conditional Recommendation** is a non-directive Statement that is used when the clinical action does not have a clear net benefit (or harm).

In addition, there are two statement types that are used
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**TABLE 1.**

**AUA Risk Stratification for Non-Muscle Invasive Bladder Cancer**

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Intermediate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>LG(^a) solitary Ta ≤ 3cm</td>
<td>Recurrence within 1 year, LG Ta</td>
<td>HG T1</td>
</tr>
<tr>
<td>PUNLMP(^b)</td>
<td>Solitary LG Ta &gt; 3cm</td>
<td>Any recurrent, HG Ta</td>
</tr>
<tr>
<td></td>
<td>LG Ta, multifocal</td>
<td>HG Ta, &gt;3cm (or multifocal)</td>
</tr>
<tr>
<td></td>
<td>HG(^c) Ta, ≤ 3cm</td>
<td>Any CIS(^d)</td>
</tr>
<tr>
<td></td>
<td>LG T1</td>
<td>Any BCG failure in HG patient</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Any variant histology</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Any LVI(^e)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Any HG prostatic urethral involvement</td>
</tr>
</tbody>
</table>

\(^a\)LG = low grade; \(^b\)PUNLMP = papillary urothelial neoplasm of low malignant potential; \(^c\)HG = high grade; \(^d\)CIS = carcinoma in situ; \(^e\)LVI = lymphovascular invasion
Guideline Statements

Diagnosis

- At the time of resection of suspected bladder cancer, a clinician should perform a thorough cystoscopic examination of a patient’s entire urethra and bladder that evaluates and documents tumor size, location, configuration, number, and mucosal abnormalities. *(Clinical Principle)*

- At initial diagnosis of a patient with bladder cancer, a clinician should perform complete visual resection of the bladder tumor(s), when technically feasible. *(Clinical Principle)*

- A clinician should perform upper urinary tract imaging as a component of the initial evaluation of a patient with bladder cancer. *(Clinical Principle)*

- In a patient with a history of NMIBC with normal cystoscopy and positive cytology, a clinician should consider prostatic urethral biopsies and upper tract imaging, as well as enhanced cystoscopic techniques (blue light cystoscopy, when available), ureteroscopy, or random bladder biopsies. *(Expert Opinion)*

Risk Stratification

- At the time of each occurrence/recurrence, a clinician should assign a clinical stage and classify a patient accordingly as “low-,” “intermediate-,” or “high-risk.” *(Moderate Recommendation; Evidence Level: Grade C)*
Variant Histologies

- An experienced genitourinary pathologist should review the pathology of a patient with any doubt in regards to variant or suspected variant histology (e.g., micropapillary, nested, plasmacytoid, neuroendocrine, sarcomatoid), extensive squamous or glandular differentiation, or the presence/absence of LVI. *(Moderate Recommendation; Evidence Level: Grade C)*

- If a bladder sparing approach is being considered in a patient with variant histology, then a clinician should perform a restaging transurethral resection of bladder tumor (TURBT) within four to six weeks of the initial TURBT. *(Expert Opinion)*

- Due to the high rate of upstaging associated with variant histology, a clinician should consider offering initial radical cystectomy. *(Expert Opinion)*

Urine Markers after Diagnosis of Bladder Cancer

- In surveillance of NMIBC, a clinician should not use urinary biomarkers in place of cystoscopic evaluation. *(Strong Recommendation; Evidence Level: Grade B)*

- In a patient with a history of low-risk cancer and a normal cystoscopy, a clinician should not routinely use a urinary biomarker or cytology during surveillance. *(Expert Opinion)*

- In a patient with NMIBC, a clinician may use biomarkers to assess response to intravesical BCG (UroVysion® FISH) and adjudicate equivocal cytology (UroVysion® FISH and ImmunoCyt™). *(Expert Opinion)*
TURBT/Repeat Resection: Timing, Technique, Goal, Indication

- In a patient with non-muscle invasive disease who underwent an incomplete initial resection (not all visible tumor treated), a clinician should perform repeat transurethral resection or endoscopic treatment of all remaining tumor if technically feasible. (*Strong Recommendation; Evidence Level: Grade B*)

- In a patient with high-risk, high-grade Ta tumors, a clinician should consider performing repeat transurethral resection of the primary tumor site within six weeks of the initial TURBT. (*Moderate Recommendation; Evidence Level: Grade C*)

- In a patient with T1 disease, a clinician should perform repeat transurethral resection of the primary tumor site to include muscularis propria within six weeks of the initial TURBT. (*Strong Recommendation; Evidence Level: Grade B*)

Intravesical Therapy; BCG/Maintenance; Chemotherapy/BCG Combinations

- In a patient with suspected or known low- or intermediate-risk bladder cancer, a clinician should consider administration of a single postoperative instillation of intravesical chemotherapy (e.g., mitomycin C or epirubicin) within 24 hours of TURBT. In a patient with a suspected perforation or extensive resection, a clinician should not use postoperative chemotherapy. (*Moderate Recommendation; Evidence Level: Grade B*)

- In a low-risk patient, a clinician should not administer induction intravesical therapy. (*Moderate Recommendation; Evidence Level: Grade C*)
- In an intermediate-risk patient a clinician should consider administration of a six week course of induction intravesical chemotherapy or immunotherapy. *(Moderate Recommendation; Evidence Level: Grade B)*

- In a high-risk patient with newly diagnosed CIS, high-grade T1, or high-risk Ta urothelial carcinoma, a clinician should administer a six-week induction course of BCG. *(Strong Recommendation; Evidence Level: Grade B)*

- In an intermediate-risk patient who completely responds to an induction course of intravesical chemotherapy, a clinician may utilize maintenance therapy. *(Conditional Recommendation; Evidence Level: Grade C)*

- In an intermediate-risk patient who completely responds to induction BCG, a clinician should consider maintenance BCG for one year, as tolerated. *(Moderate Recommendation; Evidence Level: Grade C)*

- In a high-risk patient who completely responds to induction BCG, a clinician should continue maintenance BCG for three years, as tolerated. *(Moderate Recommendation; Evidence Level: Grade B)*

**BCG Relapse and Salvage Regimens**

- In an intermediate- or high-risk patient with persistent or recurrent disease or positive cytology following intravesical therapy, a clinician should consider performing prostatic urethral biopsy and an upper tract evaluation prior to administration of additional intravesical therapy. *(Conditional Recommendation; Evidence Level: Grade C)*

- In an intermediate- or high-risk patient with persistent or recurrent Ta or CIS disease after a single course of
induction intravesical BCG, a clinician should offer a second course of BCG. *(Moderate Recommendation; Evidence Level: Grade C)*

- In a patient fit for surgery with high-grade T1 disease after a single course of induction intravesical BCG, a clinician should offer radical cystectomy. *(Moderate Recommendation; Evidence Level: Grade C)*

- A clinician should not prescribe additional BCG to a patient who is intolerant of BCG or has documented recurrence on TURBT of high-grade, non-muscle-invasive disease and/or CIS within six months of two induction courses of BCG or induction BCG plus maintenance. *(Moderate Recommendation; Evidence Level: Grade C)*

- In a patient with persistent or recurrent intermediate- or high-risk NMIBC who is unwilling or unfit for cystectomy following two courses of BCG, a clinician may recommend clinical trial enrollment. A clinician may offer this patient intravesical chemotherapy when clinical trials are unavailable. *(Expert Opinion)*

**Role of Cystectomy in NMIBC**

- In a patient with Ta low- or intermediate-risk disease, a clinician should not perform radical cystectomy until bladder-sparing modalities (staged TURBT, intravesical therapies) have failed. *(Clinical Principle)*

- In a high-risk patient who is fit for surgery with persistent high-grade T1 disease on repeat resection, or T1 tumors with associated CIS, LVI, or variant histologies, a clinician should consider offering initial radical cystectomy. *(Moderate Recommendation; Evidence Level: Grade C)*
In a high-risk patient with persistent or recurrent disease within one year following treatment with two induction cycles of BCG or BCG maintenance, a clinician should offer radical cystectomy. *(Moderate Recommendation; Evidence Level: Grade C)*

**Enhanced Cystoscopy**

- In a patient with NMIBC, a clinician should offer blue light cystoscopy at the time of TURBT, if available, to increase detection and decrease recurrence. *(Moderate Recommendation; Evidence Level: Grade B)*

- In a patient with NMIBC, a clinician may consider use of narrow band imaging to increase detection and decrease recurrence. *(Conditional Recommendation; Evidence Level: Grade C)*

**Risk Adjusted Surveillance and Follow-up Strategies**

- After completion of the initial evaluation and treatment of a patient with NMIBC, a clinician should perform the first surveillance cystoscopy within three to four months. *(Expert Opinion)*

- For a low-risk patient whose first surveillance cystoscopy is negative for tumor, a clinician should perform subsequent surveillance cystoscopy six to nine months later, and then annually thereafter; surveillance after five years in the absence of recurrence should be based on shared-decision making between the patient and clinician. *(Moderate Recommendation; Evidence Level: Grade C)*

- In an asymptomatic patient with a history of low-risk NMIBC, a clinician should not perform routine surveillance upper tract imaging. *(Expert Opinion)*
● In a patient with a history of low-grade Ta disease and a noted sub-centimeter papillary tumor(s), a clinician may consider in-office fulguration as an alternative to resection under anesthesia. (Expert Opinion)

● For an intermediate-risk patient whose first surveillance cystoscopy is negative for tumor, a clinician should perform subsequent cystoscopy with cytology every 3-6 months for 2 years, then 6-12 months for years 3 and 4, and then annually thereafter. (Expert Opinion)

● For a high-risk patient whose first surveillance cystoscopy is negative for tumor, a clinician should perform subsequent cystoscopy with cytology every three to four months for two years, then six months for years three and four, and then annually thereafter. (Expert Opinion)

● For an intermediate- or high-risk patient, a clinician should consider performing surveillance upper tract imaging at one to two year intervals. (Expert Opinion)
Non-Muscle Invasive Bladder Cancer: AUA/SUO Treatment Algorithm

**Low Risk**
- Postoperative Chemo
  - Complete response
  - Partial or no response

**Int. Risk**
- Others
  - Partial or no response
  - TURBT
    - Int. Risk
    - Others
    - Re-TURBT† +/- Chemo
      - Partial or no response
      - BCG
        - Induction Chemo
          - Others
            - Partial or no response
            - BCG
              - Reinduce
                - Partial or no response
                - Postoperative Chemo
                  - Complete response
                  - Others

**High Risk**
- Re-TURBT† +/- Chemo
  - T1, LVI, +/− variant
  - Cystectomy
    - Others
      - Partial or no response
      - BCG
        - T1
          - Partial or no response
          - Postoperative Chemo
            - Complete response
            - Others

---

*Consider fulguration in low-volume disease recurrence; otherwise reassess as intermediate risk.

†Timely re-TURBT (within six weeks) should be performed if there are concerns regarding an incomplete resection and/or if bladder sparing treatment (e.g., intravesical therapy or surveillance), is being planned.
TREATMENT OF NON-METASTATIC MUSCLE-INVASIVE BLADDER CANCER

AUA/ASCO/ASTRO/SUO GUIDELINE – 2017

Purpose

Although representing approximately 25% of patients diagnosed with bladder cancer, muscle-invasive bladder cancer (MIBC) carries a significant risk of death that has not significantly changed in decades. Increasingly, clinicians and patients recognize the importance of multidisciplinary collaborative efforts that take into account survival and quality of life concerns. For the first time for any type of malignancy, the American Urological Association (AUA), the American Society of Clinical Oncology (ASCO), the American Society for Radiation Oncology (ASTRO), and the Society of Urologic Oncology (SUO) have formulated an evidence-based guideline. This guideline provides a risk-stratified clinical framework for the management of clinically non-metastatic, muscle-invasive urothelial bladder cancer (cT2-T4N0M0) and focuses on evaluation, treatment, and surveillance guided toward curative intent. This document is designed for use in conjunction with the associated treatment algorithm.

AUA Nomenclature

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are directive statements that indicate that there is a net benefit (or harm) associated with a clinical action, while a **Conditional Recommendation** is a non-directive Statement that is used when the clinical action does not have a clear net benefit (or harm).

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**Guideline Statements**

**Initial Patient Evaluation and Counseling**

- Prior to treatment consideration, a full history and physical exam should be performed, including an exam under anesthesia, at the time of transurethral resection of bladder tumor (TURBT) for a suspected invasive cancer. *(Clinical Principle)*

- Prior to MIBC management, clinicians should perform a complete staging evaluation, including imaging of the chest and cross sectional imaging of the abdomen and pelvis with intravenous contrast if not contraindicated. Laboratory evaluation should include a comprehensive metabolic panel (complete blood count, liver function tests, alkaline phosphatase, and renal function). *(Clinical Principle)*
• An experienced genitourinary pathologist should review the pathology of a patient when variant histology is suspected or if muscle invasion is equivocal (e.g., micropapillary, nested, plasmacytoid, neuroendocrine, sarcomatoid, extensive squamous or glandular differentiation). *(Clinical Principle)*

• For patients with newly diagnosed MIBC, curative treatment options should be discussed before determining a plan of therapy that is based on both patient comorbidity and tumor characteristics. Patient evaluation should be completed using a multidisciplinary approach. *(Clinical Principle)*

• Prior to treatment, clinicians should counsel patients regarding complications and the implications of treatment on quality of life (e.g., impact on continence, sexual function, fertility, bowel dysfunction, metabolic problems). *(Clinical Principle)*

### TREATMENT

**Neoadjuvant/Adjuvant Chemotherapy**

• Utilizing a multidisciplinary approach, clinicians should offer cisplatin-based neoadjuvant chemotherapy to eligible radical cystectomy patients prior to cystectomy. *(Strong Recommendation; Evidence Level: Grade B)*

• Clinicians should not prescribe carboplatin-based neoadjuvant chemotherapy for clinically resectable stage cT2-T4aN0 bladder cancer. Patients ineligible for cisplatin-based neoadjuvant chemotherapy should proceed to definitive locoregional therapy. *(Expert Opinion)*
Clinicians should perform radical cystectomy as soon as possible following a patient’s completion of and recovery from neoadjuvant chemotherapy. *(Expert Opinion)*

Eligible patients who have not received cisplatin-based neoadjuvant chemotherapy and have non-organ confined (pT3/T4 and/or N+) disease at cystectomy should be offered adjuvant cisplatin-based chemotherapy. *(Moderate Recommendation; Evidence Level: Grade C)*

**Radical Cystectomy**

Clinicians should offer radical cystectomy with bilateral pelvic lymphadenectomy for surgically eligible patients with resectable non-metastatic (M0) MIBC. *(Strong Recommendation; Evidence Level: Grade B)*

When performing a standard radical cystectomy, clinicians should remove the bladder, prostate, and seminal vesicles in males and should remove the bladder, uterus, fallopian tubes, ovaries, and anterior vaginal wall in females. *(Clinical Principle)*

Clinicians should discuss and consider sexual function preserving procedures for patients with organ-confined disease and absence of bladder neck, urethra, and prostate (male) involvement. *(Moderate Recommendation; Evidence Level: Grade C)*

**Urinary Diversion**

In patients undergoing radical cystectomy, ileal conduit, continent cutaneous, and orthotopic neobladder urinary diversions should all be discussed. *(Clinical Principle)*

In patients receiving an orthotopic urinary diversion, clinicians must verify a negative urethral margin. *(Clinical Principle)*
Perioperative Surgical Management

- Clinicians should attempt to optimize patient performance status in the perioperative setting. *(Expert Opinion)*

- Perioperative pharmacologic thromboembolic prophylaxis should be given to patients undergoing radical cystectomy. *(Strong Recommendation; Evidence Level: Grade B)*

- In patients undergoing radical cystectomy, μ-opioid antagonist therapy should be used to accelerate gastrointestinal recovery, unless contraindicated. *(Strong Recommendation; Evidence Level: Grade B)*

- Patients should receive detailed teaching regarding care of urinary diversion prior to discharge from the hospital. *(Clinical Principle)*

Pelvic Lymphadenectomy

- Clinicians must perform a bilateral pelvic lymphadenectomy at the time of any surgery with curative intent. *(Strong Recommendation; Evidence Level: Grade B)*

- When performing bilateral pelvic lymphadenectomy, clinicians should remove, at a minimum, the external and internal iliac and obturator lymph nodes (standard lymphadenectomy). *(Clinical Principle)*
BLADDER PRESERVING APPROACHES

Patient Selection

- For patients with newly diagnosed non-metastatic MIBC who desire to retain their bladder, and for those with significant comorbidities for whom radical cystectomy is not a treatment option, clinicians should offer bladder preserving therapy when clinically appropriate. (Clinical Principle)

- In patients under consideration for bladder preserving therapy, maximal debulking TURBT and assessment of multifocal disease/carcinoma in situ should be performed. (Strong Recommendation; Evidence Level: Grade C)

Maximal TURBT and Partial Cystectomy

- Patients with MIBC who are medically fit and consent to radical cystectomy should not undergo partial cystectomy or maximal TURBT as primary curative therapy. (Moderate Recommendation; Evidence Level: Grade C)

Primary Radiation Therapy

- For patients with MIBC, clinicians should not offer radiation therapy alone as a curative treatment. (Strong Recommendation; Evidence Level: Grade C)

Multi-Modal Bladder Preserving Therapy

- For patients with MIBC who have elected multi-modal bladder preserving therapy, clinicians should offer maximal TURBT, chemotherapy combined with external beam radiation therapy, and planned cystoscopic re-evaluation. (Strong Recommendation; Evidence Level: Grade B)

- Radiation sensitizing chemotherapy regimens should
include cisplatin or 5-fluorouracil and mitomycin C. *(Strong Recommendation; Evidence Level: Grade B)*

- Following completion of bladder preserving therapy, clinicians should perform regular surveillance with CT scans, cystoscopy, and urine cytology. *(Strong Recommendation; Evidence Level: Grade C)*

**Bladder Preserving Treatment Failure**

- In patients who are medically fit and have residual or recurrent muscle-invasive disease following bladder preserving therapy, clinicians should offer radical cystectomy with bilateral pelvic lymphadenectomy. *(Strong Recommendation; Evidence Level: Grade C)*

- In patients who have a non-muscle invasive recurrence after bladder preserving therapy, clinicians may offer either local measures, such as TURBT with intravesical therapy, or radical cystectomy with bilateral pelvic lymphadenectomy. *(Moderate Recommendation; Evidence Level: Grade C)*

**PATIENT SURVEILLANCE AND FOLLOW UP**

**Imaging**

- Clinicians should obtain chest imaging and cross sectional imaging of the abdomen and pelvis with CT or MRI at 6-12 month intervals for 2-3 years and then may continue annually. *(Expert Opinion)*

**Laboratory Values and Urine Markers**

- Following therapy for MIBC, patients should undergo laboratory assessment at three to six month intervals for two to three years and then annually thereafter. *(Expert Opinion)*
Following radical cystectomy in patients with a retained urethra, clinicians should monitor the urethral remnant for recurrence. *(Expert Opinion)*

**Patient Survivorship**

- Clinicians should discuss with patients how they are coping with their bladder cancer diagnosis and treatment and should recommend that patients consider participating in cancer support groups or consider receiving individual counseling. *(Expert Opinion)*

- Clinicians should encourage bladder cancer patients to adopt healthy lifestyle habits, including smoking cessation, exercise, and a healthy diet, to improve long-term health and quality of life. *(Expert Opinion)*

**Variant Histology**

- In patients diagnosed with variant histology, clinicians should consider unique clinical characteristics that may require divergence from standard evaluation and management for urothelial carcinoma. *(Expert Opinion)*
NON-METASTASIC MUSCLE-INVASIVE BLADDER CANCER: Treatment Algorithm

**Bladder Preserving Options**

**Preferred Option**

**Multi-Modal Bladder-Sparing Protocol**
- Maximal TURBT
- Chemotherapy (cisplatin or 5-FU Mitomycin-C)
- XRT

**Mid-Treatment Restaging**

**Complete Response**

**Complete Chemotherapy/XRT**

**Patient desires bladder preservation**

**Multidisciplinary Approach**
- Neoadjuvant chemotherapy
- Radical cystectomy
- Bladder preserving options

**Radical Cystectomy, Bilateral Pelvic Lymph-Node Dissection, and Urinary Diversion**

**Persistant/Recurrent Invasive Disease**

**Partial Cystectomy with Pelvic Lymphadenectomy**
- Neoadjuvant chemotherapy recommended

CBC= complete blood count; CMP= comprehensive metabolic panel; CXR= chest X-ray; p= pathologic stage; TURBT= trans-urethral resection of bladder tumor;
Bladder Cancer: Muscle Invasive

**Staging**
- CT abdomen/pelvis with IV contrast
- Chest imaging (X-ray or CT with IV contrast)
- Laboratory evaluation (CMP, CBC)
- Exam under anesthesia

**Alternatives**
- PET scan, if indicated (equivocal staging exams and/or biopsy not feasible)
- Bone scan, if indicated (elevated alkaline phosphatase and/or pain complaints)
- MRI imaging, if indicated (CT contrast imaging cannot be performed)

**DIAGNOSIS: NON-METASTATIC MUSCLE INVASIVE BLADDER CANCER**

**Surveillance**
- Cystoscopy every 3 months for 1 year, then 6-12 months
- CT abdomen/pelvis and CXR every 3-6 months for 2 years, then annually

**Surveillance after Radical Cystectomy**
- yp> T2 or N+
  - Clinical trial
  - Labs per T2
  - CT abdomen/pelvis every 3-6 months for 3 years
  - Annual chest imaging
- p> T2 or N+
  - Consider adjuvant chemo-therapy
  - Follow-up as per <T2

**Surveillance**
- Cystoscopy every 3 months for 1 year, then 6-12 months
- CT abdomen/pelvis and CXR every 3-6 months for 2 years, then annually

**Cisplatin Eligible**

**Cisplatin-Based Neoadjuvant Chemotherapy**
- pT2 or less or yp≤T2N0
  - CMP, CBC, B12
  - CT abdomen/pelvis every 6-12 months for 2-3 years
  - Option for annual upper tract imaging with CT or ultrasound to year 5

**Palliative Care**

**Patient unwilling or unfit for treatment**

**Recurrence/Persistent Invasive Disease**

XRT= external beam radiation therapy; yp= pathologic stage after neoadjuvant chemotherapy
Purpose

This guideline’s purpose is to provide direction to clinicians and patients regarding how to work up and follow patients with the finding of asymptomatic microhematuria (AMH). The strategies and approaches recommended in this document were derived from evidence-based and consensus-based processes. This document constitutes a clinical strategy and is not intended to be interpreted rigidly. The most effective approach for a particular patient is best determined by the individual clinician and patient. As the science relevant to AMH evolves and improves, the strategies presented here will require amendment to remain consistent with the highest standards of clinical care.

Guideline Statements

- Asymptomatic microhematuria (AMH) is defined as 3 or greater red blood cells (RBC) per high powered field (HPF) on a properly collected urinary specimen in the absence of an obvious benign cause. A positive dipstick does not define AMH and evaluation should be based solely on findings from microscopic examination of urinary sediment and not on a dipstick reading. A positive
Hematuria

The assessment of the asymptomatic microhematuria patient should include a careful history, physical examination, and laboratory examination to rule out benign causes of AMH, such as infection, menstruation, vigorous exercise, medical renal disease, viral illness, trauma, or recent urological procedures.

Once benign causes have been ruled out, the presence of asymptomatic microhematuria should prompt a urologic evaluation.

At the initial evaluation, an estimate of renal function should be obtained (may include calculated eGRF, creatinine, and blood urea nitrogen [BUN]) because intrinsic renal disease may have implications for renal related risk during the evaluation and management of patients with AMH.

The presence of dysmorphic red blood cells, proteinuria, cellular casts, and/or renal insufficiency or any other clinical indicator suspicious for renal parenchymal disease warrants concurrent nephrologic workup but does not preclude the need for urologic evaluation.

Microhematuria that occurs in patients who are taking anti-coagulants requires urologic evaluation and nephrologic evaluation regardless of the type or level of anti-coagulation therapy.

For the urologic evaluation of asymptomatic microhematuria, a cystoscopy should be performed on all patients aged 35 years and older.

In patients younger than age 35 years, cystoscopy may be performed at the physician’s discretion.
A cystoscopy should be performed on all patients who present with risk factors for urinary tract malignancies (e.g., irritative voiding symptoms, current or past tobacco use, chemical exposures) regardless of age.

The initial evaluation for AMH should include a radiologic evaluation. Multi-phasic computed tomography (CT) urography (without/with IV contrast), including sufficient phases to evaluate the renal parenchyma to rule out a renal mass and an excretory phase to evaluate the urothelium of the upper tracts, is the imaging procedure of choice because it has the highest sensitivity and specificity for imaging the upper tracts.

For patients with relative or absolute contraindications that preclude use of multiphasic CT (such as renal insufficiency, contrast allergy, pregnancy), magnetic resonance urography (MRU) (without/with intravenous contrast) is an acceptable alternative imaging approach.

For patients with relative or absolute contraindications that preclude use of multiphasic CT (such as renal insufficiency, contrast allergy, pregnancy) where collecting system detail is deemed imperative, combining MRI with retrograde pyelograms (RPGs) provides alternative evaluation of the entire upper tracts.

For patients with relative or absolute contraindications that preclude use of multiphasic CT (such as renal insufficiency, contrast allergy) and MRI (presence of metal in the body) where collecting system detail is deemed imperative, combining non-contrast CT or renal ultrasound (US) with retrograde pyelograms (RPGs) provides alternative evaluation of the entire upper tracts.
• The use of urine cytology and urine markers (NMP22, BTA-stat, and UroVysion FISH) is NOT recommended as a part of the routine evaluation of the asymptomatic microhematuria patient.

• In patients with persistent microhematuria following a negative work up or those with other risk factors for carcinoma in situ (e.g., irritative voiding symptoms, current or past tobacco use, chemical exposures), cytology may be useful.

• Blue light cystoscopy should not be used in the evaluation of patients with asymptomatic microhematuria.

• If a patient with a history of persistent asymptomatic microhematuria has two consecutive negative annual urinalyses (UA) [one per year for 2 years from the time of initial evaluation or beyond], then no further UA for the purpose of evaluation of AMH is necessary.

• For persistent asymptomatic microhematuria after negative urologic work up, yearly UA should be conducted.

• For persistent or recurrent asymptomatic microhematuria after initial negative urologic work-up, repeat evaluation at 3-5 years should be considered.
## TABLE 1.

**Common Risk Factors for Urinary Tract Malignancy in Patients with Microhematuria**

<table>
<thead>
<tr>
<th>Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
</tr>
<tr>
<td>Age (&gt; 35 years)</td>
</tr>
<tr>
<td>Past or current smoking</td>
</tr>
<tr>
<td>Occupational or other exposure to chemicals or dyes (benzenes or aromatic amines)</td>
</tr>
<tr>
<td>Analgesic abuse</td>
</tr>
<tr>
<td>History of gross hematuria</td>
</tr>
<tr>
<td>History of urologic disorder or disease</td>
</tr>
<tr>
<td>History of irritative voiding symptoms</td>
</tr>
<tr>
<td>History of pelvic irradiation</td>
</tr>
<tr>
<td>History of chronic urinary tract infection</td>
</tr>
<tr>
<td>History of exposure to known carcinogenic agents or chemotherapy such as alkylating agents</td>
</tr>
<tr>
<td>History of chronic indwelling foreign body</td>
</tr>
</tbody>
</table>

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Copyright © 2012 American Urological Association Education and Research, Inc.®
Hematuria

+AMH
(≥ 3 RBC per HPF on UA with microscopy)

History & Physical Assess for other potential AMH causes
(e.g., infection, menstruation, recent urologic procedures)

Repeat UA after treatment of other cause(s)

Release from care

Concurrent nephrologic work up if proteinuria, red cell morphology or other signs indicate nephrologic causes.

Renal Function Testing
Cystoscopy
Imaging (CTU)

Follow up with at least one UA/micro yearly for at least two years

Follow up as indicated by diagnosis. Re-evaluate for MH after resolution of identified condition.

Release from care

FIGURE 1.

Diagnosis, Evaluation and Follow-up of AMH
If unable to undergo CTU, less optimal imaging options include:
- MR Urogram
- Retrograde pyelograms in combination with non-contrast CT, MRI, or US

Follow persistent MH with annual UA. Consider nephrologic evaluation. Repeat anatomic evaluation within three to five years* or sooner, if clinically indicated.

*The threshold for re-evaluation should take into account patient risk factors for urological pathological conditions such as malignancy.
Purpose

This guideline’s purpose is to provide direction to clinicians and patients regarding how to: recognize non-neurogenic overactive bladder (OAB); conduct a valid diagnostic process; and, approach treatment with the goals of maximizing symptom control and patient quality of life while minimizing adverse events and patient burden. There is continually expanding literature on OAB; the Panel notes that this document constitutes a clinical strategy and is not intended to be interpreted rigidly. The most effective approach for a particular patient is best determined by the individual clinician and patient. As the science relevant to OAB evolves and improves, the strategies presented here will require amendment to remain consistent with the highest standards of clinical care. This document was created to serve as a guide for all types of providers who evaluate and treat OAB patients, including those in general practice as well as those who specialize in various branches of medicine.

Guideline Statements

Diagnosis

- The clinician should engage in a diagnostic process to document symptoms and signs that characterize OAB
and exclude other disorders that could be the cause of the patient’s symptoms; the minimum requirements for this process are a careful history, physical exam and urinalysis.

- In some patients, additional procedures and measures may be necessary to validate an OAB diagnosis, exclude other disorders, and fully inform the treatment plan. At the clinician’s discretion, a urine culture and/or post-void residual assessment may be performed and information from bladder diaries and/or symptom questionnaires may be obtained.

- Urodynamics, cystoscopy, and diagnostic renal and bladder ultrasound should not be used in the initial workup of the uncomplicated patient.

- OAB is not a disease; it is a symptom complex that generally is not a life threatening condition. After assessment has been performed to exclude conditions requiring treatment and counseling, no treatment is an acceptable choice made by some patients and caregivers.

- Clinicians should provide education to patients regarding normal lower urinary tract function, what is known about OAB, the benefits vs. risks/burdens of the available treatment alternatives, and the fact that acceptable symptom control may require trials of multiple therapeutic options before it is achieved.

**Treatment**

**First-Line Treatments**

- Clinicians should offer behavioral therapies (e.g., bladder training, bladder control strategies, pelvic floor muscle
training, fluid management) as first line therapy to all patients with OAB.

- Behavioral therapies may be combined with pharmacologic management.

**Second-Line Treatments**

- Clinicians should offer oral anti-muscarinics, or ß3-andrenoceptor agonists as second-line therapy.

- If an immediate release (IR) and an extended release (ER) formulation are available, then ER formulations should preferentially be prescribed over IR formulations because of lower rates of dry mouth.

- Transdermal (TDS) oxybutynin (patch [now available to women ages 18 years and older without a prescription] or gel) may be offered.

- If a patient experiences inadequate symptom control and/or unacceptable adverse drug events with one anti-muscarinic medication, then a dose modification or a different anti-muscarinic medication or a ß3-andrenoceptor agonist may be tried.

- Clinicians should not use anti-muscarinics in patients with narrow angle glaucoma unless approved by the treating ophthalmologist and should use anti-muscarinics with extreme caution in patients with impaired gastric emptying or a history of urinary retention.

