AUA White Paper

NON-NEUROGENIC CHRONIC URINARY RETENTION: CONSENSUS DEFINITION, MANAGEMENT STRATEGIES, AND FUTURE OPPORTUNITIES

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INTRODUCTION

Non-neurogenic chronic urinary retention (CUR) can be challenging to diagnose and treat because there is no consensus on the criteria that define CUR. Associated with either underactive bladder or chronic outlet obstruction, the condition is important because CUR can be associated with hydronephrosis, renal failure, chronic urinary tract infections (UTIs), urinary incontinence, and can lead to a complete inability to void. However, not all patients with CUR necessarily require treatment, and for such patients, interventions can place them at risk for complications. Indwelling and intermittent catheterization can cause UTIs, urethral trauma, and negatively affect quality of life (QOL).[1] Medications and surgical procedures for reducing CUR can likewise cause temporary or permanent harm. Consequently, it is important that clinicians identify patients with CUR at risk for morbidity but not expose all patients with CUR to costly and even potentially harmful interventions.

CUR definitions using physical exam findings have been proposed but have had limited clinical adoption. Instead, many practitioners use an elevated post void residual (PVR) measurement to make a CUR diagnosis. However, a recent Agency for Healthcare Research and Quality (AHRQ) report on CUR specifically mentions a lack of standardization in the literature regarding what PVR constitutes CUR,[2] with the literature using definitions of urinary retention with PVR volumes in men ranging from 100 mL to 1000 mL.[3] The definition of CUR is also poorly documented for women.[4]

This variance in definitions complicates the understanding of the impact of CUR on patient safety and quality of life. On one end of the spectrum, CUR may present as an asymptomatic, incidental finding and patients who are not treated do not suffer morbidity. On the other end, some patients with CUR develop severe urinary symptoms or complications and may even progress to end stage

renal failure. Because CUR encompasses this wide clinical range of findings and potential morbidity, there are few consistent recommendations for practitioners on how to diagnose and manage patients with CUR in either primary or specialty care.

The American Urological Association (AUA) Quality Improvement and Patient Safety (QIPS) Committee has sought to address this knowledge gap related to CUR by creating a White Paper. The goals of this White Paper are to:

1) Characterize patients with CUR into clinically definable index populations in adult men and women (>18 years old).
2) Propose diagnostic and treatment algorithms for these index populations.
3) Propose outcome endpoints for patients with CUR.
4) Identify future areas of research for CUR.

The recommendations in this paper are limited to non-neurological CUR, defined *a priori, based on panel expert opinion and review of literature,* as an elevated PVR of >300 mL that has persisted for at least six months and is documented on two or more separate occasions. This definition differentiates CUR from either acute/transitory urinary retention or urinary retention caused by a temporally related neurologic, oncologic, or traumatic etiology. Urinary retention associated with these conditions is excluded from this definition of CUR, as these conditions require that the underlying cause of urinary retention be addressed as part of treatment and thus need individually more specific recommendations and longitudinal follow-up that address how this urinary retention impacts safety and quality of life. Recommendations for this White Paper are based on a review of the literature and consensus expert opinion of the CUR White Paper panel. The target audience for this White Paper is both primary care providers who may initially

encounter the qualifying patient with urine residuals >300 mL twice over a six-month period, as well as urology and urogynecology providers who follow and treat these patients.

METHODOLOGY

This topic was submitted for development of a comparative effectiveness review from the US Department of Health and Human Services Agency for Healthcare Research and Quality (AHRQ) and was published in September 2014, based on a thorough search of the literature from 1946 through March 2016. The AUA expanded the key questions of this evidence report, providing membership and support through the QIPS to develop this White Paper on the topic. Representatives were also included from the Society for Urodynamics and Female Pelvic Medicine and Urogential Reconstruction (SUFU) and the Society of Genitourinary Reconstructive Surgeons.

BACKGROUND

There are no accepted, standardized criteria for diagnosing CUR, and existing definitions carry significant limitations regarding universal application. The most specific urinary retention definition comes from the International Continence Society (ICS), which has defined subcategories of retention as: 1) ability of patient to release any urine (complete or partial); 2) duration (acute or chronic); 3) symptoms (painful or silent); 4) mechanism (obstructive or non-obstructive); and 5) urodynamic findings (high or low pressure).[5] This definition does not define PVR volume ranges but notes that >300 mL is commonly used because Abrams et al. reported that it is the minimal volume at which a bladder becomes palpable.[6] The UK National Institute for Health and Clinical Excellence guidelines for lower urinary tract symptoms (LUTS) imply a broader definition of CUR in men as a PVR of >1000 mL.[7] The UK National Health Service (NHS) has developed a treatment algorithm for CUR in men, but the pathway is not commonly utilized outside the NHS

and does not apply to women. Few other resources exist regarding a CUR definition, and contemporary review articles focus more on describing symptoms and heterogeneity rather than specific inclusion criteria for the condition.[8] The work group chose >300 mL as the threshold value based on previously published convention and lack of other directional guidance from the literature.