- Clinicians should manage constipation and dry mouth before abandoning effective anti-muscarinic therapy. Management may include bowel management, fluid management, dose modification, or alternative anti-muscarinics.
Clinicians must use caution in prescribing antimuscarinics in patients who are using other medications with anti-cholinergic properties.

Clinicians should use caution in prescribing antimuscarinics or ß3-andrenoceptor agonists in the frail OAB patient.

Patients who are refractory to behavioral and pharmacologic therapy should be evaluated by an appropriate specialist if they desire additional therapy.

**Third-line Treatments**

Clinicians may offer intradetrusor onabotulinumtoxinA (1000 IU) as third-line treatment in the carefully-selected and thoroughly-counseled patient who has been refractory to first- and second-line OAB treatments. The patient must be able and willing to return for frequent post-void residual evaluation and able and willing to perform self-catheterization if necessary.

Clinicians may offer peripheral tibial nerve stimulation (PTNS) as third line treatment in a carefully selected patient population.

Clinicians may offer sacral neuromodulation (SNS) as third line treatment in a carefully selected patient population characterized by severe refractory OAB symptoms or patients who are not candidates for second-line therapy and who are willing to undergo a surgical procedure.

Practitioners and patients should persist with new treatments for an adequate trial in order to determine whether the therapy is efficacious and tolerable.
Combination therapeutic approaches should be assembled methodically, with the addition of new therapies occurring only when the relative efficacy of the preceding therapy is known. Therapies that do not demonstrate efficacy after an adequate trial should be ceased.

**Additional Treatments**

- Indwelling catheters (including transurethral, suprapubic, etc.) are not recommended as a management strategy for OAB because of the adverse risk/benefit balance except as a last resort in selected patients.

- In rare cases, augmentation cystoplasty or urinary diversion for severe, refractory, complicated OAB patients may be considered.

**Follow-Up**

- The clinician should offer follow up with the patient to assess compliance, efficacy, side effects and possible alternative treatments.
Incontinence: OAB

History and Physical; Urinalysis

- Signs/symptoms of OAB, (-) urine microscopy

Patient education:
- Normal urinary tract function
- Benefits/risks of treatment alternatives
- Agree on treatment goals

- Patient desires treatment and/or treatment is in patient’s best interests

Behavioral Treatments
(consider adding pharmacologic management if partially effective)

Treatment goals not met after appropriate duration*; Patient desires further treatment, is willing to engage in treatment, and/or further treatment in patient’s best interests

Pharmacologic management With active management of adverse events; consider dose modification or alternate medication if initial treatment is effective but adverse events or other considerations preclude continuation

- Treatment goals not met after appropriate duration*; Patient desires further treatment, is willing to engage in treatment, and/or further treatment in patient’s best interests

Reassess and/or refer; consider urine culture, post-void residual, bladder diary, symptom questionnaire

The complete OAB Guideline is available at www.AUAnet.org/Guidelines.
Incontinence: OAB

Diagnosis unclear or additional information needed

Consider urine culture, post-void residual bladder diary, and/or symptom questionnaires

Not OAB or Complicated OAB; treat or refer

Signs/symptoms of OAB

Consider in carefully-selected and thoroughly-counseled patients with moderate to severe symptoms

- Intradetrusor onabotulinumtoxin (patients must be willing to perform CISC)
  OR
- Peripheral tibial nerve stimulation (PTNS) (patients must be willing and able to make frequent office visits)
  OR
- Sacral neuromodulation (SNS)

Follow-up for efficacy and adverse events

In extremely rare cases, consider urinary diversion or augmentation cystoplasty

Treatment goals met

Signs/symptoms consistent with OAB diagnosis; Treatment goals not met after appropriate duration*; Patient desires further treatment, is willing to engage in treatment, and/or further treatment in patient’s best interests

*Appropriate duration is 8 to 12 weeks for behavioral therapies and 4 to 8 weeks for pharmacologic therapies
Purpose

Stress urinary incontinence (SUI) is a common problem experienced by many women. SUI can have a significant negative impact on the quality of life (QOL) of not only those who suffer from the condition, but also potentially on those friends and family members whose lives and activities may also be limited. The surgical options for the treatment of SUI continue to evolve; as such, this guideline and the associated algorithm aims to outline the currently available treatment techniques as well as the data associated with each treatment.

AUA Nomenclature

The AUA nomenclature system links statement types to a number of factors including strength of evidence, magnitude of benefit and risks/burdens, and panel judgment. There are three evidence-based statement types: Strong Recommendations and Moderate Recommendations are directive statements that indicate that there is a net benefit (or harm) associated with a clinical action, while a Conditional Recommendation is a non-directive Statement that is used when the clinical action does not have a clear net benefit (or harm).

In addition, there are two statement types that are used when pertinent evidence is not present in the systematic review of literature associated with the guideline: Expert
Incontinence: SUI

Opinions are statements made by panel consensus based on members’ clinical training, experience, knowledge, and judgment, while a Clinical Principle is a statement about a component of clinical care that is very widely agreed upon by urologists or other clinicians.

Index Patient

The index patient for this guideline is an otherwise healthy female who is considering surgical therapy for the correction of pure stress and/or stress-predominant mixed urinary incontinence (MUI) who has not undergone previous SUI surgery. Patients with low-grade pelvic organ prolapse were also considered to be index patients. However, while the stage of prolapse was often specified in more recent trials, it was not indicated in many of the earlier studies. Where evidence was available, the data is presented separately for index patients and non-index patients. The Panel recognizes that many women who seek surgical correction of SUI do not meet the definition of the index patient. In fact, most of the studies in the literature do not enroll patients based on this definition of the index patient. Therefore, the Panel felt it was also important to review the literature regarding patients undergoing surgery for SUI who did not meet this definition of the index patient.

Non-index patient

Non-index patients reviewed in this analysis include women with SUI and pelvic prolapse (stage 3 or 4), MUI (non-stress-predominant), incomplete emptying/elevated post-void residual (PVR) and/or other voiding dysfunction, prior surgical interventions for SUI, recurrent or persistent
SUI, mesh complications, high body mass index (BMI), neurogenic lower urinary tract dysfunction, and advanced age (geriatric). Finally, the Panel felt it was important to more fully understand the literature regarding the safety of mesh products used in the surgical treatment of SUI and, therefore, included studies of women who had undergone mesh procedures regardless of whether they were index or non-index patients. The Panel also acknowledges that persistent or recurrent SUI following any SUI treatment is not uncommon; however, there is a lack of robust data to substantiate any recommendation from the Panel regarding the management of these patients.

Definitions

SUI is the symptom of urinary leakage due to increased abdominal pressure, which can be caused by activities such as sneezing, coughing, exercise, lifting, and position change. Though the utility of urethral function assessment remains controversial, some clinicians utilize leak point pressure and others utilize urethral closure pressure. Intrinsic sphincter deficiency (ISD) is often defined as a leak point pressure of less than 60 cm H$_2$O or a maximal urethral closure pressure of less than 20 cm H$_2$O, often in the face of minimal urethral mobility. Urgency urinary incontinence (UUI) is the symptom of urinary leakage that occurs in conjunction with the feeling of urgency and a sudden desire to urinate that cannot be deferred. Mixed incontinence refers to a combination of SUI and UUI.
Guideline Statements

Patient Evaluation

- In the initial evaluation of patients with SUI desiring to undergo surgical intervention, physicians should include the following components: *(Clinical Principle)*
  - History, including assessment of bother
  - Physical examination, including a pelvic examination
  - Objective demonstration of SUI with a comfortably full bladder (any method)
  - Assessment of PVR urine (any method)
  - Urinalysis

- Physicians should perform additional evaluations in patients being considered for surgical intervention who have the following conditions: *(Expert Opinion)*
  - Inability to make definitive diagnosis based on symptoms and initial evaluation
  - Inability to demonstrate SUI
  - Known or suspected neurogenic lower urinary tract dysfunction
  - Abnormal urinalysis, such as unexplained hematuria or pyuria
  - Urgency-predominant MUI
  - Elevated PVR per clinician judgment
  - High grade pelvic organ prolapse (POP-Q stage 3 or higher) if SUI not demonstrated with pelvic organ prolapse reduction
  - Evidence of significant voiding dysfunction

- Physicians may perform additional evaluations in patients with the following conditions: *(Expert Opinion)*
Concomitant overactive bladder symptoms
Failure of prior anti-incontinence surgery
Prior pelvic prolapse surgery

Cystoscopy and Urodynamics Testing

- Physicians should not perform cystoscopy in index patients for the evaluation of SUI unless there is a concern for urinary tract abnormalities. *(Clinical Principle)*

- Physicians may omit urodynamic testing for the index patient desiring treatment when SUI is clearly demonstrated. *(Conditional Recommendation; Evidence Level: Grade B)*

- Physicians may perform urodynamic testing in non-index patients. *(Expert Opinion)*

Patient Counseling

- In patients wishing to undergo treatment for SUI, the degree of bother that their symptoms are causing them should be considered in their decision for therapy. *(Expert Opinion)*

- In patients with SUI or stress-predominant MUI who wish to undergo treatment, physicians should counsel regarding the availability of the following treatment options: *(Clinical Principle)*
  - Observation
  - Pelvic floor muscle training (± biofeedback)
  - Other non-surgical options (e.g., continence pessary)
  - Surgical intervention

- Physicians should counsel patients on potential complications specific to the treatment options. *(Clinical Principle)*
• Prior to selecting midurethral synthetic sling procedures for the surgical treatment of SUI in women, physicians must discuss the specific risks and benefits of mesh as well as the alternatives to a mesh sling. (Clinical principle)

Treatment

• In patients with SUI or stress-predominant MUI, physicians may offer the following non-surgical treatment options: (Expert Opinion)
  - Continence pessary
  - Vaginal inserts
  - Pelvic floor muscle exercises

• In index patients considering surgery for SUI, physicians may offer the following options: (Strong Recommendation; Evidence Level: Grade A)
  - Midurethral sling (synthetic)
  - Autologous fascia pubovaginal sling
  - Burch colposuspension
  - Bulking agents

• In index patients who select midurethral sling surgery, physicians may offer either the retropubic or transobturator midurethral sling. (Moderate Recommendation; Evidence Level: Grade A)

• Physicians may offer single-incision slings to index patients undergoing midurethral sling surgery with the patient informed as to the immaturity of evidence regarding their efficacy and safety. (Conditional Recommendation; Evidence Level: Grade B)

• Physicians should not place a mesh sling if the urethra is inadvertently injured at the time of a planned midurethral sling procedure. (Clinical Principle)
Physicians should not offer stem cell therapy for stress incontinent patients outside of investigative protocols. (Expert Opinion)

Special Cases

In patients with SUI and a fixed, immobile urethra (often referred to as ‘intrinsic sphincter deficiency’) who wish to undergo treatment, physicians should offer pubovaginal slings, retropubic midurethral slings, or urethral bulking agents. (Expert Opinion)

Physicians should not utilize a synthetic midurethral sling in patients undergoing concomitant urethral diverticulectomy, repair of urethrovaginal fistula, or urethral mesh excision and stress incontinence surgery. (Clinical Principle)

Physicians should strongly consider avoiding the use of mesh in patients undergoing stress incontinence surgery who are at risk for poor wound healing (e.g., following radiation therapy, presence of significant scarring, poor tissue quality). (Expert Opinion)

In patients undergoing concomitant surgery for pelvic prolapse repair and SUI, physicians may perform any of the incontinence procedures (e.g., midurethral sling, pubovaginal sling, Burch colposuspension). (Conditional Recommendation; Evidence Level: Grade C)

Physicians may offer patients with SUI and concomitant neurologic disease affecting lower urinary tract function (neurogenic bladder) surgical treatment of SUI after appropriate evaluation and counseling have been performed. (Expert Opinion)
Physicians may offer synthetic midurethral slings, in addition to other sling types, to the following patient populations after appropriate evaluation and counseling have been performed: (*Expert Opinion*)

- Patients planning to bear children
- Diabetes
- Obesity
- Geriatric

**Outcomes Assessment**

- Physicians or their designees should communicate with patients within the early postoperative period to assess if patients are having any significant voiding problems, pain, or other unanticipated events. If patients are experiencing any of these outcomes, they should be seen and examined. (*Expert Opinion*)

- Patients should be seen and examined by their physicians or designees within six months post-operatively. Patients with unfavorable outcomes may require additional follow-up. (*Expert Opinion*)

  - The subjective outcome of surgery as perceived by the patient should be assessed and documented.
  - Patients should be asked about residual incontinence, ease of voiding/force of stream, recent urinary tract infection, pain, sexual function, and new onset or worsened overactive bladder symptoms.
  - A physical exam, including an examination of all surgical incision sites, should be performed to evaluate healing, tenderness, mesh extrusion (in the case of synthetic slings), and any other potential abnormalities.
A PVR should be obtained.

F

A standardized questionnaire (e.g. PGI-I) may be
considered.

Incontinence: SUI

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In patients who wish to undergo treatment, physicians should counsel regarding the availability of observation, pelvic floor muscle training, other non-surgical options, and surgical interventions. Physicians should counsel patients on potential complications specific to the treatment options.
If a midurethral sling surgery is selected, either the retropubic or transobturator midurethral sling may be offered. A single-incision sling may be offered to index patients if they are informed as to the immaturity of evidence regarding their efficacy and safety. Physicians must discuss the specific risks and benefits of mesh as well as alternatives to a mesh sling.

TREATMENT

Non-Surgical
- Continence pessary
- Vaginal inserts
- Pelvic floor muscle exercises

Surgical
- Bulking agents
- Midurethral sling (synthetic)
- Autologous fascia pubovaginal sling
- Burch colposuspension

SPECIAL CASES

1. Fixed immobile urethra
   - Pubovaginal sling
   - Retropubic midurethral sling
   - Urethral bulking agents

2. Concomitant surgery for POP repair and SUI
   Any incontinence procedure

3. Concomitant NLUTD
   Surgical treatment following appropriate evaluation and counseling

4. Child-bearing, diabetes, obesity, geriatric
   Surgical treatment following appropriate evaluation and counseling

MUI= mixed urinary incontinence; NLUTD= neurogenic lower urinary tract dysfunction; OAB= overactive bladder; POP= pelvic organ prolapse; PVR= post-void residual; SUI= stress urinary incontinence
Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) is a potentially devastating condition that impacts not only a patient’s physical function, but also their psychosocial function and quality of life. This Guideline aims to provide direction on IC/BPS recognition, appropriate diagnostic examination and treatment. IC/BPS patients experience pain, urgency, and frequency, and it is important that treatment approaches reduce these symptoms and increase patient quality of life without increasing adverse events and patient burden.

This Guideline addresses a topic which has not been addressed previously by AUA Guidelines. It provides a useful synthesis of the evidence along with panel guidance. The panel has emphasized that treatment of IC/BPS is individualized; the most effective approach for a particular patient is best determined by the individual clinician and patient. To guide physicians, the panel has developed a treatment algorithm which includes elements for a basic assessment as well as available first-line through sixth-line treatments.

Guideline Statements

Evaluation and Diagnosis of IC/BPS

- The basic assessment should include a careful history, physical examination, and laboratory examination to rule
in symptoms that characterize IC/BPS and rule out other confusable disorders.

- Baseline voiding symptoms and pain levels should be obtained in order to measure subsequent treatment effects.

- Cystoscopy and/or urodynamics should be considered as an aid to diagnosis only for complex presentations; these tests are not necessary for making the diagnosis in uncomplicated presentations.

### Strategies for the Treatment of IC/BPS

- Treatment strategies should proceed using more conservative therapies first, with less conservative therapies employed if symptom control is inadequate for acceptable quality of life; because of their irreversibility, surgical treatments (other than fulguration of Hunner’s lesions) are appropriate only after other treatment alternatives have been exhausted, or at any time in the rare instance when an end-stage small, fibrotic bladder has been confirmed and the patient’s quality of life suggests a positive risk-benefit ratio for major surgery.

- Initial treatment type and level should depend on symptom severity, clinician judgment, and patient preferences; appropriate entry points into the treatment portion of the algorithm depend on these factors.

- Multiple, simultaneous treatments may be considered if it is in the best interests of the patient; baseline symptom assessment and regular symptom level reassessment are essential to document efficacy of single and combined treatments.
• Ineffective treatments should be stopped once a clinically meaningful interval has elapsed.

• Pain management should be continually assessed for effectiveness because of its importance to quality of life. If pain management is inadequate, then consideration should be given to a multidisciplinary approach and the patient referred appropriately.

• The IC/BPS diagnosis should be reconsidered if no improvement occurs after multiple treatment approaches.

Treatments that may be offered

Treatments that may be offered are divided into first-, second-, third-, fourth-, fifth-, and sixth-line groups based on the balance between potential benefits to the patient, potential severity of adverse events (AEs), and the reversibility of the treatment. See full Guideline for protocols, study details, and rationales.

First-line treatments
(Should be performed on all patients)

• Patients should be educated about normal bladder function, what is known and not known about IC/BPS, the benefits vs. risks/burdens of the available treatment alternatives, the fact that no single treatment has been found effective for the majority of patients, and the fact that acceptable symptom control may require trials of multiple therapeutic options (including combination therapy) before it is achieved.

• Self-care practices and behavioral modifications that can improve symptoms should be discussed and implemented as feasible.
• Patients should be encouraged to implement stress management practices to improve coping techniques and manage stress-induced symptom exacerbations.

Second-line treatments

• Appropriate manual physical therapy techniques (e.g., maneuvers that resolve pelvic, abdominal and/or hip muscular trigger points, lengthen muscle contractures, and release painful scars and other connective tissue restrictions), if appropriately-trained clinicians are available, should be offered to patients who present with pelvic floor tenderness. Pelvic floor strengthening exercises (e.g., Kegel exercises) should be avoided.

• Multimodal pain management approaches (e.g., pharmacological, stress management, manual therapy if available) should be initiated.

• Amitriptyline, cimetidine, hydroxyzine, or pentosan polysulfate may be administered as second-line oral medications (listed in alphabetical order; no hierarchy is implied).

• DMSO, heparin, or lidocaine may be administered as second-line intravesical treatments (listed in alphabetical order; no hierarchy is implied).

Third-line treatments

• Cystoscopy under anesthesia with short-duration, low-pressure hydrodistension may be undertaken if first- and second-line treatments have not provided acceptable symptom control and quality of life or if the patient’s presenting symptoms suggest a more-invasive approach is appropriate.
• If Hunner’s lesions are present, then fulguration (with laser or electrocautery) and/or injection of triamcinolone should be performed.

**Fourth-line treatment**

• Intradetrusor botulinum toxin A (BTX-A) may be administered if other treatments have not provided adequate symptom control and quality of life or if the clinician and patient agree that symptoms require this approach. Patients must be willing to accept the possibility that post-treatment intermittent self-catheterization may be necessary.

• A trial of neurostimulation may be performed and, if successful, implantation of permanent neurostimulation devices may be undertaken if other treatments have not provided adequate symptom control and quality of life or if the clinician and patient agree that symptoms require this approach.

**Fifth-line treatments**

• Cyclosporine A may be administered as an oral medication if other treatments have not provided adequate symptom control and quality of life or if the clinician and patient agree that symptoms require this approach.

**Sixth-line treatment**

• Major surgery (e.g., substitution cystoplasty, urinary diversion with or without cystectomy) may be undertaken in carefully selected patients for whom all other therapies have failed to provide adequate symptom control and quality of life.
Treatments that should not be offered

The treatments below appear to lack efficacy and/or appear to be accompanied by unacceptable AE profiles. See body of Guideline for study details and rationales.

- Long-term oral antibiotic administration should not be offered.
- Intravesical instillation of bacillus Calmette-Guerin (BCG) should not be offered outside of investigational study settings.
- High-pressure, long-duration hydrodistension should not be offered.
- Systemic (oral) long-term glucocorticoid administration should not be offered.
Interstitial Cystitis/Bladder Pain Syndrome

Interstitial Cystitis Algorithm

**IC/BPS**
An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes

**BASIC ASSESSMENT**
- History
- Frequency/Volume Chart
- Post-void residual
- Physical examination
- Urinalysis, culture
- Cytology if smoking hx
- Symptom questionnaire
- Pain evaluation

**Signs/Symptoms of Complicated IC/BPS**
- Incontinence/OAB
- GI signs/symptoms
  - Microscopic/gross hematuria/sterile pyuria
- Gynecologic signs/symptoms

**CONSIDER:**
- Urine cytology
- Imaging
- Cystoscopy
- Urodynamics
- Laparoscopy
- Specialist referral (urologic or non-urologic as appropriate)

**Dx Urinary Tract Infection**

**TREAT & REASSESS**

**CONFIRMED OR UNCOMPROMICATED IC/BPS**

**CLINICAL MANAGEMENT PRINCIPLES**
- Treatments are ordered from most to least conservative; surgical treatment is appropriate only after other treatment options have been found to be ineffective (except for treatment of Hunner’s lesions if detected)
- Initial treatment level depends on symptom severity, clinician judgment, and patient preferences
- Multiple, simultaneous treatments may be considered if in best interests of patient
- Ineffective treatments should be stopped
- Pain management should be considered throughout course of therapy with goal of maximizing function and minimizing pain and side effects
- Diagnosis should be reconsidered if no improvement within clinically-meaningful time-frame

The evidence supporting the use of Neuromodulation, Cyclosporine A, and BTX for IC/BPS is limited by many factors including study quality, small sample sizes, and lack of durable follow up. None of these therapies have been approved by the U.S. Food and Drug Administration for this indication. The panel believes that none of these interventions can be recommended for generalized use for this disorder, but rather should be limited to practitioners with experience managing this syndrome and willingness to provide long term care of these patients post intervention.

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FIRST-LINE TREATMENTS
- General Relaxation/ Stress Management
- Pain Management
- Patient Education
- Self-care/Behavioral Modification

SECOND-LINE TREATMENTS
- Appropriate manual physical therapy techniques
- Oral: amitriptyline, cimetidine, hydroxyzine, PPS
- Intravesical: DMSO, Heparin, Lidocaine
- Pain Management

THIRD-LINE TREATMENTS
- Cystoscopy under anesthesia w/ hydrodistention
- Pain Management
- Tx of Hunner’s lesions if found

FOURTH-LINE TREATMENTS
- Intradetrusor botulinum toxin A
- Neuromodulation
- Pain Management

FIFTH-LINE TREATMENTS
- Cyclosporine A
- Pain Management

SIXTH-LINE TREATMENTS
- Diversion w/ or w/out cystectomy
- Pain Management
- Substitution cystoplasty

Note: For patients with end-stage structurally small bladders, diversion is indicated at any time clinician and patient believe appropriate.

RESEARCH TRAILS
Patient enrollment as appropriate at any point in treatment process
Male infertility can be due to a variety of conditions. Some of these conditions are identifiable and specifically treatable or reversible, such as ductal obstruction and hypogonadotrophic hypogonadism. Other conditions are identifiable but not reversible, such as bilateral testicular atrophy secondary to viral orchitis.

- The goals are to identify:
  - potentially correctable conditions,
  - irreversible conditions that are amenable to assisted reproductive techniques (ART) using the sperm of the male partner,
  - irreversible conditions that are not amenable to ART and for which donor insemination or adoption are possible options,
  - life- or health-threatening conditions that may underlie the infertility and require medical attention, and
  - genetic abnormalities that may affect the health of offspring if ART is employed.

- Perform initial screening evaluation if:
  - pregnancy has not occurred within one year of unprotected intercourse.
  - An earlier evaluation may be warranted if a known male or female infertility risk factor exists (e.g., cryptorchidism or female age >35 years) or if a man questions his fertility potential.
Initial screening includes:

- a reproductive history (coital frequency and timing, duration of infertility, and prior fertility, childhood illnesses and developmental history, systemic medical illnesses, prior surgeries, sexual history including sexually transmitted infections, gonadotoxin exposure including heat exposure), and
- two semen analyses (Table 1).

Perform full evaluation of male infertility if:
- the initial screening evaluation is abnormal,
- couples have unexplained infertility, and
- infertility persists following treatment of a female factor.

Full evaluation includes:

- A medical history consisting of
  - a reproductive history (see above),
  - a complete medical and surgical history,
  - a review of medications (prescription and nonprescription) and allergies, lifestyle exposures and systems, family reproductive history, and past infections such as sexually transmitted diseases and respiratory infections.
- A focused physical examination (including penis, testes, vasa, epididymes, varicocele, secondary sex characteristics, and digital rectal examination),
- at least two semen analyses,
- other procedures and tests as needed to narrow differential diagnosis or help with prognosis.
● Other procedures and tests for assessing male fertility

*Endocrine Evaluation* (Table 2)

- Perform if:
  - sperm count is <10 million/mL,
  - sexual function is impaired,
  - clinical findings suggest a specific endocrinopathy.

- The *initial* endocrine evaluation includes:
  - serum follicle-stimulating-hormone (FSH),
  - serum testosterone level; if low, repeat measurement of total and free (or bioavailable) testosterone and obtain serum luteinizing hormone (LH) and prolactin level.

- *Post-Ejaculatory Urinalysis* (UA)

- Perform to diagnose possible retrograde ejaculation in patients with ejaculate volumes < 1.0 mL, except in patients with bilateral vasal ag nesis or clinical signs of hypogonadism.

- *Transrectal Ultrasonography* (TRUS)

- Perform in:
  - azoospermic patients with palpable vasa and low ejaculate volumes to identify ejaculatory duct obstruction.

- *Scrotal Ultrasonography*

- Perform if physical examination of the scrotum is difficult or inadequate or if a testicular mass is suspected.

- Specialized Tests

  - *Sperm morphology* by rigid (strict) criteria is not consistently predictive of fecundity; do not use in isolation to make prognostic or therapeutic decisions.

  - *DNA integrity testing* (evaluation of degree of sperm DNA fragmentation): evidence to support routine use is insufficient.
- Reactive oxygen species (ROS) testing is not predictive of pregnancy independent of routine semen parameters nor are any therapies proven to correct an abnormal test result; data are insufficient to support the routine use of ROS testing.

- Specialized tests on semen (including leukocyte quantification, antisperm antibody testing, sperm viability, examination of sperm-cervical mucus interaction, zona-free hamster oocyte test/sperm penetration assay, human zona pellucid binding tests) are not required for routine diagnosis. May use individual tests in certain patients for identifying the etiology of specific semen parameter abnormalities or in cases of unexplained infertility or for selecting therapy.

- **Genetic Screening**
  - Most common genetic factors related to male infertility:
    - Cystic fibrosis gene mutations associated with congenital bilateral absence of the vas deferens (CBAVD).
    - Sex chromosomal abnormalities (aneuploidy) resulting in impaired sperm production and often with impaired testosterone production.
    - Y-chromosome microdeletions associated with isolated spermatogenic impairment.

- Inform patients with:
  - Nonobstructive azoospermia or severe oligospermia that they might have chromosomal abnormalities or Y-chromosome microdeletions.
  - Azoospermia due to CBAVD that they probably have an abnormality of the cystic fibrosis transmembrane conductance regulator (CFTR) gene.
Offer:

- Genetic counseling and CFTR mutations testing for a patient with CBAVD and to the female partner before proceeding with treatments that utilize the sperm of a man with CBAVD.
- Include at minimum a panel of common point mutations and the 5T allele; currently there is no consensus on the minimum number of mutations that should be tested.

Imaging for renal abnormalities to men with unilateral vassal agenesis or CBAVD and no evidence of CFTR abnormalities.

Gene sequencing may be considered in couples where the wife is a carrier and the husband with CBAVD tests negative on a routine panel of CFTR mutations.

Karyotyping and genetic counseling to patients with nonobstructive azoospermia and severe oligospermia (<5 million sperm/mL).

Y-chromosome microdeletion analysis to men with nonobstructive azoospermia or severe oligospermia.
- There are insufficient data to recommend a minimal number of sequence tagged sites to test for in patients undergoing Y chromosome microdeletion analysis.
- Although the prognosis for sperm retrieval is poor in patients having large deletions involving AZF region a or b, the results of Y chromosome deletion analysis cannot absolutely predict the absence of sperm.
EVALUATION OF AZOOSPERMIC MALE

AUA BEST PRACTICE STATEMENT – 2010; REVIEWED AND AMENDED – 2011

- Absence of the vasa deferentia (vasal agenesis)
  - Consider TRUS in patients with unilateral vasa deferentia agenesis for evaluation of the ampullary portion of the existing vas deferens and the seminal vesicles since these patients may have segmental atresia of the vas deferens causing obstructive azoospermia.
  - Offer genetic counseling and testing for CFTR mutations to male and also to female partner before proceeding with treatments that use sperm of a man with CBAVD.
  - Imaging of the kidneys for abnormalities should be offered to men with unilateral vasa deferentia agenesis or to men with CBAVD and no evidence of CFTR abnormalities.

- Bilateral testicular atrophy
  - Offer genetic testing (chromosomal abnormalities and Y-chromosome microdeletions) to patients with non-obstructive azoospermia due to primary testicular failure (FSH levels elevated with normal or low serum testosterone).
  - Evaluate patients with acquired hypogonadotropic hypogonadism (low FSH, bilaterally small testes and low serum testosterone levels) for functioning and nonfunctioning pituitary tumors by serum prolactin measurement and pituitary gland imaging.
• Ductal obstruction

In patients with normal ejaculate volume (> 1.0 mL), normal testicular size, at least one palpable vas deferens, and normal FSH levels:

- Perform diagnostic testicular biopsy to distinguish between obstructive and nonobstructive causes.
- Vasography should not be performed at the time of biopsy unless reconstructive surgery is undertaken at the same time.

In patients with low ejaculate volume (<1.0 mL) not caused by hypogonadism or CBAVD and palpable vasa perform:

- TRUS with or without seminal vesicle aspiration and seminal vesiculography to identify obstruction in the distal male reproductive tract,
- testis biopsy in patients with ejaculatory duct obstruction demonstrated by TRUS, if needed to confirm normal spermatogenesis.
- alternatively, vasography to identify the site of reproductive tract obstruction but not unless reconstructive surgery is undertaken at the same surgical procedure.
- CFTR and 5T testing in patients with a unilateral absence of the vas and low volume azoospermia due to the possibility of a variant of CBAVD; if positive, do not perform TRUS.
MANAGEMENT OF OBSTRUCTIVE AZOOSPERMIA

AUA Best Practice Statement – 2010; Reviewed and Validity Confirmed – 2011

- Treatment options include:
  - Surgery
    - microsurgical reconstruction of the reproductive tract
    - transurethral resection of the ejaculatory ducts (TURED)
  - Sperm retrieval techniques and in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) (Table 3)
    - There is no evidence that either fertilization or pregnancy rates are different using either fresh or thawed cryopreserved sperm. Base the timing of sperm retrieval in relation to oocyte retrieval on local preference and expertise.
    - There is no evidence that the site or method of sperm retrieval affects outcome of IVF with ICSI for patients with obstructive azoospermia. Base the choice of sperm retrieval by either percutaneous or open surgery from either the testis or epididymis on local preferences and expertise.
    - Open surgical testicular sperm retrieval with or without microscopic magnification is recommended for patients with nonobstructive azoospermia.
    - The patient should be apprised of the associated risks of IVF/ICSI.
  - Microsurgical reconstruction is preferable to sperm retrieval with IVF/ICSI in men with prior vasectomy if the obstructive interval is less than 15 years and no female fertility risk factors are present.
If epididymal obstruction is present, the decision to use either microsurgical reconstruction or sperm retrieval with IVF/ICSI should be individualized.

Vasoepididymostomy should be performed by an expert in reproductive microsurgery.

- Sperm retrieval/ICSI is preferred to surgical treatment in cases

- of advanced female age,

- of female factors requiring IVF,

- if the chance for success with sperm retrieval/ICSI exceeds the chance for success with surgical treatment, or

- if sperm retrieval/ICSI is preferred by the couple for financial reasons.

**TABLE 1.**

**Semen Analysis: Reference Values**

<table>
<thead>
<tr>
<th>On at least two occasions (&gt; 1 month apart, if possible):</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejaculate volume</td>
<td>1.5-5.0 ml</td>
</tr>
<tr>
<td>pH</td>
<td>&gt; 7.2</td>
</tr>
<tr>
<td>Sperm concentration</td>
<td>&gt;20 million/ml</td>
</tr>
<tr>
<td>Total sperm number</td>
<td>&gt;40 million/ejaculate</td>
</tr>
<tr>
<td>Percent motility</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>Forward progression</td>
<td>&gt;2 (scale 0-4)</td>
</tr>
</tbody>
</table>

**Normal morphology**

| >50% normal* |
| >30% normal** |
| >14% normal*** |

And:

| Sperm agglutination | < 2 (Scale 0-3) |
| Viscosity           | <3 (Scale 0-4) |

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TABLE 2.

Endocrine Evaluation: The Relationship of Testosterone, LH, FSH and Prolactin with Clinical Condition

<table>
<thead>
<tr>
<th>Clinical Condition</th>
<th>FSH</th>
<th>LH</th>
<th>Testosterone</th>
<th>Prolactin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal spermatogenesis</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Hypogonadotropic hypogonadism</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Abnormal spermatogenesis*</td>
<td>High/Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Complete testicular failure/ hypergonadotropic hypogonadism</td>
<td>High</td>
<td>High</td>
<td>Normal/Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Prolactin-secreting pituitary tumor</td>
<td>Normal/Low</td>
<td>Normal/Low</td>
<td>Low</td>
<td>High</td>
</tr>
</tbody>
</table>

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* Many men with abnormal spermatogenesis have a normal serum FSH, but a marked elevation of serum FSH is clearly indicative of an abnormality in spermatogenesis.
<table>
<thead>
<tr>
<th>Obstructive Azoospermia: Sperm Retrieval Techniques</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Microsurgical epididymal sperm aspiration (MESA)</strong></td>
<td>Large quantity of sperm obtained suitable for several IVF/ICSI cycles in one procedure</td>
<td>Requires microsurgical skills Incision with post-op discomfort Higher cost compared to percutaneous procedures</td>
</tr>
<tr>
<td><strong>Percutaneous epididymal sperm aspiration (PESA)</strong></td>
<td>No microsurgical skills required Fast Minimum post-op discomfort</td>
<td>Fewer sperm retrieved Risk of epididymal damage</td>
</tr>
<tr>
<td><strong>Testicular sperm extraction (TESE) and microTESE</strong></td>
<td>No microsurgical skills required except when micro TESE performed</td>
<td>Risk of testicular damage with multiple biopsies Incision with post-op discomfort Higher cost compared to percutaneous procedures</td>
</tr>
<tr>
<td><strong>Percutaneous testicular sperm aspiration (TESA)</strong></td>
<td>No microsurgical skills required Fast and easyum post-op discomfort Minimally invasive</td>
<td>Fewer sperm retrieved</td>
</tr>
</tbody>
</table>

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Purpose

Erectile Dysfunction (ED) is defined as the consistent or recurrent inability to attain and/or maintain penile erection sufficient for sexual satisfaction. The Panel believes that shared decision-making is the cornerstone of the treatment and management of ED. Using this approach, all men should be informed of all treatment options that are not medically contraindicated to determine the appropriate treatment. Men also may choose to forego treatment. In each scenario, the clinician’s role is to ensure that the man and his partner have full understanding of the benefits and risks/burdens of the various management strategies. This guideline’s purpose is to provide direction to on how to recognize ED, how to conduct a valid diagnostic process, and how to approach treatment with the goals of restoring sexual function and enhancing the man and his partner’s quality of life (QoL) while minimizing adverse events (AEs) and diagnosis- and treatment-associated burden.

AUA Nomenclature

The AUA nomenclature system links statement types to a number of factors including strength of evidence, magnitude of benefit and risks/burdens, and panel judgment. There are three evidence-based statement types: Strong Recommendations and Moderate Recommendations are directive statements that indicate that there is a net benefit (or harm) associated with a clinical action, while a Conditional Recommendation is a non-directive Statement
that is used when the clinical action does not have a clear net benefit (or harm).

In addition, there are two statement types that are used when pertinent evidence is not present in the systematic review of literature associated with the guideline: **Expert Opinions** are statements made by panel consensus based on members’ clinical training, experience, knowledge, and judgment, while a **Clinical Principle** is a statement about a component of clinical care that is very widely agreed upon by urologists or other clinicians.

### Guideline Statements

#### Evaluation and Diagnosis

- Men presenting with symptoms of ED should undergo a thorough medical, sexual and psychosocial history, a physical examination, and selective laboratory testing. *(Clinical Principle)*

- For the man with ED, validated questionnaires are recommended to assess the severity of ED, to measure treatment effectiveness, and to guide future management. *(Expert Opinion)*

- Men should be counseled that ED is a risk marker for underlying cardiovascular disease (CVD) and other health conditions that may warrant evaluation and treatment. *(Clinical Principle)*

- For men with ED, morning serum total testosterone levels should be measured. *(Moderate Recommendation; Evidence Strength Grade C)*

- For some men with ED, specialized testing and evaluation
may be necessary to guide treatment. \textit{(Expert Opinion)}

**Treatment**

- For men being treated for ED, referral to a mental health professional should be considered to promote treatment adherence, reduce performance anxiety and integrate treatments into a sexual relationship. \textit{(Moderate Recommendation; Evidence Strength Grade C)}

- Clinicians should counsel men with ED who have comorbidities known to negatively affect erectile function that lifestyle modifications, including changes in diet and increased physical activity, improve overall health and may improve erectile function. \textit{(Moderate Recommendation; Evidence Strength Grade C)}

- Men with ED should be informed regarding the treatment option of an FDA-approved oral phosphodiesterase type 5 inhibitor (PDE5i), including discussion of benefits and risks/burdens, unless contraindicated. \textit{(Strong Recommendation; Evidence Strength Grade B)}

- When men are prescribed an oral PDE5i for the treatment of ED, instructions should be provided to maximize benefit/efficacy. \textit{(Strong Recommendation; Evidence Strength Grade C)}

- For men who are prescribed PDE5i, the dose should be titrated to provide optimal efficacy. \textit{(Strong Recommendation; Evidence Strength Grade B)}

- Men who desire preservation of erectile function after treatment for prostate cancer by radical prostatectomy (RP) or radiotherapy (RT) should be informed that early use of PDE5i post-treatment may not improve
spontaneous, unassisted erectile function. *(Moderate Recommendation; Evidence Strength Grade C)*

- Men with ED and testosterone deficiency (TD) who are considering ED treatment with a PDE5i should be informed that PDE5i may be more effective if combined with testosterone therapy. *(Moderate Recommendation; Evidence Strength Grade C)*

- Men with ED should be informed regarding the treatment option of a vacuum erection device (VED), including discussion of benefits and risks/burdens. *(Moderate Recommendation; Evidence Strength Grade C)*

- Men with ED should be informed regarding the treatment option of intraurethral (IU) alprostadil, including discussion of benefits and risks/burdens. *(Conditional Recommendation; Evidence Strength Grade C)*

- For men with ED who are considering the use of IU alprostadil, an in-office test should be performed. *(Clinical Principle)*

- Men with ED should be informed regarding the treatment option of intracavernosal injections (ICI), including discussion of benefits and risks/burdens. *(Moderate Recommendation, Evidence Strength Grade C)*

- For men with ED who are considering ICI therapy, an in-office injection test should be performed. (Clinical Principle)

- Men with ED should be informed regarding the treatment option of penile prosthesis implantation, including discussion of benefits and risks/burdens. *(Strong Recommendation, Evidence Strength Grade C)*
• For men with ED who have decided on penile implantation surgery, counseling should be provided regarding post-operative expectations. (Clinical Principle)

• Penile prosthetic surgery should not be performed in the presence of systemic, cutaneous, or urinary tract infection. (Clinical Principle)

• For young men with ED and focal pelvic/penile arterial occlusion and without documented generalized vascular disease or veno-occlusive dysfunction, penile arterial reconstruction may be considered. (Conditional Recommendation, Evidence Strength Grade C)

• For men with ED, penile venous surgery is not recommended. (Moderate Recommendation, Evidence Strength C)

• For men with ED, low-intensity extracorporeal shock wave therapy (ESWT) should be considered investigational. (Conditional Recommendation; Evidence Strength Grade C)

• For men with ED, intracavernosal stem cell therapy should be considered investigational. (Conditional Recommendation; Evidence Strength Grade C)

• For men with ED, platelet-rich plasma (PRP) therapy should be considered experimental. (Expert Opinion)
COUNSEL THE MAN AND PARTNER REGARDING:
- The value of psychosocial/relationship support from trained professionals to optimize treatment satisfaction
- The importance of lifestyle change (weight loss, exercise, smoking cessation) to improve erectile function and overall health
- The benefits and risks/burdens of all available ED treatments that are not contraindicated

Using a shared decision-making framework, identify appropriate treatment\(^1\) based on values and priorities of man and partner

IF INADEQUATE EFFICACY AND/OR UNACCEPTABLE AEs AND/OR INSUFFICIENT SATISFACTION, THEN ADDRESS AS APPROPRIATE:
- Dose adjustments (for PDE5i, IU alprostadil, ICI)
- Revisit instructions to maximize efficacy (for all treatments)
- Revisit values and priorities of man and partner with mental health professional to refine values and priorities and/or to address psychosocial or relationship barriers to successful treatment
- Consider alternate treatment

\(^1\) For men with testosterone deficiency, defined as the presence of symptoms and signs and a total testosterone <300 ng/dl, counseling should emphasize that restoration of testosterone levels to therapeutic levels is likely to increase efficacy of ED treatments other than prosthesis surgery.
EVALUATION AND MANAGEMENT OF TESTOSTERONE DEFICIENCY:

AUA GUIDELINE

Purpose

Evaluation and Management of Testosterone Deficiency: AUA Guideline provides guidance to the practicing clinician on how to diagnose, treat, and monitor the adult male with testosterone deficiency. The care of testosterone deficient patients should focus on accurate assessment of total testosterone levels, symptoms, and signs as well as proper on-treatment monitoring to ensure therapeutic testosterone levels are reached and symptoms are ameliorated. Guidance is also given on the management of patients with cardiovascular disease, men who are interested in preserving their fertility, and men who are at risk for or have prostate cancer.

AUA Nomenclature

The AUA nomenclature system links statement types to a number of factors including strength of evidence, magnitude of benefit and risks/burdens, and panel judgment. There are three evidence-based statement types: Strong Recommendations and Moderate Recommendations are directive statements that indicate that there is a net benefit (or harm) associated with a clinical action, while a Conditional Recommendation is a non-directive Statement that is used when the clinical action does not have a clear net benefit (or harm).

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**Guideline Statements**

**Diagnosis of Testosterone Deficiency**

- Clinicians should use a total testosterone level below 300 ng/dL as a reasonable cut-off in support of the diagnosis of low testosterone. *(Moderate Recommendation; Evidence Level: Grade B)*

- The diagnosis of low testosterone should be made only after two total testosterone measurements are taken on separate occasions with both conducted in an early morning fashion. *(Strong Recommendation; Evidence Level: Grade A)*

- The clinical diagnosis of testosterone deficiency is only made when patients have low total testosterone levels combined with symptoms and/or signs. *(Moderate Recommendation; Evidence Level: Grade B)*

- Clinicians should consider measuring total testosterone in patients with a history of unexplained anemia, bone density loss, diabetes, exposure to chemotherapy, exposure to testicular radiation, HIV/AIDS, chronic narcotic use, male infertility, pituitary dysfunction, and chronic corticosteroid use even in the absence of symptoms or signs associated with testosterone
deficiency. *(Moderate Recommendation; Evidence Level: Grade B)*

- The use of validated questionnaires is not currently recommended to either define which patients are candidates for testosterone therapy or monitor symptom response in patients on testosterone therapy. *(Conditional Recommendation; Evidence Level: Grade C)*

**Adjunctive Testing**

- In patients with low testosterone, clinicians should measure serum luteinizing hormone levels. *(Strong Recommendation; Evidence Level: Grade A)*

- Serum prolactin levels should be measured in patients with low testosterone levels combined with low or low/normal luteinizing hormone levels. *(Strong Recommendation; Evidence Level: Grade A)*

- Patients with persistently high prolactin levels of unknown etiology should undergo evaluation for endocrine disorders. *(Strong Recommendation; Evidence Level: Grade A)*

- Serum estradiol should be measured in testosterone deficient patients who present with breast symptoms or gynecomastia prior to the commencement of testosterone therapy. *(Expert Opinion)*

- Men with testosterone deficiency who are interested in fertility should have a reproductive health evaluation performed prior to treatment. *(Moderate Recommendation; Evidence Level: Grade B)*

- Prior to offering testosterone therapy, clinicians should measure hemoglobin and hematocrit and inform patients
regarding the increased risk of polycythemia. *(Strong Recommendation; Evidence Level: Grade A)*

- PSA should be measured in men over 40 years of age prior to commencement of testosterone therapy to exclude a prostate cancer diagnosis. *(Clinical Principle)*

### Counseling Regarding Treatment of Testosterone Deficiency

- Clinicians should inform testosterone deficient patients that low testosterone is a risk factor for cardiovascular disease. *(Strong Recommendation; Evidence Level: Grade B)*

- Patients should be informed that testosterone therapy may result in improvements in erectile function, low sex drive, anemia, bone mineral density, lean body mass, and/or depressive symptoms. *(Moderate Recommendation; Evidence Level: Grade B)*

- Patients should be informed that the evidence is inconclusive whether testosterone therapy improves cognitive function, measures of diabetes, energy, fatigue, lipid profiles, and quality of life measures. *(Moderate Recommendation; Evidence Level: Grade B)*

- The long-term impact of exogenous testosterone on spermatogenesis should be discussed with patients who are interested in future fertility. *(Strong Recommendation; Evidence Level: Grade A)*

- Clinicians should inform patients of the absence of evidence linking testosterone therapy to the development of prostate cancer. *(Strong Recommendation; Evidence Level: Grade B)*
• Patients with testosterone deficiency and a history of prostate cancer should be informed that there is inadequate evidence to quantify the risk-benefit ratio of testosterone therapy. *(Expert Opinion)*

• Patients should be informed that there is no definitive evidence linking testosterone therapy to a higher incidence of venothrombotic events. *(Moderate Recommendation; Evidence Level: Grade C)*

• Prior to initiating treatment, clinicians should counsel patients that, at this time, it cannot be stated definitively whether testosterone therapy increases or decreases the risk of cardiovascular events (e.g., myocardial infarction, stroke, cardiovascular-related death, all-cause mortality). *(Moderate Recommendation; Evidence Level: Grade B)*

• All men with testosterone deficiency should be counseled regarding lifestyle modifications as a treatment strategy. *(Conditional Recommendation; Evidence Level: Grade B)*

**Treatment of Testosterone Deficiency**

• Clinicians should adjust testosterone therapy dosing to achieve a total testosterone level in the middle tertile of the normal reference range. *(Conditional Recommendation; Evidence Level: Grade C)*

• Exogenous testosterone therapy should not be prescribed to men who are currently trying to conceive. *(Strong Recommendation; Evidence Level: Grade A)*

• Testosterone therapy should not be commenced for a period of three to six months in patients with a history of cardiovascular events. *(Expert Opinion)*
• Clinicians should not prescribe alkylated oral testosterone. (Moderate Recommendation; Evidence Level: Grade B)

• Clinicians should discuss the risk of transference with patients using testosterone gels/creams. (Strong Recommendation; Evidence Level: Grade A)

• Clinicians may use aromatase inhibitors, human chorionic gonadotropin, selective estrogen receptor modulators, or a combination thereof in men with testosterone deficiency desiring to maintain fertility. (Conditional Recommendation; Evidence Level: Grade C)

• Commercially manufactured testosterone products should be prescribed rather than compounded testosterone, when possible. (Conditional Recommendation; Evidence Level: Grade C)

Follow up of Men on Testosterone Therapy

• Clinicians should measure an initial follow-up total testosterone level after an appropriate interval to ensure that target testosterone levels have been achieved. (Expert Opinion)

• Testosterone levels should be measured every 6-12 months while on testosterone therapy. (Expert Opinion)

• Clinicians should discuss the cessation of testosterone therapy three to six months after commencement of treatment in patients who experience normalization of total testosterone levels but fail to achieve symptom or sign improvement. (Clinical Principle)
EVALUATION AND MANAGEMENT OF TESTOSTERONE DEFICIENCY: DIAGNOSTIC ALGORITHM

PATIENT PRESENTS WITH SIGNS, SYMPTOMS OR CONDITIONS ASSOCIATED WITH TESTOSTERONE DEFICIENCY

MEASURE TT^*

TT < 300 ng/dL

REPEAT TT*

MEASURE LH

MEASURE Hct

ADDITIONAL TESTS FOR SPECIAL CASES **

<table>
<thead>
<tr>
<th>Test</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>Patients who present with gynecomastia or breast symptoms</td>
</tr>
<tr>
<td>FSH</td>
<td>Patients who are interested in preserving their fertility</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Patients who may be at risk for diabetes</td>
</tr>
<tr>
<td>DEXA</td>
<td>Patients who have a history of low trauma bone fracture</td>
</tr>
<tr>
<td>Karyotype</td>
<td>Patients with unexplained hypergonadatropic hypogonadism</td>
</tr>
<tr>
<td>PSA</td>
<td>If first PSA is elevated, repeat test before initiating testosterone therapy</td>
</tr>
</tbody>
</table>

^Testosterone values are measured as ng/dL

*All TT measurements ≥ 300 ng/dL are considered normal

**After testosterone deficiency is confirmed additional tests may be considered for special cases

FSH = Follicle-Stimulating Hormone
Hct = Hematocrit
LH = Luteinizing Hormone
TD = Testosterone Deficiency
TT = Total Testosterone
Withhold testosterone therapy and refer for further evaluation by a primary care physician or internist

PROLACTIN TESTING

- Hct > 50% and second TT < 300 ng/dL
- LH low or low/normal and second TT < 300 ng/dL
- Normal Prolactin and second TT < 300 ng/dL
- Hct <50%, high/normal or elevated LH and second TT < 300 ng/dL

If prolactin elevated, repeat test

Refer to endocrinologist (order pituitary MRI)

TESTOSTERONE DEFICIENCY CONFIRMED

PSA TESTING IN PATIENTS ≥ 40 YEARS

PROCEED TO TREATMENT ALGORITHM
EVALUATION AND MANAGEMENT OF TESTOSTERONE DEFICIENCY: TREATMENT ALGORITHM

PATIENT MEETS CRITERIA FOR TESTOSTERONE DEFICIENCY AND IS A CANDIDATE FOR TESTOSTERONE THERAPY

CVD RISK ASSESSMENT: PATIENTS AT HIGH RISK FOR CV EVENTS SHOULD BE REFERRED FOR FURTHER EVALUATION

DISCUSS THERAPEUTIC MODALITIES INCLUDING LIFESTYLE CHANGES

EXOGENOUS TESTOSTERONE
- Gels/creams
- Patch
- Buccal
- IM
- SQ Pellets
- Nasal spray

ALTERNATIVE STRATEGIES
- SERM
- hCG
- AI

MEASURE ON-TREATMENT TESTOSTERONE LEVELS*

- Therapeutic levels without symptom and sign improvement
- Therapeutic levels with symptom and sign improvement
- Consider testosterone cessation 3 to 6 months after commencement of therapy
- Lab testing every 6-12 months
- Dose adjustment or change modalities; if using alternative strategies consider changing to exogenous testosterone

*Testosterone levels should be driven to the normal physiological range of 450-600 ng/dL (approximately equivalent to the middle tertile of the normal range).

AI = Aromatase Inhibitor
CVD = Cardiovascular Disease
hCG = Human Chorionic Gonadotropin
IM = Intramuscular Testosterone Injection
SERM = Selective Estrogen Receptor Modulator
SQ = Subcutaneous
Purpose

Priapism, a relatively uncommon disorder, is a medical emergency. Although not all forms of priapism require immediate intervention, ischemic priapism is associated with progressive fibrosis of the cavernosal tissues and with erectile dysfunction. Therefore, all patients with priapism should be evaluated emergently in order to intervene as early as possible in those patients with ischemic priapism. The goal of the management of all patients with priapism is to achieve detumescence and preserve erectile function. Unfortunately, some of the treatments aimed at correcting priapism have the potential complication of erectile dysfunction. Current treatment modalities represent a range of options that are applied in a step-wise pattern, with increasing invasiveness and risk balanced against the likelihood of prolonged ischemia and permanent damage to the corpora cavernosa if treatment is absent or delayed.

Guideline Statements

Evaluation of Priapism

Perform historical, physical and laboratory/radiologic evaluations to differentiate ischemic from nonischemic priapism (Table 1).

- Components of the historical evaluation:
  - duration of erection
• degree of pain
• previous history of priapism and its treatment
• use of drugs that may have precipitated the episode
• history of pelvic, genital or perineal trauma
• history of sickle cell disease or other hematologic abnormality

• Components of the physical examination:
  • focused examination of the genitalia, perineum and abdomen
    • abdominal, pelvic and perineal examination may reveal evidence of trauma or malignancy

• Components of laboratory/radiologic evaluation:
  • CBC
  • reticulocyte count
  • hemoglobin electrophoresis
  • psychoactive medication screening
  • urine toxicology
  • blood gas testing (Table 2)
  • color duplex ultrasonography
  • penile arteriography

Management of Priapism

An algorithm for the management of ischemic and nonischemic priapism is presented in Figure 1.

Ischemic Priapism

Ischemic priapism is a nonsexual, persistent erection characterized by little or no cavernous blood flow and abnormal cavernous blood gases.
Male Sexual Health: Priapism

- In patients with underlying disorders (e.g., sickle cell disease, hematologic malignancy), intracavernous treatment of ischemic priapism should be undertaken concurrently with systemic treatment of the underlying disorder.

- Therapeutic aspiration (with or without irrigation), or intracavernous injection of sympathomimetics (e.g., phenylephrine) may be used as initial intervention.

- If priapism persists following aspiration/irrigation, perform intracavernous injection of sympathomimetic drugs and repeat if needed prior to initiating surgical intervention.

- Phenylephrine is recommended as the sympathomimetic agent of choice for intracavernous injection to minimize cardiovascular side effects.
  - In adult patients, dilute with normal saline to a concentration of 100 to 500 µg/mL. Inject every 3 to 5 minutes for approximately 1 hour before determining treatment failure.
  - Children and patients with severe cardiovascular diseases require smaller volumes or lower concentrations.
  - Observe patients for subjective symptoms and objective findings consistent with known undesirable effects of these agents.
  - Blood pressure and electrocardiogram monitoring are recommended in high-risk patients.

- Consider use of surgical shunts after intracavernous injections of sympathomimetics has failed.
  - Consider cavernoglanular (corporoglanular) shunt as first choice. Perform with a large biopsy needle or scalpel inserted percutaneously through the glans.
  - Oral systemic therapy is not indicated for treatment of ischemic priapism.
Nonischemic Priapism

Nonischemic priapism is an uncommon form of priapism caused by unregulated arterial flow. It may follow perineal trauma that results in laceration of the cavernous artery. In many patients, there is no underlying cause. The erections associated with nonischemic priapism are typically neither fully rigid nor painful. Nonischemic priapism is not an emergency and will often resolve without treatment.

- Corporal aspiration has only a diagnostic role. Aspiration with or without injection of sympathomimetic agents is not recommended as treatment.
- Initial management should be observation.
  ✦ Discuss the following with the patient prior to treatment: chances for spontaneous resolution, risks of treatment-related erectile dysfunction and lack of significant consequences expected from delaying intervention.
- Perform selective arterial embolization at request of patient; autologous clot and absorbable gels (nonpermanent therapies) are preferable.
- Consider surgery as a last resort: perform with intraoperative color duplex ultrasonography.

Stuttering Priapism

Stuttering (or intermittent) priapism is a recurrent form of ischemic priapism in which unwanted painful erections occur repeatedly with intervening periods of detumescence.

- Treat each episode as described for ischemic priapism.
- Trials of gonadotropin-releasing hormone agonists or antiandrogens may be used, but have not been fully tested. Hormonal agents should not be used in patients
who have not achieved full sexual maturation and adult stature.

- Consider intracavernous self-injection of phenylephrine in patients who either fail or reject systemic treatment of stuttering priapism.

**TABLE 1.**

**Key Findings in the Evaluation of Priapism**

<table>
<thead>
<tr>
<th>Finding</th>
<th>Ischemic Priapism</th>
<th>Nonischemic Priapism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corpora cavernosa fully rigid</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Penile pain</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Abnormal cavernous blood gases</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Blood abnormalities and hematologic malignancy</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Recent intracavernous vasoactive drug injections</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Chronic, well-tolerated tumescence without full rigidity</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Perineal trauma</td>
<td>●</td>
<td>●</td>
</tr>
</tbody>
</table>

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● Usually present; ● Sometimes present; ● Seldom present

**TABLE 2.**

**Typical Blood Gas Values**

<table>
<thead>
<tr>
<th>Source</th>
<th>Po2 (mm Hg)</th>
<th>Pco2 (mm Hg)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic priapism (cavernous blood)*</td>
<td>&lt;30</td>
<td>&gt;60</td>
<td>&lt;7.25</td>
</tr>
<tr>
<td>Normal arterial blood (room air)</td>
<td>&gt;90</td>
<td>&lt;40</td>
<td>7.40</td>
</tr>
<tr>
<td>Normal mixed venous blood (room air)</td>
<td>40</td>
<td>50</td>
<td>7.35</td>
</tr>
</tbody>
</table>

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**Management of Priapism**

PRIAPISM*

History & Physical → Simultaneous Treatment of Any Underlying Disease (e.g., sickle cell disease)

Cavernous Aspiration with Blood Gas or Doppler Ultrasound

Ischemic

Phenylephrine

† Distal Shunting

† Repeat Distal or Use Proximal Shunting

Nonischemic

Observation

† Arteriography & Embolization

† Surgical Ligation

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* Erection greater than 4 hours duration.
† Proceed upon treatment failure.
Purpose

This guideline’s purpose is to provide direction to clinicians and patients regarding how to recognize Peyronie’s Disease (PD), conduct a valid diagnostic process, and approach treatment with the goals of maximizing symptom control, sexual function, and patient and partner quality of life while minimizing adverse events and patient and partner burden. The strategies and approaches recommended in this document were derived from evidence-based and consensus-based processes. There is a continually expanding literature on PD; the Panel notes that this document constitutes a clinical strategy and is not intended to be interpreted rigidly. The most effective approach for a particular patient is best determined by the individual clinician and patient in the context of that patient’s history, values, and goals for treatment. As the science relevant to PD evolves and improves, the strategies presented here will be amended to remain consistent with the highest standards of clinical care.

AUA Nomenclature

The AUA nomenclature system links statement types to a number of factors including strength of evidence, magnitude of benefit and risks/burdens, and panel judgment. There are three evidence-based statement types: Strong Recommendations and Moderate Recommendations are directive statements that indicate that there is a net benefit (or harm) associated with a clinical action, while a
**Conditional Recommendation** is a non-directive Statement that is used when the clinical action does not have a clear net benefit (or harm).

In addition, there are two statement types that are used when pertinent evidence is not present in the systematic review of literature associated with the guideline: **Expert Opinions** are statements made by panel consensus based on members’ clinical training, experience, knowledge, and judgment, while a **Clinical Principle** is a statement about a component of clinical care that is very widely agreed upon by urologists or other clinicians.

**Guideline Statements**

**Diagnosis**

- Clinicians should engage in a diagnostic process to document the signs and symptoms that characterize PD. The minimum requirements for this examination are a careful history (to assess penile deformity, interference with intercourse, penile pain, and/or distress) and a physical exam of the genitalia (to assess for palpable abnormalities of the penis). *(Clinical Principle)*

- Clinicians should perform an in-office intracavernosal injection (ICI) test with or without duplex Doppler ultrasound prior to invasive intervention. *(Expert Opinion)*

- Clinicians should evaluate and treat a man with PD only when he/she has the experience and diagnostic tools to appropriately evaluate, counsel, and treat the condition. *(Expert Opinion)*
Treatment

- Clinicians should discuss with patients the available treatment options and the known benefits and risks/burdens associated with each treatment. *(Clinical Principle)*

- Clinicians may offer oral non-steroidal anti-inflammatory medications to the patient suffering from active PD who is in need of pain management. *(Expert Opinion)*

- Clinicians should not offer oral therapy with vitamin E, tamoxifen, procarbazine, omega-3 fatty acids, or a combination of vitamin E with L-carnitine. *[Moderate Recommendation; Evidence Level: Grade B (vitamin E)/B (omega-3 fatty acids)/B (Vitamin E + propionyl-L-carnitine)/C (tamoxifen)/C(procarbazine)]*

- Clinicians should not offer electromotive therapy with verapamil. *(Moderate Recommendation; Evidence Level: Grade C)*

- Clinicians may administer intraloesional collagenase clostridium histolyticum in combination with modeling by the clinician and by the patient for the reduction of penile curvature in patients with stable PD, penile curvature >30° and <90°, and intact erectile function (with or without the use of medications). *(Moderate Recommendation; Evidence Level: Grade B)*

- Clinicians should counsel patients with PD prior to beginning treatment with intraloesional collagenase regarding potential occurrence of adverse events, including penile ecchymosis, swelling, pain, and corporal rupture. *(Clinical Principle)*
• Clinicians may administer intralesional interferon α-2b in patients with PD. (*Moderate Recommendation; Evidence Level: Grade C*)

• Clinicians should counsel patients with PD prior to beginning treatment with intralesional interferon α-2b about potential adverse events, including sinusitis, flu-like symptoms and minor penile swelling. (*Clinical Principle*)

• Clinicians may offer intralesional verapamil for the treatment of patients with PD. (*Conditional Recommendation; Evidence Level: Grade C*)

• Clinicians should counsel patients with PD prior to beginning treatment with intralesional verapamil about potential adverse events, including penile bruising, dizziness, nausea and pain at the injection site. (*Clinical Principle*)

• Clinicians should not use extracorporeal shock wave therapy (ESWT) for the reduction of penile curvature or plaque size. (*Moderate Recommendation; Evidence Level: Grade B*)

• Clinicians may offer ESWT to improve penile pain. (*Conditional Recommendation; Evidence Level: Grade B*)

• Clinicians should not use radiotherapy (RT) to treat PD. (*Moderate Recommendation; Evidence Level: Grade C*)

• Clinicians should assess patients as candidates for surgical reconstruction based on the presence of stable disease. (*Clinical Principle*)

• Clinicians may offer tunical plication surgery to patients whose rigidity is adequate for coitus (with or without pharmacotherapy and/or vacuum device therapy) to
improve penile curvature. *(Moderate Recommendation; Evidence Level: Grade C)*

- Clinicians may offer plaque incision or excision and/or grafting to patients with deformities whose rigidity is adequate for coitus (with or without pharmacotherapy and/or vacuum device therapy) to improve penile curvature. *(Moderate Recommendation; Evidence Level: Grade C)*

- Clinicians may offer penile prosthesis surgery to patients with PD with erectile dysfunction (ED) and/or penile deformity sufficient to prevent coitus despite pharmacotherapy and/or vacuum device therapy. *(Moderate Recommendation; Evidence Level: Grade C)*

- Clinicians may perform adjunctive intra-operative procedures, such as modeling, plication or incision/grafting, when significant penile deformity persists after insertion of the penile prosthesis. *(Moderate Recommendation; Evidence Level: Grade C)*

- Clinicians should use inflatable penile prosthesis for patients undergoing penile prosthetic surgery for the treatment of PD. *(Expert Opinion)*
**Peyronie’s Guideline Algorithm**

**HISTORY & PHYSICAL**

**BASIC ASSESSMENT**

- Penile deformity
- Palpable abnormalities
- Interference with intercourse

- Pain
- Distress
- Establish active v. stable phase

**EXPERT OPINION**

Perform in-office intracavernosal injection (ICI) test with or without duplex ultrasound

- Document curvature, other deformities, presence/absence and degree of plaque(s) and ED

**PATIENT COUNSELING**

- Typical course of PD
- Available treatment options based on phase
- Benefits/risks of treatment options
- Agree on realistic treatment goals

**PATIENT HAS STABLE DISEASE**

Patient desires invasive treatment

**PATIENT HAS ACTIVE DISEASE**

Patient desires treatment of pain

**EXPERT OPINION**

*Offer NSAIDs*

**MODERATE RECOMMENDATIONS**

*Offer intrallesional collagenase clostridium histolyticum with modeling by clinician and patient for curvature reduction (Grade B)*

- Appropriate for patients with curvature >30 and <90 degrees
- Patient must have intact erectile function with or without use of medications

*Offer intrallesional interferon α-2b for curvature, plaque, and pain reduction (Grade C)*

**CONDITIONAL RECOMMENDATION**

*Offer intrallesional verapamil (Grade C)*

- Note: evidence for efficacy is weak
Follow and repeat assessment; if patient has reached stable disease state as indicated by absence of pain and non-progression of curvature, then may consider invasive treatments.