Both men and women may develop urinary retention from obstruction of the bladder outlet, as well as from abnormalities in detrusor contractility. A common cause of urinary retention is bladder outlet obstruction (BOO).[9] BOO may result from mechanical obstruction of the outlet because of prostate/bladder neck enlargement or urethral stricture; vaginal vault prolapse; obstructing suburethral sling; or impacted stool. The most common sources of bladder outlet obstruction in males are benign prostatic enlargement and prostate cancer,[10-12] while the most common cause of outlet obstruction in women has not been well categorized in the literature. Long-term use of medications, such as alpha agonists and tricyclic antidepressants, may also be underappreciated and underreported sources of chronic BOO. While neurologic conditions leading to CUR are not the subject of this review, detrusor sphincter dyssynergia is also an anatomic cause of BOO. Other physiologic derangements not related to an underlying neurologic condition such as primary bladder neck dysfunction, pelvic floor dyssynergia, and Fowler's syndrome can cause CUR in both sexes as well. CUR can also result from decreased bladder wall contractility. Table 1 reviews common causes of CUR.

DEFINING CUR

Although CUR is often described using terms such as atonic detrusor, this term is a urodynamic description of absence of detrusor contractility and can be used only in context of urodynamic data. However, a diagnosis of an atonic detrusor during urodynamic study (UDS) does not always

imply that the detrusor is unable to contract, only that it is not seen during the study. CUR has been more recently linked with the terms primary bladder muscle underactivity and underactive bladder. The ICS has described primary bladder muscle underactivity as "a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying within a normal time span."[6,14,15] Thus, a CUR definition overlaps with the definitions of detrusor underactivity (DU) and underactive bladder (Figure 1), but differs because CUR is a clinical definition and does not require urodynamic testing to investigate detrusor function.

Non Neurogenic CUR is empirically defined herein as an elevated PVR of >300 mL that has persisted for at least six months documented on two or more separate occasions. PVR can be measured by any modality (i.e., catheterization or bladder scanner). At least two documentations are recommended to reduce the potential of situational false positives, such as supra-physiologic fluid intake, inadequate time to complete void, and anxiety. Elevated PVRs in the literature range from >100 mL to >500 mL,[3,16] while others advocate not assigning a numerical value to PVR to diagnose urinary retention.[17] The value of >300 mL is used in much of the literature;[3,4,18-22] therefore, PVR >300 mL will be used to define CUR for the purposes of the development of this proposed treatment algorithm, while recognizing that no single PVR value independently and sufficiently defines CUR. The value will also apply for both men and women since differentiating data does not currently exist. A cutoff value of CUR has also been proposed based on a percentage of the total volume remaining after voiding. The work group recognizes the potential value of this calculation but did not include it in the current CUR definition due to a paucity of data on creating such a reference range and the added challenges associated with attempting to accurately measure and calculate true voided versus retained volumes. Future studies may be able to refine these definitions of CUR.

CATEGORIES OF CUR

Because CUR is a clinical sign and not a uniform diagnosis, CUR presents and behaves differently in different populations. For example, a 70-year-old male with CUR resulting in bilateral hydroureteronephrosis, recurrent urinary tract infections, azotemia, and elevated serum creatinine differs in prognosis from a 70-year-old asymptomatic male with an incidentally discovered elevated PVR and no additional radiologic or laboratory findings. For this reason, categories of CUR were developed based on risk (high versus low) and symptomatology (symptomatic versus asymptomatic).

High-risk CUR

The term "high-risk" defines a subset of individuals with CUR who are at potentially elevated risk for organ system harm or failure resulting from CUR. These categories were developed based on consensus expert opinion in combination with a review of the literature, and are subject to further refinement as the evidence base accrues. Table 2 demonstrates the radiologic findings, laboratory findings, and clinical signs and symptoms believed to be associated with high-risk CUR. Radiologic findings implying potential high-risk CUR include presence or development of hydronephrosis, hydroureter, and/or bladder stones. High-risk laboratory findings include indications of stage 3 chronic kidney disease (CKD), defined as an eGFR (glomerular filtration rate) of 45 to 59 mL/min/1.73 m^2 (stage 3A) or 30 percent to 44 percent (stage 3B).[23] Recurrent symptomatic UTIs, defined *a priori* as any pyelonephritis or three or more UTIs in a twelve-month period, and any episode of urosepsis in a six-month period, are additional indications of high-risk CUR.[24] Recurrent symptomatic UTI implies the presence of recurrent irritative symptoms in the setting of pyuria and a positive urine culture. The work group considers recurrent UTIs as a

high-risk category because they can result in significant morbidity to patient and burden to healthcare system.[25] The work group recommends that UTIs be documented in patients with CUR through urine microscopy and cultures to avoid confusion with other underlying urinary symptoms.

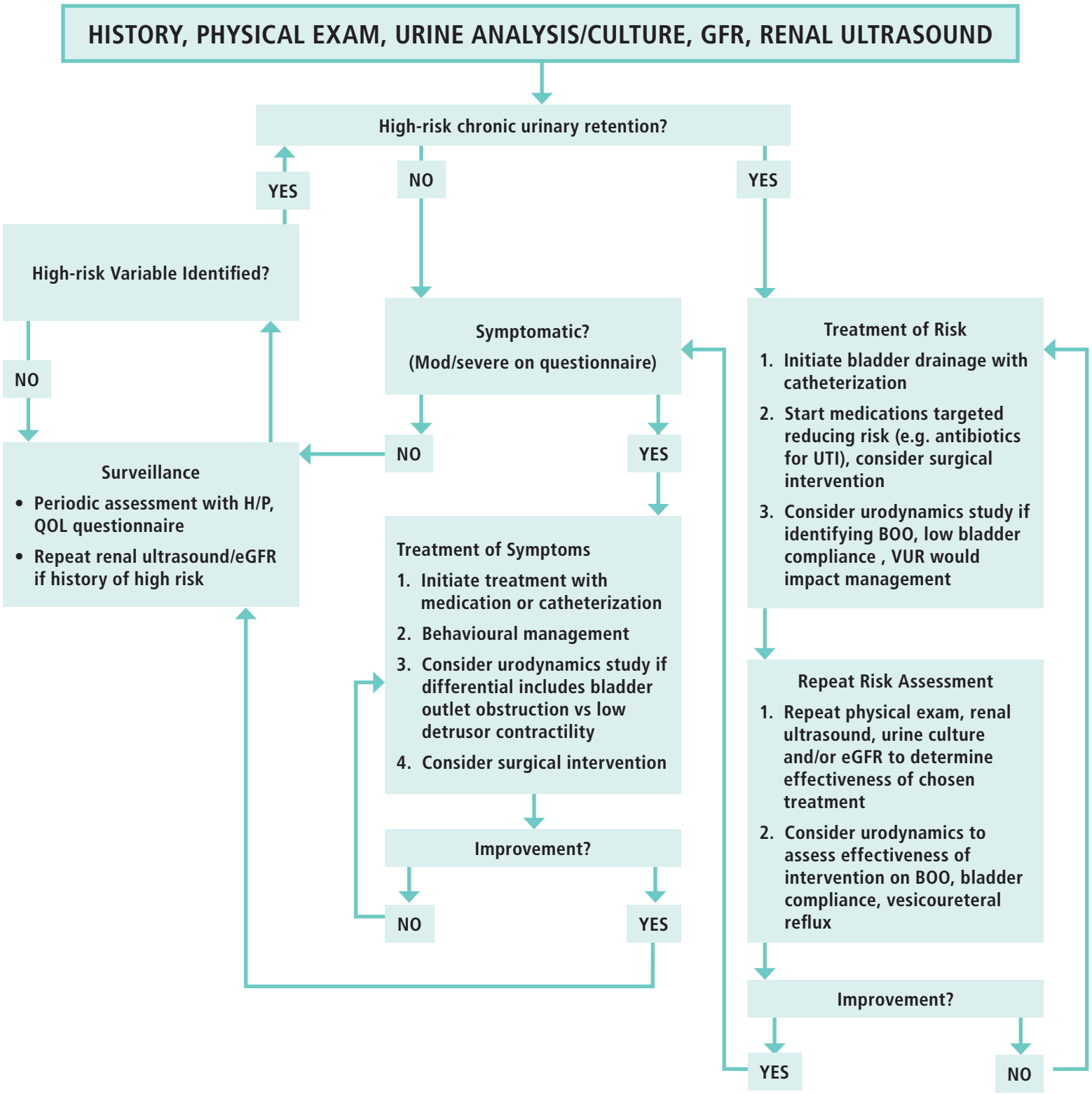
Some subjective signs and symptoms can also be considered high-risk in certain clinical scenarios. For example, overflow urinary incontinence causing perineal skin changes, ranging in severity from superficial genitocrural yeast and/or chemical dermatitis to skin ulcers.