THERAPIES THAT SHOULD NOT BE OFFERED:

Moderate Recommendations
- Oral therapy with vitamin E, omega-3 fatty acids, vitamin E plus L-carnitine (Grade B), tamoxifen, procarbazine (Grade C)
- Electromotive verapamil (Grade C)
- Radiotherapy (Grade C)

CONDITIONAL RECOMMENDATION
If inadequate pain control with oral medications, then may offer ESWT (Grade B), BUT:
- Substantial patient burden
- Rarely used in US
- Does not reduce curvature or plaque

Patient has stable disease and requires greater deformity correction than possible with intralesional treatments

Patient has intact erectile function with or without pharmacotherapy and/or vacuum device therapy

MODERATE RECOMMENDATION
Offer tunical plication or plaque incision/excision with or without grafting (Grade C)

Patient does not have intact erectile function and/or has severe penile deformity and/or shortening

MODERATE RECOMMENDATION
Offer penile prosthesis surgery with intraoperative adjunctive procedures, as necessary (Grade C)
- Use inflatable penile prosthesis (Expert Opinion)
Purpose

Premature ejaculation (PE) is one of the most common male sexual disorders. Because a universally accepted definition of PE has yet to be established, for the purposes of this Guideline, the panel defined PE as the following: ejaculation that occurs sooner than desired, either before or shortly after penetration, causing distress to either one or both partners. Although the exact etiology of PE is unknown, treatments have encompassed psychological, behavioral and pharmacologic interventions. The present recommendations address pharmacologic therapies only.

Guideline Statements

Patient Evaluation

The diagnosis of PE is based on sexual history alone.

Obtain a detailed sexual history from all patients with ejaculatory complaints.

- Components of the historical evaluation:
  - frequency and duration of PE
  - relationship to specific partners
  - occurrence with all or some attempts
  - degree of stimulus resulting in PE
• nature and frequency of sexual activity
• impact of PE on sexual activity
• types and quality of personal relationships and quality of life
• aggravating or alleviating factors
• relationship to drug use or abuse

- Determine whether erectile dysfunction (ED) is a concurrent problem. In patients with concomitant PE and ED, treat ED first.

- Laboratory or physiological testing is not required unless the history and physical examination reveal indications beyond uncomplicated PE.

**Patient Management**

Patient and partner satisfaction is the primary target outcome for treatment.

- Reassure the patient and, if possible, his partner that PE is common and treatable.

- Inform the patient of the treatment options and their risk and benefits prior to any intervention: The selective serotonin reuptake inhibitors (fluoxetine, paroxetine, and sertraline), a tricyclic antidepressant (clomipramine) and topical anesthetic agents (lidocaine/prilocaine cream) (Table 1) can be used to effectively treat PE.

- Base treatment choice on both physician judgment and patient preference.
Medical Treatment

Serotonin Reuptake Inhibitors (SRIs) – Selective and Nonselective

- Whether continuous or situational dosing is more effective is unclear. Choice of regimen is based on frequency of sexual activity. The optimal interval for situational dosing before intercourse has not been established.

- Therapy most likely will be needed on a continuing basis. PE usually returns upon discontinuing therapy.

- Although the adverse effects of the SRIs have been well-described in the management of clinical depression, consider the following facts when prescribing these agents for PE:
  - Evidence to date suggests that adverse event profiles for SRIs in the treatment of PE are similar to those reported in patients with depression (nausea, dry mouth, drowsiness and reduced libido).
  - Doses effective in the treatment of PE are usually lower than those recommended in the treatment of depression.
  - Adverse event profiles may differ among patients depending on the dosing regimen prescribed (continuous daily dosing or situational dosing).

- Pharmacodynamic drug interactions resulting in a “serotonergic syndrome” have been reported rarely with the concomitant use of monoamine oxidase inhibitors, lithium, sumatriptan and tryptophan. Pharmacokinetic interactions resulting in alterations of drug blood levels may occur with the anticonvulsants, benzodiazepines, cimetidine, tricyclic antidepressants, antipsychotic agents,
tolbutamide, antiarrhythmics and warfarin, especially in elderly patients.

- None of the SRIs have been approved by the U.S. Food and Drug Administration for the treatment of PE.

**Topical Anesthetic Agents**

- Should be applied to the penis prior to intercourse and used with or without a condom. The condom may be removed and penis washed clean prior to intercourse.

- Prolonged application (30 to 45 minutes) may result in loss of erection due to numbness. Diffusion of residual topical anesthetic into the vaginal wall may produce numbness of the partner.
TABLE 1.

Medical Therapy Options for the Treatment of Premature Ejaculation*

<table>
<thead>
<tr>
<th>Oral Therapies</th>
<th>Trade Names†</th>
<th>Recommended Dose‡§</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nonselective Serotonin Reuptake Inhibitor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clomipramine</td>
<td>Anafranil®</td>
<td>25 to 50 mg/day or 25 mg 4 to 24 h pre-intercourse</td>
</tr>
<tr>
<td><strong>Selective Serotonin Reuptake Inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Prozac®, Sarafem®</td>
<td>5 to 20 mg/day</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Paxil®</td>
<td>10, 20, 40 mg/day or 20 mg 3 to 4 h pre-intercourse</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Zoloft®</td>
<td>25 to 200 mg/day or 50 mg 4 to 8 h pre-intercourse</td>
</tr>
<tr>
<td><strong>Topical Therapies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lidocaine/prilocaine cream</td>
<td>EMLA® Cream</td>
<td>Lidocaine 2.5%/prilocaine 2.5% 20 to 30 minutes pre-intercourse</td>
</tr>
</tbody>
</table>

* This list does not reflect order of choice or efficacy.
† Trade names listed may not be all-inclusive.
‡ Peak plasma concentrations occur 2 to 8 hours (h) postdose and half-lives range from 1 to 3 days.
§ Titrate doses from low to high based on response.

Medical therapies currently employed in the management of PE have not been approved by the U.S. Food and Drug Administration for this indication. Treatment with oral antidepressants should be started at the lowest possible dose that is compatible with success.
EVALUATION AND TREATMENT OF CRYPTORCHIDISM

AUA GUIDELINE – 2014

Purpose

Cryptorchidism, or undescended testis (UDT), is one of the most common pediatric disorders of the male endocrine glands and the most common genital disorder identified at birth. The main reasons for treatment of cryptorchidism include increased risks of impairment of fertility potential, testicular malignancy, torsion and/or associated inguinal hernia. Cryptorchidism has evolved significantly over the past half century, with respect to both diagnosis and treatment. The current standard of therapy in the United States is orchidopexy (also referred to as orchiopexy in the literature), or surgical repositioning of the testis within the scrotal sac, while hormonal therapy has fewer advocates. Successful scrotal relocation of the testis, however, may reduce but does not prevent these potential long-term sequelae in susceptible individuals. The purpose of this guideline is to provide physicians and non-physician providers (primary care and specialists) with a consensus of principles and treatment plans for the management of cryptorchidism. The panel members are representative of various medical specialties (pediatric urology, pediatric endocrinology, general pediatrics).

Guideline Statements

Diagnosis

- Providers should obtain gestational history at initial evaluation of boys with suspected cryptorchidism.
• Primary care providers should palpate testes for quality and position at each recommended well-child visit.

• Providers should refer infants with a history of cryptorchidism (detected at birth) who do not have spontaneous testicular descent by six months (corrected for gestational age) to an appropriate surgical specialist for timely evaluation.

• Providers should refer boys with the possibility of newly diagnosed (acquired) cryptorchidism after six months (corrected for gestational age) to an appropriate surgical specialist.

• Providers must immediately consult an appropriate specialist for all phenotypic male newborns with bilateral, non-palpable testes for evaluation of a possible disorder of sex development (DSD).

• Providers should not perform ultrasound (US) or other imaging modalities in the evaluation of boys with cryptorchidism prior to referral as these studies rarely assist in decision making.

• Providers should assess the possibility of a disorder of sex development (DSD) when there is increasing severity of hypospadias with cryptorchidism.

• In boys with bilateral, non-palpable testes who do not have congenital adrenal hyperplasia (CAH), providers should measure Müllerian Inhibiting Substance (MIS or Anti- Müllerian Hormone [AMH]) and consider additional hormone testing to evaluate for anorchia.

• In boys with retractile testes, providers should monitor the position of the testes at least annually to monitor for secondary ascent.
Treatment

- Providers should not use hormonal therapy to induce testicular descent as evidence shows low response rates and lack of evidence for long-term efficacy.
- In the absence of spontaneous testicular descent by six months (corrected for gestational age), specialists should perform surgery within the next year.
- In pre-pubertal boys with palpable, cryptorchid testes, surgical specialists should perform scrotal or inguinal orchiopexy.
- In pre-pubertal boys with non-palpable testes, surgical specialists should perform exam under anesthesia to reassess for palpability of testes. If non-palpable, surgical exploration and, if indicated, abdominal orchiopexy should be performed.
- At the time of exploration for a non-palpable testis in boys, surgical specialists should identify the status of the testicular vessels to help determine the next course of action.
- In boys with a normal contralateral testis, surgical specialists may perform an orchiectomy (removal of the undescended testis) if a boy has a normal contralateral testis and either very short testicular vessels and vas deferens, dysmorphic or a hypoplastic testis, or post-pubertal age.
- Providers should counsel boys with a history of cryptorchidism and/or monorchidism and their parents regarding potential long-term risks and provide education on infertility and cancer risk.
Evaluation and Treatment of Cryptorchidism

- Boy with undescended testis
  - Older than 6 months (corrected for gestational age)
    - Refer to surgical specialist
    - YES
  - Still undescended testis at 6 months
    - NO
  - Reassess at 6 months (corrected for gestational age)
    - NO
    - Still undescended testis at 6 months
      - YES
      - Refer to surgical specialist
      - NO
      - PALPABLE
        - Retractile
          - Monitor yearly
        - Undescended
          - Orchiopexy - Scrotal vs Inguinal
          - YES
          - Testis identified
            - Orchiopexy - Single stage- Fowler Stephens (1 or 2 stage)
    - NO
    - Bilateral, nonpalpable
NON-PALPABLE
Examination under anesthesia

NON-PALPABLE
Consider inguinal/scrotal exploration if nubbin palpable +/- contralateral hypertrophy

PALPABLE
Abdominal exploration - Laparoscopic vs open

Vessels entering Internal ring
Inguinal exploration

Blind ending vessels
Close

Consult specialist to evaluate for DSD
Pediatric Urology: Vesicoureteral Reflux

MANAGEMENT AND SCREENING OF PRIMARY VESICOURETERAL REFLUX IN CHILDREN

AUA GUIDELINE – 2010; REVIEWED AND VALIDITY CONFIRMED – 2017

Purpose

The management of vesicoureteral reflux (VUR) has continued to evolve, with practitioners often confronted with conflicting information regarding the outcomes of medical, surgical, and endoscopic therapy, and the efficacy of continuous antibiotic prophylaxis (CAP). In addition, the role of screening has become recognized as important in detecting a population at risk and allowing timely treatment in order to decrease adverse outcomes associated with VUR. This guide discusses the initial evaluation, management and follow-up of the child with VUR along with screening in siblings, offspring, and neonates with prenatal hydronephrosis. Identification of individual risk factors should be taken into consideration when managing the child with VUR, as well as incorporating family choices in care when medical options are not clearly different.

Guideline Statements

Initial Evaluation of the Child with VUR

- General medical evaluation in all patients:
  - Measurement of height, weight, and blood pressure, and serum creatinine if bilateral renal abnormalities are found.
Urinalysis for proteinuria and bacteriuria; if urinalysis indicates infection, a urine culture and sensitivity is recommended.

A baseline serum creatinine may be obtained to establish an estimate of glomerular filtration rate.

- Imaging procedures:
  - Renal ultrasound to assess the upper urinary tract is recommended.
  - DMSA (technetium-99m-labeled dimercaptosuccinic acid) renal imaging can be obtained to assess the kidney for scarring and function.

- Assessment of voiding patterns:
  - Symptoms indicative of bladder/bowel dysfunction (BBD) should be sought including: urinary frequency and urgency, prolonged voiding intervals, daytime wetting, perineal/penile pain, holding maneuvers (posturing to prevent wetting), and constipation/encopresis.

- Family and patient education:
  - Discussion should include rationale for treating VUR, potential consequences of untreated VUR, equivalency of certain treatment approaches, assessment of likely adherence with the care plan.
  - Determination of parental concerns and accommodation of parental preferences when treatment choices offer a similar risk-benefit balance.

**Initial Management of the Child with VUR**

The goals of management are to 1) prevent recurring febrile urinary tract infection (UTI); 2) prevent renal injury; and 3) minimize morbidity of treatment and follow-up.
The child with VUR <1 year of age:

- CAP is recommended for children <1 year of age with VUR and a history of a febrile UTI.
- In the absence of a history of febrile UTI, CAP is recommended for the child <1 year of age with VUR grades III–V identified through screening.
- In the absence of a history of febrile UTI, the child <1 year of age with VUR grades I–II who is identified through screening may be offered CAP.
- Circumcision of the male infant with VUR may be considered based on an increased risk of UTI in boys who are not circumcised.
  - Parents need to be made aware of this association to permit informed decision-making.

The child with UTI and VUR >1 year of age (Table 1):

- If clinical evidence of BBD is present, treatment is indicated, preferably before any surgical intervention for VUR is undertaken.

Treatment options include behavioral therapy, biofeedback (for children >5 years of age), anticholinergic medications, alpha blockers, and treatment of constipation.

- CAP is recommended for the child with BBD and VUR due to the increased risk of UTI while BBD is present and being treated.
- CAP may be considered for the child >1 year of age with a history of UTI and VUR in the absence of BBD.
- Observational management without CAP, with prompt initiation of antibiotic therapy for UTI, may be considered for the child >1 year of age with VUR in the absence of BBD, recurrent febrile UTIs, or renal cortical abnormalities.
Surgical intervention for VUR, including both open and endoscopic methods, may be used.

**Follow-up Management of the Child with VUR**

- General follow-up in all patients:
  - General evaluation, including monitoring of blood pressure, height, and weight is recommended annually.
  - Urinalysis for proteinuria and bacteriuria is indicated annually, including a urine culture and sensitivity if the urinalysis is suggestive of infection.

- Imaging – ultrasonography and cystography:
  - Ultrasonography is recommended every 12 months to monitor renal growth and any parenchymal scarring.
  - Voiding cystography (radionuclide cystogram or low-dose fluoroscopy, when available) is recommended between 12 and 24 months.

- Longer intervals between follow-up studies are suggested in patients who may have lower rates of spontaneous resolution (i.e. those with VUR grades III-V, BBD, and older age).
  - If an observational approach without CAP is being used, follow-up cystography is an option.
  - Follow-up cystography may be performed after 1 year of age in patients with VUR grades I–II; these patients have high rates of spontaneous resolution and boys also have a low risk of recurrent UTI.
  - A single normal voiding cystogram may serve to establish resolution.

- The clinical significance of grade I VUR, and the need for ongoing evaluation is undefined.
• Imaging – DMSA:
  ✦ Recommended when renal ultrasound is abnormal, when there is a greater concern for scarring (i.e. breakthrough UTI [BT-UTI]; grade III-V VUR), or if serum creatinine is elevated.
  ✦ May be considered for follow-up of children with VUR to detect new renal scarring, especially after a febrile UTI.

**Interventions for the Child with BT-UTI**

✦ If symptomatic BT-UTI occurs, a change in therapy is recommended.
  • The clinical scenario will guide the choice of treatment alternatives; this includes VUR grade, degree of renal scarring, if any, and evidence of abnormal voiding patterns (BBD) that might contribute to UTI, as well as parental preferences.
  ✦ Patients receiving CAP with a febrile BT-UTI should be considered for open surgical ureteral reimplantation or endoscopic injection of bulking agents for intervention with curative intent.
  ✦ In patients receiving CAP with a single febrile BT-UTI and no evidence of pre-existing or new renal cortical abnormalities, changing to an alternative antibiotic agent is an option prior to intervention with curative intent.
  ✦ In patients not receiving CAP who develop a febrile UTI, initiation of CAP is recommended.
  ✦ In patients not receiving CAP who develop a non-febrile UTI, CAP is an option; not all cases of pyelonephritis are associated with fever.

**Surgical treatment of VUR**

✦ Surgical treatment of VUR, including both open and endoscopic methods, is an option.
Following open surgical or endoscopic procedures for VUR, a renal ultrasound should be obtained to assess for obstruction.

Postoperative voiding cystography following endoscopic injection of bulking agents is recommended.

Postoperative cystography may be performed following open ureteral reimplantation.

Management Following Resolution of VUR

Either spontaneously or by surgical intervention, monitoring of blood pressure, height, and weight, and urinalysis for protein and UTI is recommended annually through adolescence.

If both kidneys are normal by ultrasound or DMSA scanning, such follow-up is an option.

With the occurrence of a febrile UTI following resolution or surgical treatment of VUR, evaluation for BBD or recurrent VUR is recommended.

Discussion is recommended of the long-term concerns of hypertension (particularly during pregnancy), renal functional loss, recurrent UTI, and familial VUR in the child’s siblings and offspring with the family and child at an appropriate age.

Screening for VUR in Siblings

The incidence of VUR in siblings of children with VUR is 27% overall and decreases with age. The incidence of VUR in offspring of a parent with reflux is 37%.

For siblings of children with VUR:

A voiding cystourethrogram (VCUG) or radionuclide cystogram is recommended on evidence of renal cortical abnormalities or renal size asymmetry on ultrasound or a history of UTI in the sibling who has not been tested.
Given that the value of identifying and treating VUR is unproven:

- Ultrasound screening of the kidneys may be performed to identify significant renal scarring and to focus attention on the presence and potential further risk of VUR.
- Screening offspring of patients with VUR can be considered as similar to screening of siblings.

**Neonates with Prenatal Hydronephrosis**

The incidence of VUR in children who have had hydronephrosis detected prenatally is 16% overall. The likelihood of VUR is not predicted by the severity of the hydronephrosis either prenatally or postnatally.

- VCUG is recommended for children with high-grade (Society for Fetal Urology [SFU] grade 3 and 4) hydronephrosis, hydroureter or an abnormal bladder on ultrasound (late-term prenatal or postnatal), or who develop a UTI on observation.

- Screening for VUR in children with a history of prenatally detected hydronephrosis with low grade hydronephrosis (SFU grade 1 or 2) is an option.

- An observational approach without screening for VUR, with prompt treatment of any UTI, may be taken for children with prenatally detected hydronephrosis (SFU grade 1 or 2).
## TABLE 1.

### Management of the child with VUR and UTI >1 year of age

<table>
<thead>
<tr>
<th>Patient Presentation</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>No BBD, recurrent febrile UTI, renal cortical abnormalities</td>
<td>CAP</td>
</tr>
<tr>
<td>BBD, recurrent febrile UTI, or renal cortical abnormalities</td>
<td>Recommended</td>
</tr>
</tbody>
</table>

Option

Option

Recommended

Not recommended

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Purpose

The purpose of this guideline is to provide a clinical framework for the use of radiotherapy after prostatectomy in patients with and without evidence of prostate cancer recurrence.

Definitions

- Adjuvant radiotherapy (ART) is defined as the administration of RT to post-prostatectomy patients at a higher risk of recurrence because of adverse pathological features prior to evidence of disease recurrence (i.e., with an undetectable PSA).

- Salvage radiotherapy (SRT) is defined as the administration of RT to the prostatic bed and possibly to the surrounding tissues, including lymph nodes, in the patient with a PSA recurrence after surgery but no evidence of distant metastatic disease.

- Biochemical (PSA) recurrence after surgery is defined as a detectable PSA level $\geq 0.2$ ng/mL with a second confirmatory level $\geq 0.2$ ng/mL.
Guideline Statements

- Patients who are being considered for management of localized prostate cancer with radical prostatectomy should be informed of the potential for adverse pathologic findings that portend a higher risk of cancer recurrence and that these findings may suggest a potential benefit of additional therapy after surgery.

- Patients with adverse pathologic findings including seminal vesicle invasion, positive surgical margins, and extraprostatic extension should be informed that adjuvant radiotherapy, compared to radical prostatectomy only, reduces the risk of biochemical (PSA) recurrence, local recurrence, and clinical progression of cancer. They should also be informed that the impact of adjuvant radiotherapy on subsequent metastases and overall survival is less clear; one of two randomized controlled trials that addressed these outcomes indicated a benefit but the other trial did not demonstrate a benefit. However, the other trial was not powered to test the benefit regarding metastases and overall survival.

- Physicians should offer adjuvant radiotherapy to patients with adverse pathologic findings at prostatectomy including seminal vesicle invasion, positive surgical margins, or extraprostatic extension because of demonstrated reductions in biochemical recurrence, local recurrence, and clinical progression.

- Patients should be informed that the development of a PSA recurrence after surgery is associated with a higher risk of development of metastatic prostate cancer or death from the disease. Congruent with this clinical principle, physicians should regularly monitor PSA after radical
prostatectomy to enable early administration of salvage therapies if appropriate.

- Clinicians should define biochemical recurrence as a detectable or rising PSA value after surgery that is ≥ 0.2 ng/ml with a second confirmatory level ≥ 0.2 ng/ml.

- A restaging evaluation in the patient with a PSA recurrence may be considered.

- Physicians should offer salvage radiotherapy to patients with PSA or local recurrence after radical prostatectomy in whom there is no evidence of distant metastatic disease.

- Patients should be informed that the effectiveness of radiotherapy for PSA recurrence is greatest when given at lower levels of PSA.

- Patients should be informed of the possible short-term and long-term urinary, bowel, and sexual side effects of radiotherapy as well as of the potential benefits of controlling disease recurrence.
CASTRATION-RESISTANT PROSTATE CANCER

AUA GUIDELINE – 2013, AMENDED – 2014, 2015, 2018

Note to the Reader:

This document was amended in April 2014 and March 2015 to reflect literature that was released since the original publication of this guideline in May 2013. An additional amendment was conducted in 2018 to reflect new literature released related to the treatment of patients with non-metastatic castration-resistant prostate cancer. This document will continue to be periodically updated to reflect the growing body of literature related to this disease.

On July 26, 2013, the FDA issued a safety announcement related to the use of ketoconazole in the form of oral tablets. Side effects can include hepatotoxicity, adrenal insufficiency and dangerous drug interactions.

On July 21, 2014, the FDA issued a recommendation that health care professionals should consider the alcohol content of docetaxel when prescribing or administering the drug to patients.

Guideline Statements

Index Patient 1

Asymptomatic non-metastatic CRPC

One of the first clinical presentations of Castration-Resistant Prostate Cancer (CRPC) occurs in a patient with a rising PSA despite medical or surgical castration. This is typically defined
as a patient with a rising PSA and no radiologic evidence of metastatic prostate cancer. The Prostate Cancer Clinical Trials Working Group 2 (PCWG2) defines PSA only failure as a rising PSA that is greater than 2ng/mL higher than the nadir, the rise has to be at least 25% over nadir and the rise has to be confirmed by a second PSA at least three weeks later. In addition, the patient is required to have castrate levels of testosterone (less than 50 ng/dL) and no radiographic evidence of metastatic disease. These patients represent a relatively common clinical presentation and the earliest clinical manifestation of castration resistance.

- **Clinicians should offer apalutamide or enzalutamide with continued androgen deprivation to patients with non-metastatic CRPC at high risk for developing metastatic disease.**

- **Clinicians may recommend observation with continued androgen deprivation to patients with non-metastatic CRPC at high risk for developing metastatic disease.**

- **Clinicians may offer treatment with a second-generation androgen synthesis inhibitor (i.e. abiraterone + prednisone) to select patients with non-metastatic CRPC at high risk for developing metastatic disease who do not want or cannot have one of the standard therapies and are unwilling to accept observation.**

- **Clinicians should not offer systemic chemotherapy or immunotherapy to patients with non-metastatic CRPC outside the context of a clinical trial.**
Index Patient 2

Asymptomatic or minimally symptomatic, mCRPC without prior docetaxel chemotherapy

This patient represents a common clinical presentation seen in the CRPC setting today. These patients are characterized as having a rising PSA in the setting of castrate levels of testosterone, documented metastatic disease on radiographic imaging and no prior treatment with docetaxel chemotherapy for CRPC. The key distinction between this patient and Index Patients 3 and 4 is symptom status. Specifically, this patient is defined as having no symptoms or mild symptoms attributable to his prostate cancer. However, one must then consider whether the patient requires regular opioid pain medications for symptoms thought to be attributable to documented metastases to achieve this level of pain control. In general, if patients require regular narcotic medications for pain relief, they are not included in this category.

- Clinicians should offer abiraterone + prednisone, enzalutamide, docetaxel, or sipuleucel-T to patients with asymptomatic or minimally symptomatic mCRPC with good performance status and no prior docetaxel chemotherapy.

- Clinicians may offer first- generation anti-androgen therapy, ketoconazole + steroid or observation to patients with asymptomatic or minimally symptomatic mCRPC with good performance status and no prior docetaxel chemotherapy who do not want or cannot have one of the standard therapies.
Index Patient 3
Symptomatic, mCRPC with good performance status and no prior chemotherapy

These patients have a rising PSA in the setting of castrate levels of testosterone, documented symptomatic metastatic disease on radiographic imaging, and no prior history of docetaxel chemotherapy for prostate cancer. The definition of symptomatic disease warrants additional explanation to contrast with Index Patient 2. First, the patient must have symptoms that are clearly attributable to the metastatic disease burden, not any other medical condition. Second, if having pain, the patient should require regular opiate pain medications for symptoms attributable to documented metastases in order to achieve an acceptable level of pain control. If patients require regular narcotic medications for pain relief, then they are symptomatic from their prostate cancer and should be included in this category.

- **Clinicians should offer abiraterone+prednisone, enzalutamide or docetaxel to patients with symptomatic, mCRPC with good performance status and no prior docetaxel chemotherapy.**

- **Clinicians may offer ketoconazole + steroid, mitoxantrone or radionuclide therapy to patients with symptomatic, mCRPC with good performance status and no prior docetaxel chemotherapy who do not want or cannot have one of the standard therapies.**

- **Clinicians should offer radium-223 to patients with symptoms from bony metastases from mCRPC with good performance status and no prior docetaxel chemotherapy and without known visceral disease.**
Clinicians should not offer treatment with either estramustine or sipuleucel-T to patients with symptomatic, mCRPC with good performance status and no prior docetaxel chemotherapy.

Index Patient 4
Symptomatic, mCRPC with poor performance status and no prior docetaxel chemotherapy

Clinical trials have generally excluded patients with a poor performance status (ECOG 3-4) from participation. Thus, most data regarding management of such patients is extrapolated from randomized trials of eligible patients who had a better performance status, as well as from some smaller trials and registries. Even a phase III clinical trial that was presumptively designed for a population considered “unfit” for docetaxel (ALSYMPCA to evaluate radium-223) still only allowed a performance status of ECOG 0-1. However, treatments with acceptable safety profiles do exist and should be considered, even in poor performance status patients. This is especially true in those patients in whom the poor performance status may be considered to be directly related to the cancer itself, and thus whose status might improve with effective treatment. Treatments must be individually tailored in these patients, after a careful discussion of risks and benefits with particular attention to patient quality of life.

Clinicians may offer treatment with abiraterone + prednisone or enzalutamide to patients with symptomatic, mCRPC with poor performance status and no prior docetaxel chemotherapy.

Clinicians may offer treatment with ketoconazole + steroid or radionuclide therapy to patients with symptomatic,
mCRPC with poor performance status and no prior docetaxel chemotherapy who are unable or unwilling to receive abiraterone + prednisone or enzalutamide.

- Clinicians may offer docetaxel or mitoxantrone chemotherapy to patients with symptomatic mCRPC with poor performance status and no prior docetaxel chemotherapy in select cases, specifically when the performance status is directly related to the cancer.
- Clinicians may offer radium-223 to patients with symptoms from bony metastases from mCRPC with poor performance status and no prior docetaxel chemotherapy and without known visceral disease in select cases, specifically when the performance status is directly related to symptoms related to bone metastases.
- Clinicians should not offer sipuleucel-T to patients with symptomatic, mCRPC with poor performance status and no prior docetaxel chemotherapy.

**Index Patient 5**

**Symptomatic, mCRPC with good performance status and prior docetaxel chemotherapy**

As patients with prostate cancer receive hormonal therapy earlier in the course of the disease (frequently for non-metastatic disease), they may actually develop castrate-resistant disease (based on serologic progression) with non-metastatic or asymptomatic metastatic disease. Thus, additional agents, including docetaxel chemotherapy may be administered earlier in the course of metastatic disease. These trends have resulted in a population of mCRPC patients who have completed docetaxel and may continue to be asymptomatic or minimally symptomatic with an excellent performance
status. While such patients may be healthy enough to receive a number of subsequent therapies, a focus of therapy should also be to maintain their excellent performance status without significant toxicity from additional therapy. It is in this context that providers should choose from a number of additional therapies to offer to this patient population.

- **Clinicians should offer treatment with abiraterone + prednisone, cabazitaxel or enzalutamide to patients with mCRPC with good performance status who have received prior docetaxel chemotherapy. If the patient received abiraterone + prednisone prior to docetaxel chemotherapy, they should be offered cabazitaxel or enzalutamide.**

- **Clinicians may offer ketoconazole + steroid to patients with mCRPC with good performance status who received prior docetaxel chemotherapy if abiraterone + prednisone, cabazitaxel or enzalutamide is unavailable.**

- **Clinicians may offer retreatment with docetaxel to patients with mCRPC with good performance status who were benefitting at the time of discontinuation (due to reversible side effects) of docetaxel chemotherapy.**

- **Clinicians should offer radium-223 to patients with symptoms from bony metastases from mCRPC with good performance status who received prior docetaxel chemotherapy and without known visceral disease.**

**Index Patient 6**

**Symptomatic, mCRPC with poor performance status and prior docetaxel chemotherapy**

The American Society of Clinical Oncology (ASCO) has posted recommendations regarding treatment for patients with advanced solid tumors; particularly in the last months of life.
ASCO advocates for an increasing emphasis on a patient’s quality of life and concentrates on symptom management. Treatment given in the last months of life may delay access to end of life care, increase costs and add unnecessary symptom management. Patients with poor performance status (ECOG 3 or 4) should not be offered further treatment.

- **Clinicians should offer palliative care to patients with mCRPC with poor performance status who received prior docetaxel chemotherapy. Alternatively, for selected patients, clinicians may offer treatment with abiraterone + prednisone, enzalutamide, ketoconazole + steroid or radionuclide therapy.**

- **Clinicians should not offer systemic chemotherapy or immunotherapy to patients with mCRPC with poor performance status who received prior docetaxel chemotherapy.**

**Guideline Statements on Bone Health (not specific to any one index patient)**

Several factors conspire to place the average patient with metastatic prostate cancer at a higher risk of bone complications. First, the median age of onset of the disease is in the late 60s, meaning that the average patient with metastatic disease may be in the 70s (or beyond), clearly a population at risk of physiologic, age-related decreases in bone mineral density. Secondly, a primary therapeutic intervention in patients with recurrent disease, androgen deprivation therapy, is associated with progressive loss of bone mineral density, not infrequently to the point of measurable osteopenia or frank osteoporosis, increasing the patient’s fracture risk, even in patients with non-metastatic disease. Finally, in
patients with advanced disease, bones are the most common site of metastatic disease, with as many as 70% of patients at some point in their course demonstrating evidence of disease in this site.

- **Clinicians should offer preventative treatment (e.g. supplemental calcium, Vitamin D) for fractures and skeletal related events to CRPC patients.**

- **Clinicians may choose either denosumab or zoledronic acid when selecting a preventative treatment for skeletal related events for CRPC patients with bony metastases.**

### APPENDIX A: ECOG PERFORMANCE STATUS

#### ECOG PERFORMANCE STATUS*

<table>
<thead>
<tr>
<th>Grade</th>
<th>ECOG</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all pre-disease performance without restriction</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair</td>
</tr>
<tr>
<td>5</td>
<td>Dead</td>
</tr>
</tbody>
</table>

Castration-Resistant Prostate Cancer: AUA Guideline 2018

**STAGING/H&P/IMAGING**

- **Non-metastatic CRPC**
  - **STANDARD**
    - Apalutamide or enzalutamide with continued androgen deprivation for patients at high risk for developing metastatic disease
  - **RECOMMENDATION**
    - Observation with continued androgen deprivation for patients at high risk for developing metastatic disease
  - **OPTION**
    - Second-generation androgen synthesis inhibitor (abiraterone + prednisone) to select patients at high risk for developing metastatic disease who do not want or cannot have one of the standard therapies and are unwilling to accept observation

- **Index Patient 1**

- **No prior docetaxel**
  - **Index Patient 2**
    - **STANDARD**
      - Abiraterone + prednisone, enzalutamide, docetaxel, or sipuleucel-T
    - **OPTION**
      - First- generation anti-androgen therapy, ketoconazole + steroid or observation to patients who do not want or cannot have one of the standard therapies

- **Index Patient 3**
  - **STANDARD**
    - Abiraterone + prednisone, enzalutamide, or docetaxel
  - **OPTION**
    - Radium-223 to patients with symptoms from bony metastases from mCRPC without known visceral disease

- **Bone Health**
  - **RECOMMENDATION**
    - Preventative treatment (e.g. supplemental calcium, vitamin D) for fractures and skeletal related events
  - **OPTION**
    - Choose either denosumab or zoledronic acid when selecting a preventative treatment for skeletal related events for mCRPC patients with bony metastases

- **RECOMMENDATION AGAINST**
  - Systemic chemotherapy or immunotherapy outside the context of a clinical trial

- **RECOMMENDATION AGAINST**
  - Estramustine or sipuleucel-T

**Good performance status**
**Prostate Cancer: Castration-Resistant**

**Index Patient 4**

**OPTION**
Abiraterone + prednisone or enzalutamide
Ketoconazole + steroid or radionuclide therapy to patients who are unable or unwilling to receive abiraterone + prednisone or enzalutamide

**EXPERT OPINION**
Docetaxel or mitoxantrone chemotherapy in select cases, specifically when the performance status is directly related to the cancer
Radium-223 to patients with symptoms from bony metastases from mCRPC without known visceral disease in select cases, specifically when the performance status is directly related to symptoms related to bone metastases

**RECOMMENDATION AGAINST**
Sipuleucel-T

**Index Patient 5**

**STANDARD**
Abiraterone + prednisone, cabazitaxel, or enzalutamide; if the patient received abiraterone + prednisone prior to docetaxel chemotherapy, they should be offered cabazitaxel or enzalutamide
Radium-223 to patients with symptoms from bony metastases from mCRPC and without known visceral disease

**OPTION**
Ketoconazole + steroid if abiraterone + prednisone, cabazitaxel or enzalutamide is unavailable
Retreatment with docetaxel to patients who were benefitting at the time of discontinuation (due to reversible side effects) of docetaxel chemotherapy

**Index Patient 6**

**EXPERT OPINION**
Palliative care; alternatively, for selected patients, clinicians may offer treatment with abiraterone + prednisone, enzalutamide, ketoconazole + steroid or radionuclide therapy

**EXPERT OPINION AGAINST**
Systemic chemotherapy or immunotherapy
CLINICALLY LOCALIZED PROSTATE CANCER

AUA/ASTRO/SUO GUIDELINE – 2017

Purpose

Risk stratification for prostate cancer should include all available pertinent data, which for most patients will include PSA, clinical stage, Grade Group on biopsy, number of cores involved, maximum involvement of any single core, PSA density, and imaging.

AUA Nomenclature

The AUA nomenclature system links statement types to a number of factors including strength of evidence, magnitude of benefit and risks/burdens, and panel judgment. There are three evidence-based statement types: Strong Recommendations and Moderate Recommendations are directive statements that indicate that there is a net benefit (or harm) associated with a clinical action, while a Conditional Recommendation is a non-directive Statement that is used when the clinical action does not have a clear net benefit (or harm).

In addition, there are two statement types that are used when pertinent evidence is not present in the systematic review of literature associated with the guideline: Expert Opinions are statements made by panel consensus based on members’ clinical training, experience, knowledge, and judgment, while a Clinical Principle is a statement about a component of clinical care that is very widely agreed upon by urologists or other clinicians.
TABLE 1.

Risk Stratification for Localized Prostate Cancer

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Low Risk</td>
<td>PSA &lt;10 ng/ml AND Grade Group 1 AND clinical stage T1-T2a AND &lt;34% of biopsy cores positive AND no core with &gt;50% involved, AND PSA density &lt;0.15 ng/ml/cc</td>
</tr>
<tr>
<td>Low Risk</td>
<td>PSA &lt;10 ng/ml AND Grade Group 1 AND clinical stage T1-T2a</td>
</tr>
<tr>
<td>Intermediate Risk</td>
<td>PSA 10-&lt;20 ng/ml OR Grade Group 2-3 OR clinical stage T2b-c&lt;br&gt;&lt;li&gt;Favorable: Grade Group 1 (with PSA 10-&lt;20) OR Grade Group 2 (with PSA&lt;10)&lt;br&gt;&lt;li&gt;Unfavorable: Grade Group 2 (with either PSA 10-&lt;20 or clinical stage T2b-c) OR Grade Group 3 (with PSA &lt; 20)</td>
</tr>
<tr>
<td>High Risk</td>
<td>PSA ≥20 ng/ml OR Grade Group 4-5 OR clinical stage ≥T3*</td>
</tr>
</tbody>
</table>

*Clinical stage T3 cancer is considered locally advanced and, therefore, outside the scope of this guideline.

Guideline Statements

Shared Decision Making (SDM)

- Counseling of patients to select a management strategy for localized prostate cancer should incorporate shared decision making and explicitly consider cancer severity (risk category), patient values and preferences, life expectancy, pre-treatment general functional and genitourinary symptoms, expected post-treatment functional status, and potential for salvage treatment. *(Strong Recommendation; Evidence Level: Grade A)*
• Prostate cancer patients should be counseled regarding the importance of modifiable health-related behaviors or risk factors, such as smoking and obesity. (Expert Opinion)

• Clinicians should encourage patients to meet with different prostate cancer care specialists (e.g., urology and either radiation oncology or medical oncology or both), when possible to promote informed decision making. (Moderate Recommendation; Evidence Level: Grade B)

• Effective shared decision making in prostate cancer care requires clinicians to inform patients about immediate and long-term morbidity or side effects of proposed treatment or care options. (Clinical Principle)

• Clinicians should inform patients about suitable clinical trials and encourage patients to consider participation in such trials based on eligibility and access. (Expert Opinion)

Care Options by Cancer Severity/Risk Group

Very Low-/Low-Risk Disease

• Clinicians should not perform abdomino-pelvic CT or routine bone scans in the staging of asymptomatic very low- or low-risk localized prostate cancer patients. (Strong Recommendation; Evidence Level: Grade C)

• Clinicians should recommend active surveillance as the best available care option for very low-risk localized prostate cancer patients. (Strong Recommendation; Evidence Level: Grade A)

• Clinicians should recommend active surveillance as the preferable care option for most low-risk localized prostate cancer patients. (Moderate Recommendation; Evidence Level: Grade B)
Clinicians may offer definitive treatment (i.e. radical prostatectomy or radiotherapy) to select low-risk localized prostate cancer patients who may have a high probability of progression on active surveillance. *(Conditional Recommendation; Evidence Level: Grade B)*

Clinicians should not add androgen deprivation therapy (ADT) along with radiotherapy for low-risk localized prostate cancer with the exception of reducing the size of the prostate for brachytherapy. *(Strong Recommendation; Evidence Level: Grade B)*

Clinicians should inform low-risk prostate cancer patients considering whole gland cryosurgery that consequent side effects are considerable and survival benefit has not been shown in comparison to active surveillance. *(Conditional Recommendation; Evidence Level: Grade C)*

Clinicians should inform low-risk prostate cancer patients who are considering focal therapy or high intensity focused ultrasound (HIFU) that these interventions are not standard care options because comparative outcome evidence is lacking. *(Expert Opinion)*

Clinicians should recommend observation or watchful waiting for men with a life expectancy ≤5 years with low-risk localized prostate cancer. *(Strong Recommendation; Evidence Level: Grade B)*

Among most low-risk localized prostate cancer patients, tissue based genomic biomarkers have not shown a clear role in the selection of candidates for active surveillance. *(Expert Opinion)*
Intermediate-Risk Disease

- Clinicians should consider staging unfavorable intermediate-risk localized prostate cancer patients with cross-sectional imaging (CT or MRI) and bone scan. *(Expert Opinion)*

- Clinicians should recommend radical prostatectomy or radiotherapy plus ADT as standard treatment options for patients with intermediate-risk localized prostate cancer. *(Strong Recommendation; Evidence Level: Grade A)*

- Clinicians should inform patients that favorable intermediate-risk prostate cancer can be treated with radiation alone, but that the evidence basis is less robust than for combining radiotherapy with ADT. *(Moderate Recommendation; Evidence Level: Grade B)*

- In select patients with intermediate-risk localized prostate cancer, clinicians may consider other treatment options such as cryosurgery. *(Conditional Recommendation; Evidence Level: Grade C)*

- Active surveillance may be offered to select patients with favorable intermediate-risk localized prostate cancer; however, patients should be informed that this comes with a higher risk of developing metastases compared to definitive treatment. *(Conditional Recommendation; Evidence Level: Grade C)*

- Clinicians should recommend observation or watchful waiting for men with a life expectancy ≤5 years with intermediate-risk localized prostate cancer. *(Strong Recommendation; Evidence Level: Grade A)*

- Clinicians should inform intermediate-risk prostate cancer patients who are considering focal therapy or HIFU
that these interventions are not standard care options because comparative outcome evidence is lacking. *(Expert Opinion)*

**High-Risk Disease**

- Clinicians should stage high-risk localized prostate cancer patients with cross sectional imaging (CT or MRI) and bone scan. *(Clinical Principle)*

- Clinicians should recommend radical prostatectomy or radiotherapy plus ADT as standard treatment options for patients with high-risk localized prostate cancer. *(Strong Recommendation; Evidence Level: Grade A)*

- Clinicians should not recommend active surveillance for patients with high-risk localized prostate cancer. Watchful waiting should only be considered in asymptomatic men with limited life expectancy $\leq 5$ years). *(Moderate Recommendation; Evidence Level: Grade C)*

- Cryosurgery, focal therapy and HIFU treatments are not recommended for men with high-risk localized prostate cancer outside of a clinical trial. *(Expert Opinion)*

- Clinicians should not recommend primary ADT for patients with high-risk localized prostate cancer unless the patient has both limited life expectancy and local symptoms. *(Strong Recommendation; Evidence Level: Grade A)*

- Clinicians may consider referral for genetic counseling for patients (and their families) with high-risk localized prostate cancer and a strong family history of specific cancers (e.g., breast, ovarian, pancreatic, other gastrointestinal tumors, lymphoma). *(Expert Opinion)*
Recommended Approaches and Details of Specific Care Options.

Active Surveillance

- Localized prostate cancer patients who elect active surveillance should have accurate disease staging including systematic biopsy with ultrasound or MRI-guided imaging. *(Clinical Principle)*

- Localized prostate cancer patients undergoing active surveillance should have routine surveillance PSA testing and digital rectal exams. *(Strong Recommendation; Evidence Level: Grade B)*

- Localized prostate cancer patients undergoing active surveillance should be encouraged to have a confirmatory biopsy within the initial two years and surveillance biopsies thereafter. *(Clinical Principle)*

- Clinicians may consider multiparametric prostate MRI as a component of active surveillance for localized prostate cancer patients. *(Expert Opinion)*

- Tissue based genomic biomarkers have not shown a clear role in active surveillance for localized prostate cancer and are not necessary for follow up. *(Expert Opinion)*

- Clinicians should offer definitive treatment to localized prostate cancer patients undergoing active surveillance who develop adverse reclassification. *(Moderate Recommendation; Evidence Level: Grade B)*

Prostatectomy

- Clinicians should inform localized prostate cancer patients that younger or healthier men (e.g., <65 years of age or >10 year life expectancy) are more likely to
experience cancer control benefits from prostatectomy than older men. *(Strong Recommendation; Evidence Level: Grade B)*

- Clinicians should inform localized prostate cancer patients that open and robot-assisted radical prostatectomy offer similar cancer control, continence recovery, and sexual recovery outcomes. *(Moderate Recommendation; Evidence Level: Grade C)*

- Clinicians should inform localized prostate cancer patients that robotic/laparoscopic or perineal techniques are associated with less blood loss than retropubic prostatectomy. *(Strong Recommendation; Evidence Level: Grade B)*

- Clinicians should counsel localized prostate cancer patients that nerve-sparing is associated with better erectile function recovery than non-nerve sparing. *(Strong Recommendation; Evidence Level: Grade A)*

- Clinicians should not treat localized prostate cancer patients who have elected to undergo radical prostatectomy with neoadjuvant ADT or other systemic therapy outside of clinical trials. *(Strong Recommendation; Evidence Level: Grade A)*

- Clinicians should inform localized prostate cancer patients considering prostatectomy that older men experience higher rates of permanent erectile dysfunction and urinary incontinence after prostatectomy compared to younger men. *(Strong Recommendation; Evidence Level: Grade B)*

- Pelvic lymphadenectomy can be considered for any localized prostate cancer patients undergoing radical
prostatectomy and is recommended for those with unfavorable intermediate-risk or high-risk disease. Patients should be counseled regarding the common complications of lymphadenectomy, including lymphocele development and its treatment. (Expert Opinion)

- Clinicians should inform localized prostate cancer patients with unfavorable intermediate-risk or high-risk prostate cancer about benefits and risks related to the potential option of adjuvant radiotherapy when locally extensive prostate cancer is found at prostatectomy. (Moderate Recommendation; Evidence Level: Grade B)

**Radiotherapy**

- Clinicians may offer single modality external beam radiotherapy or brachytherapy for patients who elect radiotherapy for low-risk localized prostate cancer. (Clinical Principle)

- Clinicians may offer external beam radiotherapy or brachytherapy alone or in combination for favorable intermediate-risk localized prostate cancer. (Clinical Principle)

- Clinicians should offer 24-36 months of ADT as an adjunct to either external beam radiotherapy alone or external beam radiotherapy combined with brachytherapy to patients electing radiotherapy for high-risk localized prostate cancer. (Strong Recommendation; Evidence Level: Grade A)

- Clinicians should inform localized prostate cancer patients that use of ADT with radiation increases the likelihood and severity of adverse treatment-related
events on sexual function in most men and can cause other systemic side effects. *(Strong Recommendation; Evidence Level: Grade B)*

- Clinicians should consider moderate hypofractionation when the localized prostate cancer patient (of any risk category) and clinician decide on external beam radiotherapy to the prostate (without nodal radiotherapy). *(Moderate Recommendation; Evidence Level: Grade B)*

- For localized prostate cancer patients with obstructive, non-cancer-related lower urinary function, surgical approaches may be preferred. If radiotherapy is used for these patients or those with previous significant transurethral resection of the prostate, low-dose rate brachytherapy should be discouraged. *(Moderate Recommendation; Evidence Level: Grade C)*

- Clinicians should inform localized prostate cancer patients who are considering proton beam therapy that it offers no clinical advantage over other forms of definitive treatment. *(Moderate Recommendation; Evidence Level: Grade C)*

- Clinicians should inform localized prostate cancer patients considering brachytherapy that it has similar effects as external beam radiotherapy with regard to erectile dysfunction and proctitis but can also exacerbate urinary obstructive symptoms. *(Expert Opinion)*

**Whole Gland Cryosurgery**

- Clinicians may consider whole gland cryosurgery in low- and intermediate-risk localized prostate cancer patients who are not suitable for either radical prostatectomy or radiotherapy due to comorbidities yet have >10 year life expectancy. *(Expert Opinion)*
• Clinicians should inform localized prostate cancer patients considering whole gland cryosurgery that cryosurgery has similar progression-free survival as did non-dose escalated external beam radiation (also given with neoadjuvant hormonal therapy) in low- and intermediate-risk disease, but conclusive comparison of cancer mortality is lacking. (*Conditional Recommendation; Evidence Level: Grade C*)

• Defects from prior transurethral resection of the prostate are a relative contraindication for whole gland cryosurgery due to the increased risk of urethral sloughing. (*Clinical Principle*)

• For whole gland cryosurgery treatment, clinicians should utilize a third or higher generation, argon-based cryosurgical system. (*Clinical Principle*)

• Clinicians should inform localized prostate cancer patients considering cryosurgery that it is unclear whether or not concurrent ADT improves cancer control, though it can reduce prostate size to facilitate treatment. (*Clinical Principle*)

• Clinicians should inform localized prostate cancer patients considering whole gland cryosurgery that erectile dysfunction is an expected outcome. (*Clinical Principle*)

• Clinicians should inform localized prostate cancer patients considering whole gland cryosurgery about the adverse events of urinary incontinence, irritative and obstructive urinary problems. (*Strong Recommendation; Evidence Level: Grade B*)
Prostate Cancer: Clinically Localized

HIFU and Focal Therapy

- Clinicians should inform those localized prostate cancer patients considering focal therapy or HIFU that these treatment options lack robust evidence of efficacy. *(Expert Opinion)*

- Clinicians should inform localized prostate cancer patients who are considering HIFU that even though HIFU is approved by the FDA for the destruction of prostate tissue, it is not approved explicitly for the treatment of prostate cancer. *(Expert Opinion)*

- Clinicians should advise localized prostate cancer patients considering HIFU that tumor location may influence oncologic outcome. Limiting apical treatment to minimize morbidity increases the risk of cancer persistence. *(Moderate Recommendation; Evidence Level: Grade C)*

- As prostate cancer is often multifocal, clinicians should inform localized prostate cancer patients considering focal therapy that focal therapy may not be curative and that further treatment for prostate cancer may be necessary. *(Expert Opinion)*

Outcome Expectations and Management

Treatment Side Effects and Health Related Quality of Life

- Clinicians should inform localized prostate cancer patients that erectile dysfunction occurs in many patients following prostatectomy or radiation, and that ejaculate will be lacking despite preserved ability to attain orgasm, whereas observation does not cause such sexual dysfunction. *(Strong Recommendation; Evidence Level: Grade B)*
Clinicians should inform localized prostate cancer patients that long-term obstructive or irritative urinary problems occur in a subset of patients following observation or active surveillance or following radiation, whereas prostatectomy can relieve pre-existing urinary obstruction. *(Strong Recommendation; Evidence Level: Grade B)*

Clinicians should inform localized prostate cancer patients that whole-gland cryosurgery is associated with worse sexual side effects and similar urinary and bowel/rectal side effects as those after radiotherapy. *(Strong Recommendation; Evidence Level: Grade B)*

Clinicians should inform localized prostate cancer patients that temporary urinary incontinence occurs in most patients after prostatectomy and persists long-term in a small but significant subset, more than during observation or active surveillance or after radiation. *(Strong Recommendation; Evidence Level: Grade A)*

Clinicians should inform localized prostate cancer patients that temporary proctitis following radiation persists in some patients long-term in a small but significant subset and is rare during observation or active surveillance or after prostatectomy. *(Strong Recommendation; Evidence Level: Grade A)*

**Post-Treatment Follow Up**

Clinicians should monitor localized prostate cancer patients post therapy with PSA, even though not all PSA recurrences are associated with metastatic disease and prostate cancer specific death. *(Clinical Principle)*
• Clinicians should inform localized prostate cancer patients of their individualized risk-based estimates of post-treatment prostate cancer recurrence. *(Clinical Principle)*

• Clinicians should support localized prostate cancer patients who have survivorship or outcomes concerns by facilitating symptom management and encouraging engagement with professional or community-based resources. *(Clinical Principle)*
### TABLE 2.

**Care Options for Localized Prostate Cancer by Level of Evidence and Strength of Recommendation**

<table>
<thead>
<tr>
<th>Evidence Level/Recommendation Strength</th>
<th>Prostate Cancer Severity/Aggressiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Risk</td>
</tr>
<tr>
<td></td>
<td>Very Low Risk</td>
</tr>
</tbody>
</table>

A / Strong
- Active Surveillance
- Radical Prostatectomy OR Radiotherapy with Androgen Deprivation Therapy
- Radical Prostatectomy OR Radiotherapy with Androgen Deprivation Therapy
- Radical Prostatectomy OR Radiotherapy with Androgen Deprivation Therapy

B / Moderate
- NA
- Active Surveillance
- Radiotherapy without Androgen Deprivation Therapy
- NA

B / Conditional
- NA
- Radical Prostatectomy OR Radiotherapy
- NA

C / Conditional
- NA
- Cryosurgery (whole gland)
- Active Surveillance OR Cryosurgery (whole gland)
- Cryosurgery (whole gland)

No evidence/ Clinical principle or expert opinion
- NA
- Focal Ablative Therapy OR High Intensity Focused Ultrasound
- Focal Ablative Therapy OR High Intensity Focused Ultrasound
- Focal Ablative Therapy OR High Intensity Focused Ultrasound

1**Multicenter randomized clinical trials that constitute the basis for evidence:**
- EORTC-Bolla (XRT+ADT vs XRT): Evidence supporting XRT+ADT (intermediate-risk, high-risk)
- SPCG4 (RP vs WW): Evidence supporting RP (intermediate-risk, high-risk)
- RTOG 9408 (XRT+ADT vs XRT): Evidence supporting XRT+ADT (intermediate risk)
- PIVOT (RP vs WW): Evidence supporting AS (very low-risk, low-risk); RP (intermediate-risk, high-risk)
- EORTC (Widmark XRT+ADT vs ADT alone): Evidence supporting XRT+ADT (intermediate-risk, high-risk)
- PROTECT (AS vs RP vs XRT+ADT): Evidence supporting AS (very low-risk, low-risk, favorable intermediate-risk); RP or XRT+ADT (low-risk, favorable intermediate-risk)
- Single-center RCT: Donnelly et al. (Cryo+ADT vs XRT+ADT): Evidence supporting whole gland cryotherapy (low-risk, intermediate-risk)

2**Radiotherapy** includes a range of various forms of radiotherapy delivery (e.g. IMRT, brachytherapy, other) for which details of evidence and recommendation strength are presented in the Radiotherapy section of this guideline.
Purpose

This guideline addresses prostate cancer early detection for the purpose of reducing prostate cancer mortality with the intended user as the urologist. This document does not make a distinction between early detection and screening for prostate cancer. Early detection and screening both imply detection of disease at an early, pre-symptomatic stage when a patient would have no reason to seek medical care—an intervention referred to as secondary prevention. It is important to note that the guideline statements listed in this document target patients at average risk, defined as a man without risk factors, such as a family history of prostate cancer in multiple generations and/or family history of early onset below age 55 years, or African American race. This document does not address detection of prostate cancer in symptomatic men, where symptoms imply those that could be related to locally advanced or metastatic prostate cancer (e.g., new onset bone pain and/or neurological symptoms involving the lower extremities, etc.).

Guideline Statements

- The panel recommends against PSA screening in men under age 40 years.

None of the prospective randomized studies evaluating the benefits of PSA based screening for prostate cancer included
men under age 40 years. Hence there are no data available to estimate the benefit of prostate cancer screening in this population. However, the harms that can accrue from screening, which include the side effects of diagnostic biopsies, and perhaps subsequent treatment will certainly apply to men in this age group who would be subject to screening. Therefore, due to the relatively low prevalence of clinically detectable prostate cancer in men below age 40 years, the absence of any evidence demonstrating benefits of screening and the known harms, screening is discouraged for men under age 40 years of age.

- **The panel does not recommend routine screening in men between ages 40 to 54 years at average risk.**

Given the panel’s interpretation of the evidence concerning the benefits and harms of annual screening in men age 40 to 54 years who are not at an increased risk for prostate cancer and the rarity of fatal prostate cancers arising in this age group, we do not recommend this practice as a routine. The panel recognizes that certain subgroups of men age 40 to 54 years may realize added benefit from earlier screening. For example, men at increased risk for prostate cancer, such as those with a strong family history or those of African-American race, may benefit from earlier detection, given their higher incidence of disease.

The panel recognizes that there may be other benefits associated with screening that we either did not consider or have not been demonstrated by the current literature. The “absence of evidence does not constitute evidence of absence” and, as such, we are not explicitly stating that
screening should be actively discouraged in this group of patients. The literature in this area is quite dynamic and future studies may document additional benefits in this younger population.

- For men ages 55 to 69 years the panel recognizes that the decision to undergo PSA screening involves weighing the benefits of preventing prostate cancer mortality in 1 man for every 1,000 men screened over a decade against the known potential harms associated with screening and treatment. For this reason, the panel strongly recommends shared decision-making for men age 55 to 69 years that are considering PSA screening, and proceeding based on men’s values and preferences.

Although there are considerable harms associated with screening, the panel feels that in men age 55 to 69 years, there was sufficient certainty that the benefits of screening could outweigh the harms that a recommendation of shared decision-making in this age group was justified. The panel believes that the test should not be offered in a setting where this is not practical, for example community-based screening by health systems or other organizations.

Shared decision making should include a discussion of the man's baseline mortality risk from other co-morbid conditions, his individual risk for prostate cancer given his race/ethnicity and family history, and the degree to which screening might influence his overall life expectancy and chance of experiencing morbidity from prostate cancer or its treatment.
• To reduce the harms of screening, a routine screening interval of two years or more may be preferred over annual screening in those men who have participated in shared decision-making and decided on screening. As compared to annual screening, it is expected that screening intervals of two years preserve the majority of the benefits and reduce overdiagnosis and false positives.

Modeling studies have projected that screening men every two years preserves the majority (at least 80%) of lives saved compared with annual screening while materially reducing the number of tests, the chance of a false positive test and overdiagnosis. This is supported by indirect evidence from the two largest screening trials, although there is no direct evidence from these trials supporting a specific screening interval.

• The panel does not recommend routine PSA screening in men age 70+ years or any man with less than a 10 to 15 year life expectancy.

The panel recognizes that men age 70+ years can have a life-expectancy over 10 to 15 years and that a small sub-group of men age 70+ years who are in excellent health may benefit from PSA screening, but evidence to support the magnitude of benefit in this age group is extremely limited. The rationale for this recommendation is based on the absence of evidence of a screening benefit in this population with clear evidence of harms. Men in this age group who choose to be screened should recognize that there is strong evidence that the ratio of harm to benefit increases with
age and that the likelihood of overdiagnosis is extremely high, particularly among men with low-risk disease. In order to identify the older man more likely to benefit from treatment if screening takes place, the panel recommends two approaches: 1) increasing the prostate biopsy threshold (e.g., 10ng/ml); and 2) discontinuation of PSA screening among men with a PSA below 3ng/ml.

**FIGURE 1.**

Influence of evidence and interpretation on policy creation

- Randomized trials
- Population data
- Modeled data
- Public health perspective
- Individual perspective

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TABLE 2.

Evidence profile for mortality outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Source &amp; setting*</th>
<th>Relative risk</th>
<th>Absolute effect</th>
<th>Quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate cancer-specific mortality</td>
<td>1 RCT (ERSPC)(^\text{17}) 162,243 men Age 55-69, PSA every four years</td>
<td>0.80 (0.65–0.98)(^\text{±})</td>
<td>1 death fewer per 1000 men screened</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>1 RCT (PLCO)(^\text{18}) 76,693 men Age 55-74, annual PSA screening for six years and digital rectal examination annually for four years</td>
<td>1.14 (0.76, 1.70)</td>
<td>From 1 death fewer to 1 death more per 1000 men screened</td>
<td>Low*</td>
</tr>
</tbody>
</table>

*The quality of evidence regarding prostate cancer-specific mortality derived from PLCO is low due to methodological limitations relating to the degree of contamination in the control arm. Therefore, PLCO does not provide a direct comparison of screening v. not screening. Rates of screening in the control group increased from 40% in the first year to 52% in the sixth year for PSA testing and ranged from 41 to 46% for digital rectal examination.

\(^\text{±}\) After a median follow-up of 11 years in the core age group, relative risk reduction 21% (RR, 0.79; 0.68 to 0.91), and 29% after adjustment for contamination and noncompliance. Absolute risk reduction 1.07/1000 screened.
## TABLE 3.

### Harm Outcomes

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Estimate</th>
<th>Definition (data source)</th>
<th>Quality of evidence supporting association*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>False positive tests</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>False positive tests</td>
<td>75.9%</td>
<td>Proportion of men with PSA &gt;3.0 ng/mL and no cancer on subsequent biopsy (ERSPC)(^\text{17})</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12%</td>
<td>Cumulative risk of at least 1 false-positive test (PSA&gt; 4.0 µg/L) after 3 rounds of testing every four years (Finnish center, ERSPC)(^\text{17})</td>
<td>Moderate to High</td>
</tr>
<tr>
<td></td>
<td>13%</td>
<td>Cumulative risk of at least 1 false-positive test (PSA&gt; 4.0 µg/L) after 4 rounds of annual testing (PLCO)(^\text{18})</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.5%</td>
<td>Risk for undergoing at least 1 biopsy due to a false-positive test (PLCO)(^\text{18})</td>
<td></td>
</tr>
<tr>
<td><strong>Overdiagnosis</strong></td>
<td>66%</td>
<td>Cases overdiagnosed as a fraction of screen-detected cases (ERSPC (Rotterdam) age 55-67 years, four year screening interval)(^\text{22})</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>23-42%</td>
<td>Cases overdiagnosed as a fraction of screen-detected cases (SEER-9, 1987-2000)(^\text{25})</td>
<td></td>
</tr>
<tr>
<td><strong>Lead time</strong></td>
<td>5.4-6.9</td>
<td>Average time by which screening advances diagnosis among cases who would have been diagnosed during their lifetimes in the absence of screening (SEER-9, 1987-2000)(^\text{25})</td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>Minor (hematuria/hematosper-mia)</strong></td>
<td>20-50%</td>
<td>20-50% (first time sextant biopsy, Netherland site, ERSPC)(^\text{17}) 24-45% (ERSPC, Rotterdam)(^\text{27})</td>
<td>High</td>
</tr>
<tr>
<td><strong>Composite medical complications (infection, bleeding, urinary difficulties)</strong></td>
<td>68/10,000</td>
<td>PLCO(^\text{33})</td>
<td>High</td>
</tr>
<tr>
<td><strong>Fever post biopsy</strong></td>
<td>3.5-4.2%</td>
<td>3.5% (ERSPC)(^\text{17}) 4.2%(^\text{27}) (ERSPC, Rotterdam)</td>
<td>High</td>
</tr>
<tr>
<td><strong>Hospitalization post biopsy</strong></td>
<td>4%</td>
<td>Loeb et al. and Nam et al.(^\text{27,28})</td>
<td>High</td>
</tr>
</tbody>
</table>

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The core age group, 136,689 screening tests were performed (average, 2.27 per subject). Of these tests, 16.6% were positive, and 85.9% of the men with positive tests underwent prostate biopsy.

*The quality of evidence means how much confidence we have in the reported quantitative estimate. It does not mean the methodological quality of the study(s) although the latter is one factor that affects confidence in the estimate.
PSA TESTING FOR THE PRETREATMENT STAGING AND POSTTREATMENT MANAGEMENT OF PROSTATE CANCER

AUA BEST PRACTICE STATEMENT – 2009; AMENDED – 2013

This revised document contains the content of the "Prostate-Specific Antigen Best Practice Statement: 2009 Update" deleting that which pertains to the detection of prostate cancer. An updated guideline, available on the auanet.org website, is the 2013 AUA document "Early Detection of Prostate Cancer: AUA Guideline." Statements related to the detection of prostate cancer have been deleted, such that this revised document addresses only the use of PSA testing for the pretreatment staging and posttreatment management of prostate cancer. No other major changes have been made.

Use of PSA for Pre-treatment Staging Risk Stratification and Prognosis

PSA level and rate of rising are linked to the extent and biological potential of prostate cancer. The proportion of men with higher volume cancers, extraprostatic disease, higher-grade disease, and biochemical failure after treatment all increase as the PSA level increases. **Routine radiographic staging, such as with bone scan, computed tomography (CT), or magnetic resonance imaging (MRI), or surgical staging with pelvic lymph node dissection are**
Prostate Cancer: Prostate-Specific Antigen

not necessary in all cases of newly diagnosed prostate cancer. Clinical examination can determine appropriate patients for such staging.

- Proportion of men with pathologically organ-confined disease is about 80% when the PSA level at diagnosis is <4.0 ng/ml; about 70% when the PSA level is between 4.0 and 10.0 ng/ml; and about 50% when the PSA level is >10.0 ng/ml. The proportion of men with metastases to the pelvic lymph nodes is around 5% when the PSA level at diagnosis is 10.0 ng/ml or less, 18% when the PSA level is between 10.0 and 20.0 ng/ml, and 36% when the PSA level is above 20.0 ng/ml.

- The integration of clinical stage, histologic tumor grade, and PSA level may further refine the ability to predict outcomes after treatment for prostate cancer.

- Nomograms incorporating pretreatment PSA may help to calculate the probability of clinical endpoints and outcomes of treatment.

- Men with a PSAV above 2.0 ng/ml/year may have an approximate 10-fold greater risk of death from prostate cancer in the decade after radical prostatectomy than men with a PSAV of 2.0 ng/ml/year or less in the year before diagnosis.

Radiographic Considerations

- Bone scan:

- not required for staging asymptomatic men with clinically localized prostate cancer when their PSA is <20.0 ng/ml unless history or clinical examination suggests bony involvement.
• consider with Gleason 8 or greater disease, or stage ≥T3 prostate cancer, even if the PSA is <10.0 ng/ml.
  ❖ CT or MRI scans:

• for staging high-risk clinically localized prostate cancer when PSA is greater than 20.0 ng/ml, with locally advanced cancer or with a Gleason score greater than or equal to 8

• CT scan identification of pelvic adenopathy depends upon lymph node enlargement, and the correlation between nodal size and metastatic involvement is poor.
  ❖ Pelvic lymph node dissection:

• may not be necessary for clinically localized prostate cancer if PSA is less than 10.0 ng/ml and the Gleason score is less than or equal to 6.

• lymphadenectomy is not needed in low-risk patients. Patients with higher risk disease may benefit from lymphadenectomy. However, careful patient selection and risk/benefit analysis are crucial due to the potential for morbidity.

The Use of PSA in the Post-treatment Management of Prostate Cancer

• Offer periodic PSA determinations to detect disease recurrence

**Post-Prostatectomy:**

PSA levels post-radical prostatectomy should decrease and remain undetectable. Detectable levels indicate disease recurrence in some patients but also may be due to presence of benign glands. Biochemical recurrence (according to AUA)
is an initial PSA value $\geq 0.2$ ng/ml followed by a subsequent confirmatory PSA value $\geq 0.2$ ng/ml.

- PSA level is significantly associated with the risk of biochemical failure after surgical treatment of prostate cancer; for each 2-point increase in PSA level, the risk of biochemical progression increases by approximately 2-fold.

- Biochemical recurrence of cancer is evident within 10 years of surgery in approximately 10% of men with a preoperative PSA level below 2.6 ng/ml, 20% when the PSA level is between 2.6 and 10.0 ng/ml, and 50% when the PSA level is above 10.0 ng/ml.

- A cut-point of 0.4 ng/ml followed by another increase may better predict risk of metastatic relapse. (This cut-point was selected as a means of reporting outcomes, rather than a threshold for initiation of treatment.)

**Post-Radiation:**

PSA levels should fall to a low level and remain stable. PSA values <0.2 are uncommon after external beam radiotherapy, which does not ablate all prostate tissue. Consistently rising PSA levels often indicate cancer recurrence.

- The change in PSA following interstitial prostate brachytherapy is complex and characterized by intermittent rises called "benign bounces." The median PSA level of these patients is <0.1 ng/ml.

- The number of rises needed to define a failure is under debate: any rise in PSA level of 2.0 ng/ml or more, over and above the nadir, predicts failure after both external beam radiotherapy and interstitial prostate brachytherapy, irrespective of androgen deprivation.
The time of failure should not be backdated to the first rise in PSA. Although a “target PSA” was not possible after external beam radiotherapy, a PSA level of <0.7 ng/ml at five years is reasonable for brachytherapy. PSA levels continue to decline more than five years after interstitial prostate brachytherapy.

**PSA nadir after androgen suppression:**
- PSA kinetics correlated with outcomes. In patients with metastatic disease receiving androgen suppression therapy, failure to achieve a PSA nadir of <4.0 ng/ml seven months after initiation of therapy is associated with median survival of one year.
- Patients with a PSA nadir of <0.2 ng/ml have a median survival of six+ years.
- For patients with a PSA rise following radical prostatectomy or radiation and no radiologic evidence of metastases, a PSA nadir of >0.2 ng/ml within eight months of androgen suppression is associated with a 20-fold greater risk of prostate cancer-specific mortality as compared to patients with a PSA nadir of <0.2 ng/ml.
- PSA nadir of >0.2 ng/ml in the setting of a PSADT of <3 months is ominous.
- The prognostic importance of the value of the PSA nadir after androgen deprivation therapy is clear. Careful PSA monitoring after the initiation of such therapy can effectively identify those patients with a poor prognosis.

**PSA kinetics and salvage therapy**
- Problematic to distinguish local from distant recurrence after local treatments:
  - Most patients with a PSA rise have a negative physical exam and non-informative imaging tests.
- When PSA is low (i.e., 0.5 to 1.5 ng/ml) even patients with multiple adverse risk factors may respond to salvage radiation after prostatectomy, especially those with positive surgical margins.
- Strongly consider salvage radiation given that it is the only potentially curative treatment in this setting.

- Predictors of favorable response to post-radiation salvage prostatectomy are less well defined compared with those for salvage radiation following radical prostatectomy.
  - Recurrent disease noted on prostate biopsy, PSA less than 10.0 ng/ml (preferably PSA less than 5.0 ng/ml), a clinically localized cancer (i.e. T1C or T2), and no evidence of metastases on prior evaluation or pre-operative imaging are reasonable criteria.
  - Patients with a long PSADT (>15 months) have a low likelihood of prostate cancer-specific mortality over a 10 year period
  - Active surveillance may be considered for those with a life expectancy of <10 years. In contrast, patients with a PSADT <3 months have a median overall survival of 6 years following PSA failure, and are likely have distant disease.
  - Patients experiencing a relapse after local therapy may be candidates for clinical trials.
Prostate Cancer: Prostate-Specific Antigen

Staging—Once Prostate Cancer is Diagnosed

**Determine tumor grade** –
(based on the Gleason grading system)

- Gleason score 6: low potential for progression
- Gleason score 7: intermediate potential for progression
- Gleason score 8 - 10: high potential for progression

**Additional tests, based on preliminary staging, include:**

**Radiologic Staging:**
CT or MRI, Generally unnecessary if the PSA is < 20.0 ng/mL.

**Surgical Staging:**
Generally unnecessary in low risk patients as defined by PSA < 10 ng/mL and cT1/T2a disease and no pattern 4 or 5 disease.

**Bone Scan:**
Generally unnecessary with clinically localized prostate cancer when the PSA is < 20.0 ng/mL.

**Management Discussion**

**Treatment or Surveillance**

See Post-treatment Management, Figure 3

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FIGURE 3.

Posttreatment Assessment and Management

Goal: Monitor recurrence and treat as necessary

Post-Surgery
Serum PSA and selective use of imaging
Risk assessment and counseling
Options: salvage radiation therapy, androgen deprivation, clinical trials, surveillance

Post-radiotherapy
Recurrence if serum PSA \( \geq 2.0 \text{ ng/mL} \) above nadir or 3 consecutive rises in serum PSA. Serum PSA and selective use of imaging and prostate biopsy.
Risk assessment and counseling
Salvage radical prostatectomy, androgen deprivation, cryotherapy, radiation, clinical trials, surveillance

Surveillance
Serum PSA, DRE, prostate biopsy and selective use of imaging
Risk assessment and counseling
Radical prostatectomy, radiation therapy, androgen deprivation, cryotherapy, clinical trials, surveillance

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Purpose
This AUA Guidelines focuses primarily on the evaluation and management of clinically localized sporadic renal masses suspicious for renal cell carcinoma (RCC) in adults, including solid enhancing renal tumors and Bosniak 3 and 4 complex cystic renal masses. Some patients with clinically localized renal masses may present with findings suggesting aggressive tumor biology or may be upstaged on exploration or final pathology. Management considerations pertinent to the urologist in such patients will also be addressed. Practice patterns regarding such tumors vary considerably. The literature regarding evaluation and management has been rapidly evolving. Notable examples include controversies about the role of renal mass biopsy and concerns about overutilization of radical nephrectomy. Please also refer to the associated Renal Mass and Localized Renal Cancer treatment algorithm.

AUA Nomenclature
The AUA nomenclature system links statement types to a number of factors including strength of evidence, magnitude of benefit and risks/burdens, and panel judgment. There are three evidence-based statement types: Strong Recommendations and Moderate Recommendations are directive statements that indicate that there is a net benefit (or harm) associated with a clinical action, while a Conditional Recommendation is a non-directive Statement that is used when the clinical action does not have a clear net benefit (or harm).
In addition, there are two statement types that are used when pertinent evidence is not present in the systematic review of literature associated with the guideline: Expert Opinions are statements made by panel consensus based on members’ clinical training, experience, knowledge, and judgment, while a Clinical Principle is a statement about a component of clinical care that is very widely agreed upon by urologists or other clinicians.

**Guideline Statements**

**Evaluation and Diagnosis**
- In patients with a solid or complex cystic renal mass, physicians should obtain high quality, multiphase, cross-sectional abdominal imaging to optimally characterize and clinically stage the renal mass. Characterization of the renal mass should include assessment of tumor complexity, degree of contrast enhancement (where applicable), and presence or absence of fat. *(Clinical Principle)*
- In patients with suspected renal malignancy, physicians should obtain comprehensive metabolic panel, complete blood count, and urinalysis. Metastatic evaluation should include chest imaging to evaluate for possible thoracic metastases. *(Clinical Principle)*
- For patients with a solid or complex cystic renal mass, physicians should assign CKD stage based on GFR and degree of proteinuria. *(Expert Opinion)*

**Counseling**
- In patients with a solid or Bosniak 3/4 complex cystic renal mass, a urologist should lead the counseling process and should consider all management strategies. A multidisciplinary team should be included when necessary. *(Expert Opinion)*
• Physicians should provide counseling that includes current perspectives about tumor biology and a patient-specific risk assessment inclusive of sex, tumor size/complexity, histology (when obtained), and imaging characteristics. For cT1a tumors, the low oncologic risk of many small renal masses should be reviewed. *(Clinical Principle)*

• During counseling of patients with a solid or Bosniak 3/4 complex cystic renal mass, physicians must review the most common and serious urologic and non-urologic morbidities of each treatment pathway and the importance of patient age, comorbidities/frailty, and life expectancy. *(Clinical Principle)*

• Physicians should review the importance of renal functional recovery related to renal mass management, including the risk of progressive CKD, potential short- or long-term need for renal replacement therapy, and long-term overall survival considerations. *(Clinical Principle)*

• Physicians should consider referral to nephrology in patients with a high risk of CKD progression. Such patients may include those with eGFR less than 45 ml/min/1.73m², confirmed proteinuria, diabetics with preexisting CKD, or whenever eGFR is expected to be less than 30 ml/min/1.73m² after intervention. *(Expert Opinion)*

• Physicians should recommend genetic counseling for all patients ≤ 46 years of age with renal malignancy and consider genetic counseling for patients with multifocal or bilateral renal masses, or if personal or family history suggests a familial renal neoplastic syndrome. *(Expert Opinion)*
Renal Mass Biopsy (RMB)

- Renal mass biopsy should be considered when a mass is suspected to be hematologic, metastatic, inflammatory, or infectious. (*Clinical Principle*)

- In the setting of a solid renal mass, RMB is not required for young or healthy patients who are not willing to accept the uncertainties associated with RMB or for older or frail patients who will be managed conservatively independent of RMB findings. (*Expert Opinion*)

- When considering the utility of RMB, patients should be counseled regarding rationale, positive and negative predictive values, potential risks and non-diagnostic rates of RMB. (*Clinical Principle*)

- For patients with a solid renal mass who elect RMB, multiple core biopsies are preferred over fine needle aspiration. (*Moderate Recommendation; Evidence Level: Grade C*)

Management

Partial Nephrectomy (PN) and Nephron-Sparing Approaches

- Physicians should prioritize PN for the management of the cT1a renal mass when intervention is indicated. In this setting, PN minimizes risk of CKD or CKD progression and is associated with favorable oncologic outcomes, including excellent local control. (*Moderate Recommendation; Evidence Level: Grade B*)

- Physicians should prioritize nephron-sparing approaches for patients with solid or Bosniak 3/4 complex cystic renal masses and an anatomic or functionally solitary kidney, bilateral tumors, known familial RCC, preexisting CKD, or proteinuria. (*Moderate Recommendation; Evidence Level: Grade C*)
Physicians should consider nephron-sparing approaches for patients with solid or Bosniak 3/4 complex cystic renal masses who are young, have multifocal masses, or comorbidities that are likely to impact renal function in the future, such as moderate to severe hypertension, diabetes mellitus, recurrent urolithiasis, or morbid obesity. *(Conditional Recommendation; Evidence Level: Grade C)*

In patients who elect PN, physicians should prioritize preservation of renal function through efforts to optimize nephron mass preservation and avoidance of prolonged warm ischemia. *(Expert Opinion)*

For patients undergoing PN, negative surgical margins should be a priority. The extent of normal parenchyma removed should be determined by surgeon discretion taking into account the clinical situation, tumor characteristics including growth pattern, and interface with normal tissue. Tumor enucleation should be considered in patients with familial RCC, multifocal disease, or severe CKD to optimize parenchymal mass preservation. *(Expert Opinion)*

**Radical Nephrectomy (RN)**

Physicians should consider RN for patients with a solid or Bosniak 3/4 complex cystic renal mass where increased oncologic potential is suggested by tumor size, RMB, and/or imaging characteristics and in whom active treatment is planned. *(Conditional Recommendation; Evidence Level: Grade B)*. In this setting, RN is preferred if all of the following criteria are met: 1) high tumor complexity and PN would be challenging even in experienced hands; 2) no preexisting CKD or proteinuria; and 3) normal contralateral kidney and new baseline eGFR will likely be greater than 45 ml/min/1.73m². *(Expert Opinion)*
**Surgical Principles**

- For patients who are undergoing surgical excision of a renal mass with clinically concerning regional lymphadenopathy, physicians should perform a lymph node dissection for staging purposes. *(Expert Opinion)*

- For patients who are undergoing surgical excision of a renal mass, physicians should perform adrenalectomy if imaging and/or intraoperative findings suggest metastasis or direct invasion of the adrenal gland. *(Clinical Principle)*

- In patients undergoing surgical excision of a renal mass, a minimally invasive approach should be considered when it would not compromise oncologic, functional, and perioperative outcomes. *(Expert Opinion)*

- Pathologic evaluation of the adjacent renal parenchyma should be performed after PN or RN to assess for possible intrinsic renal disease, particularly for patients with CKD or risk factors for developing CKD. *(Clinical Principle)*

**Thermal Ablation (TA)**

- Physicians should consider thermal ablation (TA) as an alternate approach for the management of cT1a renal masses <3 cm in size. For patients who elect TA, a percutaneous technique is preferred over a surgical approach whenever feasible to minimize morbidity. *(Conditional Recommendation; Evidence Level: Grade C)*

- Both radiofrequency ablation and cryoablation are options for patients who elect thermal ablation. *(Conditional Recommendation; Evidence Level: Grade C)*

- A renal mass biopsy should be performed prior to ablation to provide pathologic diagnosis and guide subsequent surveillance. *(Expert Opinion)*
Counseling about thermal ablation should include information regarding an increased likelihood of tumor persistence or local recurrence after primary thermal ablation relative to surgical extirpation, which may be addressed with repeat ablation if further intervention is elected. *(Strong Recommendation; Evidence Level: Grade B)*

**Active Surveillance (AS)**

- For patients with small solid or Bosniak 3/4 complex cystic renal masses, especially those <2cm, AS is an option for initial management. *(Conditional Recommendation; Evidence Level: Grade C)*

- For patients with a solid or Bosniak 3/4 complex cystic renal mass, physicians should prioritize active surveillance/expectant management when the anticipated risk of intervention or competing risks of death outweigh the potential oncologic benefits of active treatment. *(Clinical Principle)*

- For patients with a solid or Bosniak 3/4 complex cystic renal mass in whom the risk/benefit analysis for treatment is equivocal and who prefer AS, physicians should repeat imaging in 3-6 months to assess for interval growth and may consider RMB for additional risk stratification. *(Expert Opinion)*

- For patients with a solid or Bosniak 3/4 complex cystic renal mass in whom the anticipated oncologic benefits of intervention outweigh the risks of treatment and competing risks of death, physicians should recommend active treatment. In this setting, AS with potential for delayed intervention may be pursued only if the patient understands and is willing to accept the associated oncologic risk. *(Moderate Recommendation; Evidence Level: Grade C)*
Renal Mass and Localized Renal Cancer

EVALUATION/DIAGNOSIS
1. Obtain high quality, multiphase, cross-sectional abdominal imaging to optimally characterize/stage the renal mass.
2. Obtain CMP, CBC, and UA. If malignancy suspected, metastatic evaluation should include chest imaging and careful review of abdominal imaging.
3. Assign CKD stage based on GFR and degree of proteinuria.

COUNSELING
1. A urologist should lead the counseling process and should consider all management strategies. A multidisciplinary team should be included when necessary.
2. Counseling should include current perspectives about tumor biology and a patient-specific oncologic risk assessment. For cT1a tumors, the low oncologic risk of many small renal masses should be reviewed.
3. Counseling should review the most common and serious urologic and non-urologic morbidities of each treatment pathway and the importance of patient age, comorbidities/frailty, and life expectancy.
4. Physicians should review the importance of renal functional recovery related to renal mass management, including risk of progressive CKD, potential short/long-term need for dialysis, and long-term overall survival considerations.
5. Consider referral to nephrology in patients with a high risk of CKD progression, including those with GFR < 45, confirmed proteinuria, diabetics with preexisting CKD, or whenever GFR is expected to be < 30 after intervention.
6. Recommend genetic counseling for all patients ≤ 46 years of age and consider genetic counseling for patients with multifocal or bilateral renal masses, or if personal/family history suggests a familial renal neoplastic syndrome.

RENAL MASS BIOPSY (RMB)
1. RMB should be considered when a mass is suspected to be hematologic, metastatic, inflammatory, or infectious.
2. RMB is not required for young/healthy patients who are not willing to accept the uncertainties associated with RMB or for older/frail patients who will be managed conservatively independent of RMB.
3. Counsel regarding rationale, positive/negative predictive values, potential risks and non-diagnostic rates of RMB.
4. Multiple core biopsies are preferred over FNA.

---

1 Focus is on clinically localized renal masses suspicious for RCC in adults, including solid enhanced tumors and Bosniak 3 and 4 complex cystic lesions.
2 ml/min/1.73m²
Management

PARTIAL NEPHRECTOMY (PN) AND NEPHRON-SPARING APPROACHES
1. Prioritize PN for the management of the cT1a renal mass when intervention is indicated.
2. Prioritize nephron-sparing approaches for patients with an anatomic or functionally solitary kidney, bilateral tumors, known familial RCC, preexisting CKD, or proteinuria.
3. Consider nephron-sparing approaches for patients who are young, have multifocal masses, or comorbidities that are likely to impact renal function in the future.

PRINCIPLES RELATED TO PN
1. Prioritize preservation of renal function through efforts to optimize nephron mass preservation and avoidance of prolonged warm ischemia.
2. Negative surgical margins should be a priority. The extent of normal parenchyma removed should be determined by surgeon discretion taking into account the clinical situation; tumor characteristics including growth pattern, and interface with normal tissue. Enucleation should be considered in patients with familial RCC, multifocal disease, or severe CKD to optimize parenchymal mass preservation.

RADICAL NEPHRECTOMY (RN)
1. Physicians should consider RN for patients where increased oncologic potential is suggested by tumor size, RMB, and/or imaging characteristics. In this setting, RN is preferred if all of the following criteria are met:
   a) high tumor complexity and PN would be challenging even in experienced hands;
   b) no preexisting CKD/proteinuria; and
   c) normal contralateral kidney and new baseline eGFR will likely be > 45.
2. Prioritize nephron-sparing approaches for patients with an anatomic or functionally solitary kidney, bilateral tumors, known familial RCC, preexisting CKD, or proteinuria.
3. Consider nephron-sparing approaches for patients who are young, have multifocal masses, or comorbidities that are likely to impact renal function in the future.

SURGICAL PRINCIPLES
1. In the presence of clinically concerning regional lymphadenopathy, lymph node dissection should be performed for staging purposes.
2. Adrenalectomy should be performed if imaging and/or intraoperative findings suggest metastasis or direct invasion.
3. A minimally invasive approach should be considered when it would not compromise oncologic, functional, and perioperative outcomes.
4. Pathologic evaluation of the adjacent renal parenchyma should be performed after PN or RN to assess for possible nephrologic disease, particularly for patients with CKD or risk factors for developing CKD.

THERMAL ABLATION (TA)
1. Consider TA an alternate approach for management of cT1a renal masses <3 cm in size. A percutaneous approach is preferred.
2. Both radiofrequency ablation and cryoablation are options.
3. A RMB should be performed prior to TA.
4. Counseling about TA should include information regarding increased likelihood of tumor persistence/recurrence after primary TA, which may be addressed with repeat TA if further intervention is elected.

ACTIVE SURVEILLANCE (AS)
1. For patients with renal masses suspicious for cancer, especially those <2 cm, AS is an option for initial management.
2. Prioritize AS/Expectant Management when the anticipated risk of intervention or competing risks of death outweigh the potential oncologic benefits of active treatment.
3. When the risk/benefit analysis for treatment is equivocal and the patient prefers AS, physicians should repeat imaging in 3-6 months to assess for interval growth and may consider RMB for additional risk stratification.
4. When the oncologic benefits of intervention outweigh the risks of treatment and competing risks of death, physicians should recommend active treatment. In this setting, AS may be pursued only if the patient understands and is willing to accept the associated oncologic risk.

Factors Favoring AS/Expectant Management

<table>
<thead>
<tr>
<th>Patient-related</th>
<th>Tumor-related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elderly</td>
<td>Tumor size &lt;3 cm</td>
</tr>
<tr>
<td>Life expectancy &lt;5 years</td>
<td>Tumor growth &lt;5 mm/year</td>
</tr>
<tr>
<td>High comorbidities</td>
<td>Non-infiltrative</td>
</tr>
<tr>
<td>Excessive perioperative risk</td>
<td>Low complexity</td>
</tr>
<tr>
<td>Frailty (poor functional status)</td>
<td>Favorable histology</td>
</tr>
<tr>
<td>Patient preference for AS</td>
<td></td>
</tr>
<tr>
<td>Marginal renal function</td>
<td></td>
</tr>
</tbody>
</table>
Algorithm for active surveillance or expectant management of localized renal masses suspicious for malignancy

Baseline Assessment

<table>
<thead>
<tr>
<th>PATIENT FACTORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Co-morbidity/life expectancy (Comorbidity Index/Frailty Score)</td>
</tr>
<tr>
<td>• Patient expectations/QOL and psychosocial assessment</td>
</tr>
<tr>
<td>• Renal functional assessment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TUMOR FACTORS (ONCOLOGIC POTENTIAL OF SOLID OR COMPLEX CYSTIC RENAL MASSES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Imaging features (degree of enhancement, infiltrative appearance, vascular or fat invasion)</td>
</tr>
<tr>
<td>• Tumor complexity</td>
</tr>
<tr>
<td>• Prior imaging (if available) to compare size and features</td>
</tr>
<tr>
<td>• Renal mass biopsy (subtype, grade, biomarkers)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MANAGEMENT RELATED FACTORS (RISKS AND BENEFITS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Evidence regarding oncologic, renal function, and peri-procedural outcomes for each type of treatment</td>
</tr>
<tr>
<td>• ACS/NSQIP calculator</td>
</tr>
<tr>
<td>• Evidence regarding expected growth rates, efficacy of surveillance, triggers and risk of delayed intervention</td>
</tr>
</tbody>
</table>
COMMUNICATION
SHARED DECISION MAKING

Frequency* & Imaging Modality+

ACTIVE SURVEILLANCE:
• Approximately every 3-6 months
• Use cross sectional imaging and/or US

EXPECTANT MANAGEMENT:
• Approximately every 6-12 months
• Use US more frequently

Potential triggers for change in management (Rx or AS intensity)

• Tumor size >3 cm
• Stage progression
• Kinetics (>5mm / year)
• Clinical changes in patient/tumor factors

PROGRESSION TO mRCC

TREATMENT

* Consider concurrent renal functional assessment (sCr, proteinuria), metabolic assessment (LFTs) and chest imaging
* Consider alternatives to contrast when possible or necessary (doppler, diffusion weighted images etc.)
FOLLOW-UP FOR CLINICALLY LOCALIZED RENAL NEOPLASMS

AUA GUIDELINE – 2013

Purpose

The panel sought to create evidence-based guidelines for the follow-up and surveillance of clinically localized renal cancers treated with surgery or renal ablative procedures, biopsy-proven untreated clinically localized renal cancers followed on surveillance, and radiographically suspicious but biopsy-unproven renal neoplasms either treated with renal ablative procedures or followed on active surveillance. The panel focused on the early detection of cancer recurrence based on the traditional presumption that treatment of a lower tumor burden would result in better patient outcomes, although the evidentiary data supporting this presumption is limited. These guidelines are not meant to address hereditary or pediatric kidney cancers, although they must take into account that a proportion of adult patients may harbor a yet unrecognized hereditary form of renal cancer. The panel also recognizes the essential elements of adult cancer survivorship care now include not only monitoring for cancer recurrence, secondary cancers and treatment effects, but also the prevention of recurrences or new tumors, medical interventions for the consequences of cancer and its treatment effects, and the coordination between specialists and primary care physicians to meet survivors’ needs.

Guideline Statements

• Patients undergoing follow-up for treated or observed
renal masses should undergo a history and physical examination directed at detecting signs and symptoms of metastatic spread or local recurrence.

- Patients undergoing follow-up for treated or observed renal masses should undergo basic laboratory testing to include blood urea nitrogen (BUN)/creatinine, urine analysis (UA) and estimated glomerular filtration rate (eGFR). Other laboratory evaluations, including complete blood count (CBC), lactate dehydrogenase (LDH), liver function tests (LFTs), alkaline phosphatase (ALP) and calcium level, may be used at the discretion of the clinician.

- Patients with progressive renal insufficiency on follow-up laboratory evaluation should be referred to nephrology.

- The panel recommends a bone scan in patients with an elevated alkaline phosphatase (ALP), clinical symptoms such as bone pain, and/or if radiographic findings are suggestive of a bony neoplasm.

- The panel recommends against the performance of a bone scan in the absence of an elevated alkaline phosphatase (ALP) or clinical symptoms, such as bone pain, or radiographic findings suggestive of a bone neoplasm.

- Patients with a history of a renal neoplasm presenting with acute neurological signs or symptoms must undergo prompt neurologic cross sectional CT or MRI scanning of the head or spine based on localization of symptomatology.

- The panel recommends against the routine use of molecular markers, such Ki-67, p-53 and VEGF, as benefits remain unproven at this time.
Surgery

Low risk patients (pT1, N0, Nx): Low risk is defined as organ-confined tumors (pT1, N0 or Nx) with negative or radiographically normal lymph nodes. These tumors have a risk of metastasis of less than 15% and an extremely low risk of local recurrence (less than 5%) in the absence of a positive surgical margin.

- Patients should undergo a baseline abdominal scan (CT or MRI) for nephron sparing surgery and abdominal imaging (US, CT or MRI) for radical nephrectomy within three to twelve months following renal surgery.
- Additional abdominal imaging (US, CT or MRI) may be performed in patients with low risk (pT1, N0, Nx) disease following a radical nephrectomy if the initial postoperative baseline image is negative.
- Abdominal imaging (US, CT, or MRI) may be performed yearly for three years in patients with low risk (pT1, N0, Nx) disease following a partial nephrectomy based on individual risk factors if the initial postoperative scan is negative.
- The panel recommends that patients with a history of low risk (pT1, N0, Nx) renal cell carcinoma undergo yearly chest x-ray to assess for pulmonary metastases for three years and only as clinically indicated beyond that time period.

Moderate to High Risk Patients (pT2-4N0 Nx or any stage N+): Moderate to high risk is defined as organ-confined tumors greater than 7cm (pT2 N0 or Nx), non-organ confined tumors (pT3-4 N0 or Nx) with evidence of extension
beyond the renal capsule, into the perinephric fat, renal sinus, renal vein or inferior vena cava, or adjacent organ invasion including the ipsilateral adrenal gland, and/or any stage tumor with positive regional nodes (N+). Patients with these tumors have a higher risk of both local and metastatic recurrence, in the range of 30% to 70% and, therefore, are recommended to have an increased frequency of examinations due to a higher likelihood of primary treatment failure.

- The panel recommends that moderate to high risk patients undergo baseline chest and abdominal scan (CT or MRI) within three to six months following surgery with continued imaging (US, CXR, CT or MRI) every six months for at least three years and annually thereafter to year five.

- The panel recommends site-specific imaging as warranted by clinical symptoms suggestive of recurrence or metastatic spread.

- Imaging (US, CXR, CT or MRI) beyond five years may be performed at the discretion of the clinician for moderate to high risk patients.

- Routine FDG-PET scan is not indicated in the follow-up for renal cancer.

**Active Surveillance**

- Percutaneous biopsy may be considered in patients planning to undergo active surveillance.

- The panel recommends that patients undergo cross-sectional abdominal scanning (CT or MRI) within six months of active surveillance initiation to establish a growth rate. The panel further recommends continued
imaging (US, CT or MRI) at least annually thereafter.

- Importantly, with respect to tumor size measurements, differences of < 3.1 mm for inter-observer or < 2.3 mm for intra-observer evaluations are within the variability of measurement and should, therefore, not be attributed to tumor growth, unless in the case where there are persistent increases over two or more interval exams.

- The panel recommends that patients on active surveillance with biopsy proven renal cell carcinoma or a tumor with oncocytic features undergo an annual chest x-ray to assess for pulmonary metastases.

**Ablation**

A local tumor recurrence following ablative therapy was defined as any localized disease remaining in the treated kidney at any point after the first ablation, as determined by a tumor with contrast enhancement after ablation, a visually enlarging lesion in the same area of treatment with or without the presence of contrast enhancement, the failure of an ablated lesion to regress in size over time, and or the development of new satellite or port site soft tissue nodules.

- A urologist should be involved in the clinical management of all patients undergoing renal ablative procedures including percutaneous ablation.

- The panel recommends that all patients undergoing ablation procedures for a renal mass undergo a pretreatment diagnostic biopsy.

- The standardized definition of “treatment failure or local recurrence” suggested in the Clinical T1 Guideline document should be adopted by clinicians. This should be further clarified to include a visually enlarging neoplasm.
or new nodularity in the same area of treatment whether determined by enhancement of the neoplasm on post-treatment contrast imaging, or failure of regression in size of the treated lesion over time, new satellite or port site soft tissue nodules, or biopsy proven recurrence.

- The panel recommends that patients undergo cross-sectional imaging (CT or MRI) with and without IV contrast unless otherwise contraindicated at three and six months following ablative therapy to assess treatment success. This should be followed by annual abdominal scans (CT or MRI) thereafter for five years.

- Patients may undergo further scanning (CT or MRI) beyond five years based on individual patient risk factors.

- Patients undergoing ablative procedures who have either biopsy proven low risk renal cell carcinoma, oncocytoma, a tumor with oncocyctic features, nondiagnostic biopsies or no prior biopsy, should undergo annual chest x-ray to assess for pulmonary metastases for five years. Imaging beyond five years is optional based on individual patient risk factors and the determination of treatment success.

- The panel recommends against further radiologic scanning in patients who underwent an ablative procedure with pathological confirmation of benign histology at or before treatment and who have radiographic confirmation of treatment success and no evidence of treatment related complications requiring further imaging.
The alternatives of observation, repeat treatment and surgical intervention should be discussed, and repeat biopsy should be performed if there is radiographic evidence of treatment failure within six months if the patient is a treatment candidate.

A progressive increase in size of an ablated neoplasm, with or without contrast enhancement, new nodularity in or around the treated zone, failure of the treated lesion to regress in size over time, satellite or port side lesions, should prompt lesion biopsy.
**APPENDIX A: FOLLOW-UP PROTOCOL SUMMARY**

**Follow-Up Measure — Active Surveillance**

<table>
<thead>
<tr>
<th>Follow-Up Measure</th>
<th>Active Surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Exam and History</td>
<td>• History and physical examination directed at detecting signs and symptoms of metastatic spread or local progression</td>
</tr>
<tr>
<td>Laboratory Testing</td>
<td>• Basic laboratory testing to include BUN/creatinine, UA and eGFR;</td>
</tr>
<tr>
<td></td>
<td>• CBC, LDH, LFTs, ALP and calcium level tests may be used at the discretion of the physician;</td>
</tr>
<tr>
<td></td>
<td>• Progressive renal insufficiency should prompt a nephrology referral</td>
</tr>
<tr>
<td>CNS Scan¹</td>
<td>• Acute neurological signs should undergo prompt neurologic cross sectional (CT or MRI) scan¹ of the head or spine based on localized symptomatology</td>
</tr>
<tr>
<td>Bone Scan</td>
<td>• Elevated ALP, clinical symptoms such as bone pain, and/or radiographic findings suggestive of a bony neoplasm should prompt a bone scan;</td>
</tr>
<tr>
<td></td>
<td>• A bone scan should not be performed in the absence of these symptoms</td>
</tr>
<tr>
<td>Percutaneous Biopsy</td>
<td>• Percutaneous biopsy should be considered prior to active surveillance</td>
</tr>
<tr>
<td>Abdominal Scan¹/Imaging²</td>
<td>• Cross-sectional abdominal scanning¹ (CT or MRI) within six months of active surveillance initiation to establish a growth rate with continued imaging² (US, CT or MRI) at least annually thereafter</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>• Patients with biopsy proven RCC or a tumor with oncocytic features on active surveillance should undergo an annual chest x-ray to assess for pulmonary metastases</td>
</tr>
</tbody>
</table>

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¹ In the context of this document, “scan” dictates the use of CT or MRI.
² In the context of this document “imaging” dictates the use of abdominal or renal US, CT or MRI.
## APPENDIX A: FOLLOW-UP PROTOCOL SUMMARY

### Follow-Up Measure — Renal Ablation

<table>
<thead>
<tr>
<th>Follow-Up Measure</th>
<th>Renal Ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical Exam and History</strong></td>
<td>• History and physical exam directed at detecting signs and symptoms of metastatic spread or local recurrence</td>
</tr>
</tbody>
</table>
| **Laboratory Testing** | • Basic laboratory testing to include BUN/creatinine, UA and eGFR;  
• CBC, LDH, LFTs, ALP and calcium level tests may be used at the discretion of the physician;  
• Progressive renal insufficiency should prompt a nephrology referral |
| **CNS Scan¹** | • Acute neurological signs should prompt neurologic cross sectional (CT or MRI) scan¹ of the head or spine based on localized symptomaticity |
| **Bone Scan** | • Elevated ALP, clinical symptoms such as bone pain, and/or radiographic findings suggestive of a bony neoplasm should prompt a bone scan;  
• A bone scan should not be performed in the absence of these symptoms |
| **Diagnostic Biopsy** | • Patients should undergo a pretreatment diagnostic biopsy |
| **Abdominal Scan¹** | • Cross-sectional scanning¹ (CT or MRI) with and without IV contrast unless otherwise contraindicated at three and six months following ablative therapy with continued scanning annually thereafter for five years;  
• Scanning¹ beyond five years is optional based on individual risk factors |
| **Chest Imaging²** | • Patients who have either biopsy proven low risk RCC, oncocytoma, a tumor with oncocytic features, nondiagnostic biopsies or no prior biopsy should undergo annual chest x-ray to assess for pulmonary metastases for five years;  
• Imaging² (CXR or CT) beyond five years is optional based on individual patient risk factors and the determination of treatment success;  
• Radiologic scanning is not recommended with pathological confirmation of benign disease at or before treatment and post treatment radiographic confirmation of treatment success and no evidence of treatment-related complications |
| **Repeat Biopsy** | • New enhancement, a progressive increase in size of an ablated neoplasm with or without contrast enhancement, new nodularity in or around the treated zone, failure of the treated lesion to regress over time, satellite or port side lesions, should prompt a repeat lesion biopsy;  
• Observation, repeat treatment and surgical intervention should be discussed |

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1 In the context of this document, “scan” dictates the use of CT or MRI.  
2 In the context of this document, “chest imaging” indicates the use of CXR or chest CT.
## APPENDIX A:
### FOLLOW-UP PROTOCOL SUMMARY

### Follow-Up Measure — Nephrectomy

<table>
<thead>
<tr>
<th>Physical Exam and History</th>
<th>Low Risk</th>
<th>Moderate to High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• History and physical examination directed at detecting signs/symptoms of metastatic spread or local recurrence</td>
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</table>

<table>
<thead>
<tr>
<th>Laboratory Testing</th>
<th>Low Risk</th>
<th>Moderate to High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Basic laboratory testing to include BUN/creatinine, UA and eGFR;</td>
<td></td>
<td></td>
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<tr>
<td>• CBC, LDH, LFTs, ALP and calcium level tests may be used at the discretion of the physician;</td>
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<tr>
<td>• Progressive renal insufficiency should prompt a nephrology referral</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>CNS Scan</th>
<th>Low Risk</th>
<th>Moderate to High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Acute neurological signs should prompt neurologic cross sectional (CT or MRI) scan(^1) of the head or spine based on localized symptomatology</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Bone Scan</th>
<th>Low Risk</th>
<th>Moderate to High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Elevated ALP, clinical symptoms such as bone pain, and/or radiographic findings suggestive of a bony neoplasm should prompt a bone scan;</td>
<td></td>
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<tr>
<td>• A bone scan should not be performed in the absence of these symptoms</td>
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<table>
<thead>
<tr>
<th>Follow-Up Measure</th>
<th>Low Risk</th>
<th>Moderate to High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Scanning/Imaging</td>
<td>Partial Nephrectomy</td>
<td>Radical Nephrectomy</td>
</tr>
<tr>
<td>• Partial Nephrectomy—Obtain a baseline abdominal scan(^1) (CT or MRI) within three to twelve months following surgery;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• If the initial postoperative scan is negative, abdominal imaging(^2) (US, CT or MRI) may be performed yearly for three years based on individual risk factors</td>
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</tr>
<tr>
<td>• Radical Nephrectomy—Patients should undergo abdominal imaging(^2) (US, CT or MRI) within three to twelve months following renal surgery;</td>
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</tr>
<tr>
<td>• If the initial postoperative imaging is negative, abdominal imaging(^2) beyond twelve months may be performed at the discretion of the clinician</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Chest Imaging/Scan</th>
<th>Low Risk</th>
<th>Moderate to High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Obtain a yearly chest x-ray for three years and only as clinically indicated beyond that time period</td>
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</tbody>
</table>

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1 In the context of this document, “scan” dictates the use of CT or MRI.
2 In the context of this document, “imaging” dictates the use of abdominal or renal US, CT or MRI.
3 In the context of this document, “chest imaging” indicates the use of CXR or chest CT.
APPENDIX D: DEFINITIONS USED IN THIS DOCUMENT

**Indications for active surveillance:** Indications for active surveillance include elderly patients, those with decreased life expectancy or those with medical comorbidities that would be associated with increased risk if a therapeutic intervention were to be undertaken. Alternatively, a strategy of observation with delayed intervention as indicated may be elected in order to determine the growth rate or to obtain alternative diagnostic imaging.

**Standardized incidence ratio:** incidence estimate (i.e. number of new cases in period of observation) in which the number of events (numerator) and the number of individuals at risk during the period of observation (denominator) are summarized across strata formed by the combination of adjustment variables (e.g. age groups, sex, race). (For more information the reader could be directed to: http://seer.cancer.gov/seerstat/WebHelp/Standardized_Incidence_Ratio_and_Confidence_Limits.htm)
MEDICAL MANAGEMENT OF KIDNEY STONES

AUA GUIDELINE – 2014

Purpose

Kidney stone disease is a common malady, affecting nearly 1 in 11 individuals in the United States at some point in their lives, and there is evidence that the number of those who have had a stone is rising. Unlike appendicitis and other surgical conditions, surgical treatment of stones is not the endpoint of the disease process, as stones are likely to recur, with at least 50% of individuals experiencing another stone within 10 years of the first occurrence. For those who have experienced a stone or undergone surgical intervention for a stone, there is strong motivation to avoid a repeat episode. Consequently, these patients often seek advice from a variety of practitioners on how to prevent recurrent stones. However, misinformation abounds in the lay community and on the internet, and even medical providers often promulgate recommendations that are contrary to evidence-based medicine. This Guideline is aimed at practitioners from a variety of disciplines who are confronted with patients afflicted with stone disease, and it is based on a systematic review of the literature with respect to the evaluation, treatment and follow-up of first-time and recurrent stone formers. Patient preferences and goals must be taken into account by the practitioner when considering these guidelines, as the cost, inconvenience and side effects of drugs and dietary measures to prevent stone disease must be weighed against the benefit of preventing a recurrent stone.
Guideline Statements

Evaluation

- A clinician should perform a screening evaluation consisting of a detailed medical and dietary history, serum chemistries and urinalysis on a patient newly diagnosed with kidney or ureteral stones.

- Clinicians should obtain serum intact parathyroid hormone (PTH) level as part of the screening evaluation if primary hyperparathyroidism is suspected.

- When a stone is available, clinicians should obtain a stone analysis at least once.

- Clinicians should obtain or review available imaging studies to quantify stone burden.

- Clinicians should perform additional metabolic testing in high-risk or interested first-time stone formers and recurrent stone formers.

- Metabolic testing should consist of one or two 24-hour urine collections obtained on a random diet and analyzed at minimum for total volume, pH, calcium, oxalate, uric acid, citrate, sodium, potassium and creatinine.

- Clinicians should not routinely perform “fast and calcium load” testing to distinguish among types of hypercalciuria.

Diet Therapies

- Clinicians should recommend to all stone formers a fluid intake that will achieve a urine volume of at least 2.5 liters daily.
Clinicians should counsel patients with calcium stones and relatively high urinary calcium to limit sodium intake and consume 1,000-1,200 mg per day of dietary calcium.

Clinicians should counsel patients with calcium oxalate stones and relatively high urinary oxalate to limit intake of oxalate-rich foods and maintain normal calcium consumption.

Clinicians should encourage patients with calcium stones and relatively low urinary citrate to increase their intake of fruits and vegetables and limit non-dairy animal protein.

Clinicians should counsel patients with uric acid stones or calcium stones and relatively high urinary uric acid to limit intake of non-dairy animal protein.

Clinicians should counsel patients with cystine stones to limit sodium and protein intake.

**Pharmacologic Therapies**

Clinicians should offer thiazide diuretics to patients with high or relatively high urine calcium and recurrent calcium stones.

Clinicians should offer potassium citrate therapy to patients with recurrent calcium stones and low or relatively low urinary citrate.

Clinicians should offer allopurinol to patients with recurrent calcium oxalate stones who have hyperuricosuria and normal urinary calcium.

Clinicians should offer thiazide diuretics and/or potassium citrate to patients with recurrent calcium stones in whom other metabolic abnormalities are absent or have been appropriately addressed and stone formation persists.
• Clinicians should offer potassium citrate to patients with uric acid and cystine stones to raise urinary pH to an optimal level.

• Clinicians should not routinely offer allopurinol as first-line therapy to patients with uric acid stones.

• Clinicians should offer cystine-binding thiol drugs, such as alpha-mercaptopropionylglycine (tiopronin), to patients with cystine stones who are unresponsive to dietary modifications and urinary alkalization, or have large recurrent stone burdens.

• Clinicians may offer acetohydroxamic acid (AHA) to patients with residual or recurrent struvite stones only after surgical options have been exhausted.

Follow-up

• Clinicians should obtain a single 24-hour urine specimen for stone risk factors within six months of the initiation of treatment to assess response to dietary and/or medical therapy.

• After the initial follow-up, clinicians should obtain a single 24-hour urine specimen annually or with greater frequency, depending on stone activity, to assess patient adherence and metabolic response.

• Clinicians should obtain periodic blood testing to assess for adverse effects in patients on pharmacological therapy.

• Clinicians should obtain a repeat stone analysis, when available, especially in patients not responding to treatment.
• Clinicians should monitor patients with struvite stones for reinfection with urease-producing organisms and utilize strategies to prevent such occurrences.

• Clinicians should periodically obtain follow-up imaging studies to assess for stone growth or new stone formation based on stone activity (plain abdominal imaging, renal ultrasonography or low dose computed tomography [CT]).
SURGICAL MANAGEMENT OF STONES

AMERICAN UROLOGICAL ASSOCIATION/ENDOUROLOGICAL SOCIETY GUIDELINE – 2016

Purpose

The purpose of this Guideline is to provide a clinical framework for the surgical management of patients with kidney and/or ureteral stones.

AUA Nomenclature

The AUA nomenclature system links statement types to a number of factors including strength of evidence, magnitude of benefit and risks/burdens, and panel judgment. There are three evidence-based statement types: **Strong Recommendations** and **Moderate Recommendations** are directive statements that indicate that there is a net benefit (or harm) associated with a clinical action, while a **Conditional Recommendation** is a non-directive Statement that is used when the clinical action does not have a clear net benefit (or harm).

In addition, there are two statement types that are used when pertinent evidence is not present in the systematic review of literature associated with the guideline: **Expert Opinions** are statements made by panel consensus based on members’ clinical training, experience, knowledge, and judgment, while a **Clinical Principle** is a statement about a component of clinical care that is very widely agreed upon by urologists or other clinicians.
Index Patients

The surgical management of patients with various stones is described below and divided into 13 respective patient profiles. Index Patients 1-10 are non-morbidly obese; non-pregnant adults (≥ 18 years of age) with stones not thought to be composed of uric acid or cystine; normal renal, coagulation and platelet function; normally positioned kidneys; intact lower urinary tracts without ectopic ureters; no evidence of sepsis; and no anatomic or functional obstruction distal to the stone(s). Index Patients 13 and 14 are children (<18 years if age) with similar characteristics to Index Patients 1-10. Index Patient 15 is a pregnant female with symptomatic renal or ureteral stone(s) with normal renal function without urinary tract infection (UTI). The proximal ureter is defined as the segment distal to the ureteropelvic junction (UPJ) and above the upper border of the sacroiliac joint. The middle ureter is that which overlies the sacroiliac joint and the distal ureter that lies below it.


Index Patients
Index Patient 1: Adult, ≤10mm proximal ureteral stone
Index Patient 2: Adult, ≤10mm mid ureteral stone
Index Patient 3: Adult, ≤10mm distal ureteral stone
Index Patient 4: Adult, >10mm proximal ureteral stone
Index Patient 5: Adult, >10mm mid ureteral stone
Index Patient 6: Adult, >10mm distal ureteral stone
Index Patient 7: Adult, ≤20mm total non-lower pole renal stone burden
Index Patient 8: Adult, >20mm total renal stone burden
Index Patient 9: Adult, ≤10mm lower pole renal stone(s)
Index Patient 10: Adult, >10mm lower pole renal stone(s)
Index Patient 11: Adult, with residual stone(s)
Index Patient 12: Adult, renal stone(s) with pain and no obstruction
Index Patient 13: Child, not known to have cystine or uric acid ureteral stone(s)
Index Patient 14: Child, not known to have cystine or uric acid renal stone(s)
Index Patient 15: Pregnant female, renal or ureteral stone(s)

Guideline Statements

Imaging, Pre-Operative Testing

- Clinicians should obtain a non-contrast CT scan on patients prior to performing percutaneous nephrolithotomy. (Strong Recommendation; Evidence Level: Grade C)

- Clinicians may obtain a non-contrast CT scan to help select the best candidate for shock-wave lithotripsy versus ureteroscopy. (Conditional Recommendation; Evidence Level: Grade C)

- Clinicians may obtain a functional imaging study (DTPA or MAG-3) if clinically significant loss of renal function in the involved kidney or kidneys is suspected. (Conditional Recommendation; Evidence Level: Grade C)

- Clinicians are required to obtain a urinalysis prior to intervention. In patients with clinical or laboratory signs of infection, urine culture should be obtained. (Strong Recommendation; Evidence Level: Grade B)
• Clinicians should obtain a complete blood count and platelet count on patients undergoing procedures where there is a significant risk of hemorrhage or for patients with symptoms suggesting anemia, thrombocytopenia, or infection; serum electrolytes and creatinine should be obtained if there is suspicion of reduced renal function. *(Expert Opinion)*

• In patients with complex stones or anatomy, clinicians may obtain additional contrast imaging if further definition of the collecting system and the ureteral anatomy is needed. *(Conditional Recommendation; Evidence Level: Grade C)*

**Treatment of Adult Patients with Ureteral Stones**

• Patients with uncomplicated distal ureteral stones ≤10 mm should be offered observation, and those with distal stones of similar size should be offered medical expulsive therapy with α-blockers. *(Index Patient 3)* *(Strong Recommendation; Evidence Level: Grade B)*

• Clinicians should offer reimaging to patients prior to surgery if passage of stones is suspected or if stone movement will change management. Reimaging should focus on the region of interest and limit radiation exposure to uninvolved regions. *(Clinical Principle)*

• In most patients, if observation with or without medical expulsive therapy is not successful after four to six weeks and/or the patient/clinician decide to intervene sooner based on a shared decision making approach, clinicians should offer definitive stone treatment. *(Index Patients 1-3)* *(Moderate Recommendation; Evidence Level: Grade C)*
Clinicians should inform patients that shock-wave lithotripsy is the procedure with the least morbidity and lowest complication rate, but ureteroscopy has a greater stone-free rate in a single procedure. (Index Patients 1-6) (*Strong Recommendation; Evidence Level: Grade B*)

In patients with mid or distal ureteral stones who require intervention (who were not candidates for or who failed medical expulsive therapy), clinicians should recommend ureteroscopy as first-line therapy. For patients who decline ureteroscopy, clinicians should offer shock-wave lithotripsy. (Index Patients 2,3,5,6) (*Strong Recommendation; Evidence Level: Grade B*)

Ureteroscopy is recommended for patients with suspected cystine or uric acid ureteral stones who fail medical expulsive therapy or desire intervention. (*Expert Opinion*)

Routine stenting should not be performed in patients undergoing shock-wave lithotripsy. (Index Patients 1-6) (*Strong Recommendation; Evidence Level: Grade B*)

Following ureteroscopy, clinicians may omit ureteral stenting in patients meeting all of the following criteria: those without suspected ureteric injury during ureteroscopy, those without evidence of ureteral stricture or other anatomical impediments to stone fragment clearance, those with a normal contralateral kidney, those without renal functional impairment, and those in whom a secondary ureteroscopy procedure is not planned. (Index Patients 1-6) (*Strong Recommendation; Evidence Level: Grade A*)

Placement of a ureteral stent prior to ureteroscopy should not be performed routinely. (Index Patient 1-6) (*Strong Recommendation; Evidence Level: Grade B*)
• Clinicians may offer α-blockers and antimuscarinic therapy to reduce stent discomfort. (Index Patients 1-6) (Moderate Recommendation; Evidence Level: Grade B)

• In patients who fail or are unlikely to have successful results with shock-wave lithotripsy and/or ureteroscopy, clinicians may offer percutaneous nephrolithotomy, laparoscopic, open, or robotic assisted stone removal. (Index Patient 1-6) (Moderate Recommendation; Evidence Level: Grade C)

• Clinicians performing ureteroscopy for proximal ureteral stones should have a flexible ureteroscope available. (Index Patients 1, 4) (Clinical Principle)

• Clinicians should not utilize electrohydraulic lithotripsy as the first-line modality for intra-ureteral lithotripsy. (Index Patients 1-6, 13, 15) (Expert Opinion)

• In patients with obstructing stones and suspected infection, clinicians must urgently drain the collecting system with a stent or nephrostomy tube and delay stone treatment. (Strong Recommendation; Evidence Level: Grade C)

**Treatment of Adult Patients with Renal Stones**

• In symptomatic patients with a total non-lower pole renal stone burden ≤ 20 mm, clinicians may offer shock-wave lithotripsy or ureteroscopy. (Index Patient 7) (Strong Recommendation; Evidence Level: Grade B)

• In symptomatic patients with a total renal stone burden > 20 mm, clinicians should offer percutaneous nephrolithotomy as first-line therapy. (Index Patient 8) (Strong Recommendation; Evidence Level: Grade C)
• In patients with total renal stone burden >20 mm, clinicians should not offer shock-wave lithotripsy as first-line therapy. (Index Patient 8) (Moderate Recommendation; Evidence Level: Grade C)

• Clinicians may perform nephrectomy when the involved kidney has negligible function in patients requiring treatment. (Index Patients 1-14) (Conditional Recommendation; Evidence Level: Grade C)

• For patients with symptomatic (flank pain), non-obstructing, caliceal stones without another obvious etiology for pain, clinicians may offer stone treatment. (Index Patient 12) (Moderate Recommendation; Evidence Level: Grade C)

• For patients with asymptomatic, non-obstructing caliceal stones, clinicians may offer active surveillance. Conditional Recommendation; Evidence Level: Grade C

• Clinicians should offer shock-wave lithotripsy or ureteroscopy to patients with symptomatic ≤ 10 mm lower pole renal stones. (Index Patient 9) (Strong Recommendation; Evidence Level: Grade B)

• Clinicians should not offer shock-wave lithotripsy as first-line therapy to patients with >10mm lower pole stones. (Index Patient 10) (Strong Recommendation; Evidence Level: Grade B)

• Clinicians should inform patients with lower pole stones >10 mm in size that percutaneous nephrolithotomaty has a higher stone-free rate but greater morbidity. (Index Patient 10). (Strong Recommendation; Evidence Level: Grade B)
• In patients undergoing uncomplicated percutaneous nephrolithotomy who are presumed stone-free, placement of a nephrostomy tube is optional. (Conditional Recommendation; Evidence Level: Grade C)

• Flexible nephroscopy should be a routine part of standard percutaneous nephrolithotomy. (Strong Recommendation; Evidence Level: Grade B)

• Clinicians must use normal saline irrigation for percutaneous nephrolithotomy and ureteroscopy. (Strong Recommendation; Evidence Level: Grade B)

• In patients not considered candidates for percutaneous nephrolithotomy, clinicians may offer staged ureteroscopy. (Moderate Recommendation; Evidence Level: Grade C)

• Clinicians may prescribe α-blockers to facilitate passage of stone fragments following shock-wave lithotripsy. (Moderate Recommendation; Evidence Level: Grade B)

• Shock-wave lithotripsy should not be used in the patient with anatomic or functional obstruction of the collecting system or ureter distal to the stone. (Strong Recommendation; Evidence Level: Grade C)

• In patients with symptomatic caliceal diverticular stones, endoscopic therapy (ureteroscopy, percutaneous nephrolithotomy, laparoscopic, robotic) should be preferentially utilized. (Strong Recommendation; Evidence Level: Grade C)

• Staghorn stones should be removed if attendant comorbidities do not preclude treatment. (Clinical Principle)
Treatment for Pediatric Patients with Ureteral or Renal Stones

- In pediatric patients with uncomplicated ureteral stones ≤10 mm, clinicians should offer observation with or without medical expulsive therapy using α-blockers. (Index Patient 13) (Moderate Recommendation; Evidence Level: Grade B)

- Clinicians should offer ureteroscopy or shock-wave lithotripsy for pediatric patients with ureteral stones who are unlikely to pass the stones or who failed observation and/or medical expulsive therapy, based on patient-specific anatomy and body habitus. (Index Patient 13) (Strong Recommendation; Evidence Level: Grade B)

- Clinicians should obtain a low-dose CT scan on pediatric patients prior to performing percutaneous nephrolithotomy. (Index Patient 13) (Strong Recommendation; Evidence Level: Grade C)

- In pediatric patients with ureteral stones, clinicians should not routinely place a stent prior to ureteroscopy. (Index Patient 13) (Expert Opinion)

- In pediatric patients with a total renal stone burden ≤20 mm, clinicians may offer shock-wave lithotripsy or ureteroscopy as first-line therapy. (Index Patient 14) (Moderate Recommendation; Evidence Level: Grade C)

- In pediatric patients with a total renal stone burden >20 mm, both percutaneous nephrolithotomy and shock-wave lithotripsy are acceptable treatment options. If shock-wave lithotripsy is utilized, clinicians should place an internalized ureteral stent or nephrostomy tube. (Index Patient 14) (Expert Opinion)
• In pediatric patients, except in cases of coexisting anatomic abnormalities, clinicians should not routinely perform open/laparoscopic/robotic surgery for upper tract stones. (Index Patients 13, 14) (Expert Opinion)

• In pediatric patients with asymptomatic and non-obstructing renal stones, clinicians may utilize active surveillance with periodic ultrasonography. (Index Patient 14) (Expert Opinion)

Treatment for Pregnant Patients with Ureteral or Renal Stones

• In pregnant patients, clinicians should coordinate pharmacological and surgical intervention with the obstetrician. (Index Patient 15) (Clinical Principal)

• In pregnant patients with ureteral stones and well controlled symptoms, clinicians should offer observation as first-line therapy. (Index Patient 15) (Strong Recommendation; Evidence Level: Grade B)

• In pregnant patients with ureteral stones, clinicians may offer ureteroscopy to patients who fail observation. Ureteral stent and nephrostomy tube are alternative options with frequent stent or tube changes usually being necessary. (Index Patient 15) (Strong Recommendation; Evidence Level: Grade C)

Treatment for All Patients with Ureteral or Renal Stones

• When residual fragments are present, clinicians should offer patients endoscopic procedures to render the patients stone free, especially if infection stones are suspected. (Index Patient 11) (Moderate Recommendation; Evidence Level: Grade C)
• Stone material should be sent for analysis. (*Clinical Principle*)

• Open/ laparoscopic /robotic surgery should not be offered as first-line therapy to most patients with stones. Exceptions include rare cases of anatomic abnormalities, with large or complex stones, or those requiring concomitant reconstruction. (Index Patients 1-15) (*Strong Recommendation; Evidence Level: Grade C*)

• A safety guide wire should be used for most endoscopic procedures. (Index Patients 1-15) (*Expert Opinion*)

• Antimicrobial prophylaxis should be administered prior to stone intervention and is based primarily on prior urine culture results, the local antibiogram, and in consultation with the current Best Practice Policy Statement on Urologic Surgery Antibiotic Prophylaxis. (*Clinical Principle*)

• Clinicians should abort stone removal procedures, establish appropriate drainage, continue antibiotic therapy, and obtain a urine culture if purulent urine is encountered during endoscopic intervention. (Index Patients1-15) (*Strong Recommendation; Evidence Level: Grade C*)

• If initial shock-wave lithotripsy fails, clinicians should offer endoscopic therapy as the next treatment option. (Index Patient 1-14) (*Moderate Recommendation; Evidence Level: Grade C*)

• Clinicians should use ureteroscopy as first-line therapy in most patients who require stone intervention in the setting of uncorrected bleeding diatheses or who require continuous anticoagulation/antiplatelet therapy. (Index Patients1-15) (*Strong Recommendation; Evidence Level: Grade C*)
Purpose

Urethral stricture is chronic fibrosis and narrowing of the urethral lumen caused by acute injury, inflammatory conditions, and iatrogenic interventions including urethral instrumentation or surgery and prostate cancer treatment. The symptoms of urethral stricture are non-specific, and may overlap with other common conditions including lower urinary tract symptoms (LUTS) and urinary tract infection (UTI) to confound timely diagnosis. Urologists play a key role in the initial evaluation of urethral stricture and currently provide all accepted treatments. Thus, urologists must be familiar with the diagnostic tests for urethral stricture as well as endoscopic and open approaches to initial presentation and management of treatment failure. This guideline provides evidence based direction to clinicians and patients regarding how to recognize symptoms and signs of a urethral stricture, carry out appropriate testing to determine the location and severity of the stricture, and recommend the best options for treatment. The most effective approach for a particular patient is best determined by the individual clinician and patient in the context of that patient’s history, values, and goals for treatment. As the science relevant to urethral stricture evolves and improves, the strategies presented here will be amended to remain consistent with the highest standards of clinical care.
AUA Nomenclature

The AUA nomenclature system links statement types to a number of factors including strength of evidence, magnitude of benefit and risks/burdens, and panel judgment. There are three evidence-based statement types: Strong Recommendations and Moderate Recommendations are directive statements that indicate that there is a net benefit (or harm) associated with a clinical action, while a Conditional Recommendation is a non-directive Statement that is used when the clinical action does not have a clear net benefit (or harm).

In addition, there are two statement types that are used when pertinent evidence is not present in the systematic review of literature associated with the guideline: Expert Opinions are statements made by panel consensus based on members’ clinical training, experience, knowledge, and judgment, while a Clinical Principle is a statement about a component of clinical care that is very widely agreed upon by urologists or other clinicians.

Guideline Statements:

Diagnosis/Initial Management

- Clinicians should include urethral stricture in the differential diagnosis of men who present with decreased urinary stream, incomplete emptying, dysuria, urinary tract infection (UTI), and after rising post void residual. (Moderate Recommendation; Evidence Level: Grade C)

- After performing a history, physical examination and urinalysis, clinicians may use a combination of patient
reported measures, uroflowmetry, and ultrasound post void residual assessment in the initial evaluation of suspected urethral stricture. *(Clinical Principle)*

- Clinicians should use urethro-cystoscopy, retrograde urethrography, voiding cystourethrography or ultrasound urethography to make a diagnosis of urethral stricture. *(Moderate Recommendation; Evidence Level: Grade C)*

- Clinicians planning non-urgent intervention for a known stricture should determine the length and location of the urethral stricture. *(Expert Opinion)*

- Surgeons may utilize urethral endoscopic management (e.g. urethral dilation or direct visual internal urethrotomy [DVIU]) or immediate suprapubic cystostomy for urgent management of urethral stricture, such as discovery of systematic urinary retention or catheterization prior to another surgical procedure. *(Expert Opinion)*

- Surgeons may place a suprapubic (SP) cystostomy prior to definitive urethroplasty in patients dependent on an indwelling urethral catheter or intermittent self-dilation. *(Expert Opinion)*

**Dilation/Internal Urethrotomy/Urethroplasty**

- Surgeons may offer urethral dilation, DVIU, or urethroplasty for the initial treatment of a short (< 2 cm) bulbar urethral stricture. *(Conditional Recommendation; Evidence Level: Grade C)*

- Surgeons may perform either dilation or DVIU when performing endoscopic treatment of a urethral stricture. *(Conditional Recommendation; Evidence Level: Grade C)*
Surgeons may safely remove the urethral catheter within 72 hours following uncomplicated dilation or DVIU. *(Conditional Recommendation; Evidence Level: Grade C)*

In selected patients who are not candidates for urethroplasty, clinicians may recommend self-catheterization after DVIU to maintain urethral patency. *(Conditional Recommendation; Evidence Level: Grade C)*

Surgeons should offer urethroplasty, instead of repeated endoscopic management for recurrent anterior urethral strictures following failed dilation or DVIU. *(Moderate Recommendation; Evidence Level: Grade C)*

Surgeons who do not perform urethroplasty should offer patients referral to centers with expertise. *(Expert Opinion)*

**Anterior Urethral Reconstruction**

Surgeons may initially treat meatal or fossa navicularis strictures with either dilation or meatotomy. *(Clinical Principle)*

Surgeons should offer urethroplasty to patients with recurrent meatal or fossa navicularis strictures. *(Moderate Recommendation; Evidence Level: Grade C)*

Surgeons should offer urethroplasty to patients with penile urethral strictures, because of the expected high recurrence rates with endoscopic treatments. *(Moderate Recommendation; Evidence Level: Grade C)*

Surgeons should offer urethroplasty as the initial treatment for patients with long (≥2cm) bulbar urethral strictures, given the low success rate of DVIU or dilation. *(Moderate Recommendation; Evidence Level: Grade C)*
• Surgeons may reconstruct long multi-segment strictures with one stage or staged techniques using oral mucosal grafts, penile fasciocutaneous flaps or a combination of these techniques. *(Moderate Recommendation; Evidence Level: Grade C)*

• Surgeons may offer perineal urethrostomy as a long term treatment option to patients as an alternative to urethroplasty. *(Conditional Recommendation; Evidence Level: Grade C)*

• Surgeons should use oral mucosa as the first choice when using grafts for urethroplasty. *(Expert Opinion)*

• Surgeons should not perform substitution urethroplasty with allograft, xenograft, or synthetic materials except under experimental protocols. *(Expert Opinion)*

• Surgeons should not perform a single-stage tubularized graft urethroplasty. *(Expert Opinion)*

• Surgeons should not use hair-bearing skin for substitution urethroplasty. *(Clinical Principle)*

**Pelvic Fracture Urethral Injury**

• Clinicians should use retrograde urethrography with voiding cystourethrogram and/or retrograde + antegrade cystoscopy for preoperative planning of urethroplasty after pelvic fracture urethral injury (PFUI). *(Moderate Recommendation; Evidence Level: Grade C)*

• Surgeons should perform delayed urethroplasty instead of delayed endoscopic procedures after urethral obstruction/obliteration due to PFUI. *(Expert Opinion)*

• Definitive urethral reconstruction for PFUI should be planned only after major injuries stabilize. *(Expert Opinion)*
Bladder Neck Contracture/Vesicourethral Stenosis

- Surgeons may perform a dilation, bladder neck incision or transurethral resection for bladder neck contracture after endoscopic prostate procedure. (*Expert Opinion*)
- Surgeons may perform a dilation, vesicourethral incision, or transurethral resection for post-prostatectomy vesicourethral anastomotic stenosis. (*Conditional Recommendation; Evidence Level: Grade C*)
- Surgeons may perform open reconstruction for recalcitrant stenosis of the bladder neck or post-prostatectomy vesicourethral anastomotic stenosis. (*Conditional Recommendation; Evidence Level: Grade C*)

Special Circumstances

- In men who require chronic self-catheterization (e.g. neurogenic bladder), surgeons may offer urethroplasty as a treatment option for urethral stricture causing difficulty with intermittent self-catheterization. (*Expert Opinion*)
- Clinicians may perform biopsy for suspected lichen sclerosus (LS), and must perform biopsy if urethral cancer is suspected. (*Clinical Principle*)
- In LS proven urethral stricture, surgeons should not use genital skin for reconstruction. (*Strong Recommendation; Evidence Level: Grade B*)

Post-operative Follow-up

- Clinicians should monitor urethral stricture patients to identify symptomatic recurrence following dilation, DVIU or urethroplasty. (*Expert Opinion*)
ADULT URODYNAMICS

AUA/SUFU GUIDELINE – 2012

This AUA Guideline on Urodynamics is intended to review the literature regarding the use of urodynamic testing in common lower urinary tract disorders. It presents the principles of urodynamic application and technique in order to guide the clinician in the most effective utilization of these studies. Urodynamics (UDS) is the dynamic study of the transport, storage and evacuation of urine. UDS is an interactive diagnostic study of the lower urinary tract composed of a number of tests that can be used to obtain functional information about urine storage and emptying. Urodynamic studies are only one part of the comprehensive evaluation of lower urinary tract symptoms (LUTS). The findings of this guideline are intended to assist the clinician in the appropriate selection of urodynamic tests following an appropriate evaluation and symptom characterization. Clinicians evaluating these disorders utilize history, physical examination, questionnaires and pad testing data collectively in the evaluation of these symptoms.

This systematic review evaluated the following urodynamic tests: post-void residual (PVR); uroflowmetry, cystometry, pressure-flow studies; videourodynamics; EMG; urethral function tests: abdominal leak point pressure (ALPP) or valsalva leak point pressure (VLPP), urethral pressure profile, maximum urethral closure pressure (MUCP); or any combination of the above tests. This review examined the role of these tests in: diagnosis, prognosis, clinical management decisions and patient outcomes.
The target populations comprised adults with the following: stress urinary incontinence (SUI) and pelvic organ prolapse; overactive bladder (OAB), urgency urinary incontinence, mixed incontinence; lower urinary tract symptoms (LUTS); and neurogenic bladder (NGB).

**Guideline Statements**

**SUI/Prolapse**

- Clinicians who are making the diagnosis of urodynamic stress incontinence should assess urethral function.
  - During multi-channel UDS, the clinical tools necessary for the assessment of urethral function are already in place.
  - A quantitative assessment, such as VLPP or MUCP, should be performed.
  - Information regarding urethral function may be used to guide surgical treatment decisions.

- Surgeons considering invasive therapy in patients with SUI should assess post-void residual (PVR) urine volume.
  - An elevated PVR suggests an abnormality of bladder emptying.
  - Patients with an elevated preoperative PVR may be at an increased risk for transient or permanent postoperative voiding difficulties following intervention.

- Clinicians may perform multi-channel urodynamics in patients with both symptoms and physical findings of stress incontinence who are considering invasive, potentially morbid or irreversible treatments.
  - Multi-channel UDS are an optional preoperative study in the patient considering surgery for SUI.
  - UDS may confirm or refute a clinical diagnosis, facilitate treatment selection and patient counseling.
- UDS may be particularly helpful in complicated patients: previous surgery, mixed storage symptoms or symptoms of impaired emptying.

- Clinicians should perform repeat stress testing with the urethral catheter removed in patients suspected of having SUI who do not demonstrate this finding with the catheter in place during urodynamic testing.

- Some patients with SUI determined during the physical examination will not have the finding of SUI with a urethral catheter in place.

- Removal of the urodynamic catheter will allow demonstration of SUI with repeat stress maneuvers.

- Care must be taken to preserve the sterility of the urethral catheter.

- In women with high grade pelvic organ prolapse (POP) but without the symptom of SUI, clinicians should perform stress testing with reduction of the prolapse. Multi-channel urodynamics with prolapse reduction may be used to assess for occult stress incontinence and detrusor dysfunction in these women with associated LUTS.

- A significant proportion of women with high grade POP who do not have the symptom of SUI will be found to have occult SUI, after reduction of the prolapse.

- If the presence of SUI would change the surgical treatment plan, stress testing with reduction of the prolapse to evaluate for occult SUI should be performed.

- Multi-channel UDS can also assess for the presence of detrusor dysfunction in women with high grade POP. In women with clinical suspicion(s) of bladder dysfunction, UDS may be helpful in the prediction of postoperative bladder function following surgery.
Overactive Bladder (OAB), Urgency Urinary Incontinence (UUI), Mixed Incontinence

- Clinicians may perform multi-channel filling cystometry when it is important to determine if altered compliance, detrusor overactivity or other urodynamic abnormalities are present (or not) in patients with urgency urinary incontinence in whom invasive, potentially morbid or irreversible treatments are considered.
  - Multi-channel cystometry is preferred over a single channel “simple” cystometrogram.
  - Urodynamic findings of storage abnormalities include: detrusor overactivity, increased filling sensation, and abnormalities of compliance.
  - Compliance determination is a very important measurement, particularly in patients with neurogenic conditions.
  - UDS may have a role in the clinical circumstances where conservative and drug therapies fail in a patient who desires more invasive treatment options for OAB. UDS findings may ultimately effect treatment decision.

- Clinicians may perform pressure flow studies (PFS) in patients with refractory urgency urinary incontinence after bladder outlet procedures to evaluate for bladder outlet obstruction (BOO).
  - Symptoms of bladder storage failure may present as a consequence of bladder outlet obstruction following anti-incontinence surgeries.
  - PVR volumes alone cannot diagnose bladder outlet obstruction.
  - In women with storage symptoms refractory to treatment following anti-incontinence surgery, UDS can be utilized to identify outlet obstruction.
Clinicians should counsel patients with urgency urinary incontinence and mixed incontinence that the absence of detrusor overactivity (DO) on a single urodynamic study does not exclude it as a causative agent for their symptoms.

- UDS may not diagnose DO even in patients who are very symptomatic. UDS in these patients should be interpreted in the context of overall clinical assessment.
- UDS may be useful in determining the presence or absence of other factors (SUI, BOO) that could influence treatment decisions.

**Neurogenic Bladder**

Clinicians should perform PVR assessment, either as part of a complete urodynamic study or separately, during the initial urological evaluation of patients with relevant neurological conditions (such as spinal cord injury and myelomeningocele) and as part of ongoing follow-up when appropriate.

- PVR is a useful tool for assessing the possibility of significant bladder and/or outlet dysfunction.
- Evaluation with PVR assessment is appropriate both at the time of diagnosis and after to monitor for changes in bladder emptying ability periodically.
- PVR assessment has been shown to influence treatment planning in a variety of neurological conditions.
- The implications of an elevated PVR in neurogenic voiding dysfunction include the development of UTIs, urosepsis, upper tract deterioration and stone disease.

Clinicians should perform a complex cystometrogram (CMG) during initial urological evaluation of patients with relevant neurological conditions with or without
symptoms, and as part of ongoing follow-up when appropriate. In patients with other neurologic diseases, physicians may consider CMG as an option in the urological evaluation of patients with LUTS.

- CMG in patients with neurogenic bladder disorders will give an accurate assessment of bladder storage.
- The maintenance of low intravesical pressures is a clinical principle, originally described in patients with myelomeningocele that has been adopted for other neurological conditions, such as spinal cord injury.
- CMG provides diagnostic, therapeutic and prognostic information in select patients with neurogenic bladder.

- Clinicians should perform pressure flow analysis in patients with relevant neurologic disease with or without symptoms, or in patients with other neurologic disease and elevated PVR or urinary symptoms.
  - Pressure flow studies (PFS) are an appropriate component of the work-up of NGB, particularly for patients at risk for or found to have elevated PVR, hydronephrosis, pyelonephritis, complicated UTIs and frequent episodes of autonomic dysreflexia.
  - PFS can accurately distinguish between BOO and detrusor hypocontractility/acontractility in NGB patients with emptying disorders.
  - PFS can be used to delineate possible treatment options and monitor outcomes.

- When available, clinicians may perform fluoroscopy at the time of urodynamics (videourodynamic) in patients with relevant neurologic disease at risk for neurogenic bladder, or in patients with other neurologic disease and elevated PVR or urinary symptoms.
Videourodynamic assessment provides anatomic imaging correlation with the functional assessment of PFS.

Videourodyamics improves the diagnosis of: vesicoureteral reflux, bladder trabeculation/diverticuli, bladder stones and bladder neck abnormalities.

Videourodyamics aids in precise localization of the level of obstruction.

**Clinicians should perform electromyography (EMG) in combination with CMG with or without pressure-flow study in patients with relevant neurologic disease at risk for neurogenic bladder, or in patients with other neurologic disease and elevated PVR or urinary symptoms.**

- EMG testing is a useful modality to assist in the diagnosis of detrusor external sphincter dyssynergia (DESD), characterized by involuntary contractions of the external sphincter during detrusor contraction.

- Artifacts are common, and interpretation of EMG requires close interaction between the clinician and the patient.

**Lower Urinary Tract Symptoms**

- Clinicians may perform PVR in patients with LUTS as a safety measure to rule out significant urinary retention both initially and during follow up.

- PVR assessment may identify patients with significant urinary retention, thus decreasing potential morbidity.

- PVR assessment may be utilized to monitor the response to treatment of voiding disorders.

- PVR assessment may be safely performed by ultrasound, without the need for catheterization.
- Uroflow may be used by clinicians in the initial and ongoing evaluation of male patients with LUTS that suggest an abnormality of voiding/emptying.
  - Uroflow measurement provides an objective and quantitative indication of bladder and outlet function.
  - Abnormalities in uroflow may indicate the need for further urodynamic testing, as this indicates a dysfunction in the voiding phase of micturition.
  - Uroflowmetry can also be used for monitoring treatment outcomes and correlating symptoms with objective findings.
  - Clinicians should be aware that uroflow studies (both peak and mean) can be affected by the volume voided and the circumstances of the test.

- Clinicians may perform multi-channel filling cystometry when it is important to determine if detrusor overactivity or other abnormalities of bladder filling/urine storage are present in patients with LUTS, particularly when invasive, potentially morbid or irreversible treatments are considered.
  - The presence of DO or impaired compliance, which may be diagnosed by cystometry, remains an important piece of information in determining treatment options.

- Clinicians should perform pressure flow studies in men when it is important to determine if urodynamic obstruction is present in men with LUTS, particularly when invasive, potentially morbid or irreversible treatments are considered.
  - Bladder outlet obstruction in men is a urodynamic diagnosis.
A diagnosis of obstruction on a PFS may predict a better outcome following surgery than those who are unobstructed.

PFS can be recommended in men seeking surgical therapy for relief of LUTS.

- Clinicians may perform pressure flow studies in women when it is important to determine if obstruction is present.
- PFS should always be correlated with symptoms and other diagnostic tests to obtain the most accurate diagnosis of bladder outlet obstruction in women.
- Documentation of obstruction in women will likely influence treatment decisions, and PFS are one way to obtain this diagnosis.

- Clinicians may perform videourodynamics in properly selected patients to localize the level of obstruction, particularly for the diagnosis of primary bladder neck obstruction (PBNO).
  - Primary bladder neck obstruction is a disorder characterized by a delay or failure of the bladder neck to open during a voluntary detrusor contraction.
  - In young men and women without an obvious anatomic cause of obstruction like benign prostatic obstruction (BPO) in men or POP in women, videourodynamics can differentiate between functional causes of obstruction like PBNO and dysfunctional voiding.
  - PBNO is a videourodynamic diagnosis in which the hallmark is relatively high detrusor pressures in association with low flow and radiographic evidence of obstruction at the bladder neck.
UROTRAUMA

AUA GUIDELINE – 2014; AMENDED – 2017

Purpose

Urologic injury often occurs in the context of severe multisystem trauma that requires close cooperation with trauma surgeons. The urologist remains an important consultant to the trauma team, helping to ensure that the radiographic evaluation of urogenital structures is performed efficiently and accurately, and that the function of the genitourinary system is preserved whenever possible. Immediate interventions for acute urologic injuries often require flexibility in accordance with damage control principles in critically ill patients. In treating urotrauma patients, urologists must be familiar with both open surgical techniques and minimally invasive techniques for achieving hemostasis and/or urinary drainage. The Panel’s purpose is to review the existing literature pertaining to the acute care of urologic injuries in an effort to develop effective guidelines for appropriate diagnosis and intervention strategies in the setting of urotrauma.

Guideline Statements

Renal Trauma

- Clinicians should perform diagnostic imaging with intravenous (IV) contrast enhanced computed tomography (CT) in stable blunt trauma patients with gross hematuria or microscopic hematuria and systolic blood pressure < 90mmHg.

- Clinicians should perform diagnostic imaging with IV contrast enhanced CT in stable trauma patients with
mechanism of injury or physical exam findings concerning for renal injury (e.g., rapid deceleration, significant blow to flank, rib fracture, significant flank ecchymosis, penetrating injury of abdomen, flank, or lower chest).

- Clinicians should perform IV contrast enhanced abdominal/pelvic CT with immediate and delayed images when there is suspicion of renal injury.
- Clinicians should use non-invasive management strategies in hemodynamically stable patients with renal injury.
- The surgical team must perform immediate intervention (surgery or angioembolization in selected situations) in hemodynamically unstable patients with no or transient response to resuscitation.
- Clinicians may initially observe patients with renal parenchymal injury and urinary extravasation.
- Clinicians should perform follow-up CT imaging for renal trauma patients having either (a) deep lacerations (AAST Grade IV-V) or (b) clinical signs of complications (e.g., fever, worsening flank pain, ongoing blood loss, abdominal distention).
- Clinicians should perform urinary drainage in the presence of complications such as enlarging urinoma, fever, increasing pain, ileus, fistula or infection.
- Drainage should be achieved via ureteral stent and may be augmented by percutaneous urinoma drain, percutaneous nephrostomy or both.
Ureteral Trauma

- Clinicians should perform IV contrast enhanced abdominal/pelvic CT with delayed imaging (urogram) for stable trauma patients with suspected ureteral injuries.

- Clinicians should directly inspect the ureters during laparotomy in patients with suspected ureteral injury who have not had preoperative imaging.

- Surgeons should repair traumatic ureteral lacerations at the time of laparotomy in stable patients.

- Surgeons may manage ureteral injuries in unstable patients with temporary urinary drainage followed by delayed definitive management.

- Surgeons should manage traumatic ureteral contusions at the time of laparotomy with ureteral stenting or resection and primary repair depending on ureteral viability and clinical scenario.

- Surgeons should attempt ureteral stent placement in patients with incomplete ureteral injuries diagnosed postoperatively or in a delayed setting.

- Surgeons should perform percutaneous nephrostomy with delayed repair as needed in patients when stent placement is unsuccessful or not possible.

- Clinicians may initially manage patients with ureterovaginal fistula using stent placement. In the event of stent failure, clinicians may pursue surgical intervention.

- Surgeons should repair ureteral injuries located proximal to the iliac vessels with primary repair over a ureteral stent, when possible.
● Surgeons should repair ureteral injuries located distal to the iliac vessels with ureteral reimplantation or primary repair over a ureteral stent, when possible.

● Surgeons should manage endoscopic ureteral injuries with a ureteral stent and/or percutaneous nephrostomy tube, when possible.

● Surgeons may manage endoscopic ureteral injuries with open repair when endoscopic or percutaneous procedures are not possible or fail to adequately divert the urine.

**Bladder Trauma**

● Clinicians must perform retrograde cystography (plain film or CT) in stable patients with gross hematuria and pelvic fracture.

● Clinicians should perform retrograde cystography in stable patients with gross hematuria and a mechanism concerning for bladder injury, or in those with pelvic ring fractures and clinical indicators of bladder rupture.

● Surgeons must perform surgical repair of intraperitoneal bladder rupture in the setting of blunt or penetrating external trauma.

● Clinicians should perform catheter drainage as treatment for patients with uncomplicated extraperitoneal bladder injuries.

● Surgeons should perform surgical repair in patients with complicated extraperitoneal bladder injury.

● Clinicians should perform urethral catheter drainage without suprapubic (SP) cystostomy in patients following surgical repair of bladder injuries.
Urethral Trauma

- Clinicians should perform retrograde urethrography in patients with blood at the urethral meatus after pelvic trauma.
- Clinicians should establish prompt urinary drainage in patients with pelvic fracture associated urethral injury.
- Surgeons may place suprapubic tubes (SPTs) in patients undergoing open reduction internal fixation (ORIF) for pelvic fracture.
- Clinicians may perform primary realignment (PR) in hemodynamically stable patients with pelvic fracture associated urethral injury.
- Clinicians should not perform prolonged attempts at endoscopic realignment in patients with pelvic fracture associated urethral injury.
- Clinicians should monitor patients for complications (e.g., stricture formation, erectile dysfunction, incontinence) for at least one year following urethral injury.
- Surgeons should perform prompt surgical repair in patients with uncomplicated penetrating trauma of the anterior urethra.
- Clinicians should establish prompt urinary drainage in patients with straddle injury to the anterior urethra.

Genital Trauma

- Clinicians must suspect penile fracture when a patient presents with penile ecchymosis, swelling, pain cracking or snapping sound during intercourse or manipulation and immediate detumescence.
• Surgeons should perform prompt surgical exploration and repair in patients with acute signs and symptoms of penile fracture.

• Clinicians may perform ultrasound in patients with equivocal signs and symptoms of penile fracture.

• Clinicians must perform evaluation for concomitant urethral injury in patients with penile fracture or penetrating trauma who present with blood at the urethral meatus, gross hematuria or inability to void.

• Surgeons should perform scrotal exploration and debridement with tunical closure (when possible) or orchiectomy (when non-salvagable) in patients with suspected testicular rupture.

• Surgeons should perform exploration and limited debridement of non-viable tissue in patients with extensive genital skin loss or injury from infection, shearing injuries, or burns (thermal, chemical, electrical).

• Surgeons should perform prompt penile replantation in patients with traumatic penile amputation, with the amputated appendage wrapped in saline-soaked gauze, in a plastic bag and placed on ice during transport.

• Clinicians should initiate ancillary psychological, reproductive, and/or interpersonal counseling and therapy for patients with genital trauma when loss of sexual, urinary, and/or reproductive function is anticipated.
VASECOTOMY

AUA GUIDELINE – 2012; AMENDED – 2015

The purpose of this guideline is to aid clinicians who offer vasectomy services by providing a set of approaches and procedures that maximizes successful vasectomy outcomes and minimizes failure and other adverse events.

Preoperative Practice

- A preoperative interactive consultation should be conducted, preferably in person. If an in-person consultation is not possible, then preoperative consultation by telephone or electronic communication is an acceptable alternative.

- The minimum and necessary concepts that should be discussed in a preoperative vasectomy consultation include the following:
  - Vasectomy is intended to be a permanent form of contraception.
  - Vasectomy does not produce immediate sterility.
  - Following vasectomy, another form of contraception is required until vas occlusion is confirmed by post-vasectomy semen analysis (PVSA).
  - Even after vas occlusion is confirmed, vasectomy is not 100% reliable in preventing pregnancy.
  - The risk of pregnancy after vasectomy is approximately 1 in 2,000 for men who have post-vasectomy azoospermia or PVSA showing rare non-motile sperm (RNMS).
  - Repeat vasectomy is necessary in ≤1% of vasectomies, provided that a technique for vas occlusion known to have a low occlusive failure rate has been used.
- Patients should refrain from ejaculation for approximately one week after vasectomy.
- Options for fertility after vasectomy include vasectomy reversal and sperm retrieval with in vitro fertilization. These options are not always successful, and they may be expensive.
- The rates of surgical complications such as symptomatic hematoma and infection are 1-2%. These rates vary with the surgeon’s experience and the criteria used to diagnose these conditions.
- Chronic scrotal pain associated with negative impact on quality of life occurs after vasectomy in about 1-2% of men. Few of these men require additional surgery.
- Other permanent and non-permanent alternatives to vasectomy are available.

- Clinicians do not need to routinely discuss prostate cancer, coronary heart disease, stroke, hypertension, dementia or testicular cancer in pre-vasectomy counseling of patients because vasectomy is not a risk factor for these conditions.
- Prophylactic antimicrobials are not indicated for routine vasectomy unless the patient presents a high risk of infection.

**Anesthesia for Vasectomy**

- Vasectomy should be performed with local anesthesia with or without oral sedation. If the patient declines local anesthesia or if the surgeon believes that local anesthesia with or without oral sedation will not be adequate for a particular patient, then vasectomy may be performed with intravenous sedation or general anesthesia.
Vas Isolation

- Isolation of the vas should be performed using a minimally-invasive vasectomy (MIV) technique such as the no-scalpel vasectomy (NSV) technique or other MIV technique.

Vas Occlusion

The Panel defined the acceptable rate of vas occlusion failure to be \( \leq 1\% \) across multiple studies conducted by different surgeons with large numbers of patients. Failure of vas occlusion includes failure to achieve azoospermia and failure to achieve RNMS. The Panel found four techniques that satisfy the criterion of \( \leq 1\% \) failure rate and, therefore, recommends these four techniques for vas occlusion. These, along with other optional techniques for surgeons with training and/or experience that may produce acceptable failure rates, can be found in Figure 1.

- The ends of the vas should be occluded by one of three divisional methods:
  - Mucosal cautery (MC) with fascial interposition (FI) and without ligatures or clips applied on the vas;
  - MC without FI and without ligatures or clips applied on the vas;
  - Open ended vasectomy leaving the testicular end of the vas unoccluded, using MC on the abdominal end and FI;

**OR** by the non-divisional method of extended electrocautery.

- The divided vas may be occluded by ligatures or clips applied to the ends of the vas, with or without FI, and with or without excision of a short segment of the vas, by surgeons whose personal training and/or experience
enable them to consistently obtain satisfactory results with such methods.

- Routine histologic examination of the excised vas segments is not required.

**Postoperative Practice**

- Men or their partners should use other contraceptive methods until vasectomy success is confirmed by PVSA.

- To evaluate sperm motility, a fresh uncentrifuged semen sample should be examined within two hours after ejaculation.

- Patients may stop using other methods of contraception when examination of one well-mixed, uncentrifuged, fresh post-vasectomy semen specimen shows azoospermia or only rare non-motile sperm (RNMS or ≤ 100,000 non-motile sperm/mL).

- Eight to sixteen weeks after vasectomy is the appropriate time range for the first PVSA. The choice of time to do the first PVSA should be left to the judgment of the surgeon.

- Vasectomy should be considered a failure if any motile sperm are seen on PVSA at six months after vasectomy, in which case repeat vasectomy should be considered.

- If >100,000 non-motile sperm/mL persist beyond six months after vasectomy, then trends of serial PVSAs and clinical judgment should be used to decide whether the vasectomy is a failure and whether repeat vasectomy should be considered.
FIGURE 1.

Most commonly used vas occlusion techniques and their occlusive failure rates

Definitions and Diagrams:

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