CUR in association with immunosuppression from medications or disease, including diabetes, does not currently place patients into a high-risk category, due to the lack of data. Longitudinal and comparative data are needed to discern risks. Similarly, apart from renal disease and upper tract obstruction, concurrent other medical conditions *a priori* do not move the patient into a high-risk category.

Symptomatic CUR

Symptomatic CUR is defined as: 1) having subjectively moderate to severe urinary symptoms impacting QOL on a validated urinary questionnaire and/or 2) history of requiring catheterization for treatment of a symptomatic episode of inability to void within last six months, excluding acute onset or urinary retention caused by oncologic, traumatic, or any neurologic event. The use of a specific individual questionnaire is not mandated; however, questionnaires should be validated, useable longitudinally to assess symptomatic change, and able to differentiate mild from moderate/severe symptoms. The AUA Symptom Index (AUA-SI) is one example of a readily available and widely used index that would be appropriate to use for this purpose in men.[26]

Non Neurogenic Chronic Urinary Retention Treatment Algorithm



TREATMENT ALGORITHM

The proposed CUR Treatment Algorithm is predicated on stratifying CUR patients first by risk and then by symptoms. All patients with urinary retention should undergo a thorough history and physical examination, including an exam of genitals and rectum, as multiple medical conditions can present with CUR, including pelvic malignancies in both males and females. Urine should be assessed with a urine analysis for possible urinary tract infection and confirmed with a urine culture if needed. Due to the inability to determine risk to the upper tracts at time of presentation, it is recommended by the work group that patients with CUR undergo serum creatinine evaluation and upper tract imaging with a renal ultrasound. Although it is the AUA's recommendation that men with benign prostatic hyperplasia (BPH) should not be routinely screened with ultrasound for hydronephrosis (*Choosing Wisely* Campaign),[27] this work group recommends a renal ultrasound for individuals with CUR as the relationship between PVR volume and upper tract risk has not been defined in the literature. We recognize that the majority of these studies will not demonstrate upper tract changes from obstruction, but the prevalence of upper tract changes in a large cohort of patients with CUR is unknown at the present time. More prospective research is needed to accurately discern phenotypes at risk for CUR-related renal failure.

In high-risk individuals, a trial length of bladder drainage, such as intermittent catheterization or indwelling catheter, should be considered to determine if improved bladder emptying will reduce the identified high risk variable. Similarly, a trial of intermittent catheterization may facilitate the treatment of a UTI and/or reduce urinary incontinence. Weak evidence suggests that intermittent catheterization is preferable to indwelling catheters for bladder drainage.[28-31] While often assumed, the absolute risk reduction of UTI is unknown when CUR is treated with intermittent catheterization. Comparative studies defining the prevalence of symptomatic UTIs and the long-

term risks associated with urosepsis remain poorly defined in the treated CUR population. Future studies should determine the success rates of different treatment strategies.

Although indwelling catheterization can be used as immediate short-term management for CUR associated with high risk, it is the panel's expert opinion that intermittent catheterization is preferable long-term care for patients who can physically perform the task or have a caregiver available to assist. Long-term bladder drainage with an indwelling catheter is associated with risk of morbidity,[28,32] regardless of whether the catheter is placed intraurethral or as a suprapubic tube.[33]

Urodynamic assessment may be considered if a potential therapeutic intervention may be appropriate. Urodynamic assessment should also be considered if the provider suspects low bladder compliance (<15 mL/cm H_2O)[34] since this may be associated with observed hydronephrosis or chronic UTIs. Video urodynamics should be used if vesicoureteral reflux is thought to be contributing to high-risk symptoms, signs, or findings.

High risk variables should be assessed, addressed and improvement should be observed if present. CUR patients are then stratified by remaining urinary symptoms, although symptoms may also improve through treatment of an identified high risk variable. Based on lack of evidence for efficacy and a known probability of developing complications, the CUR work group recommends that patients falling under the low-risk, asymptomatic CUR designation should not be offered intermittent catheterization or any procedure designed to reduce the measured post void residual.

Furthermore, when evaluating and managing low-risk asymptomatic CUR, non-invasive measurement is preferable to catheterization in these patients since catheterization can lead to morbidity such as infection, bleeding, or trauma.

Symptomatic patients should be managed conservatively if the urinary symptoms cause low impact on a person's quality of life. If bothersome symptoms are present, the patient and physician

should target symptoms for treatment, discuss risk and benefits of the treatment plan, and propose a follow-up plan to determine effectiveness of the treatment [35,36] If a symptomatic CUR patient does not respond to catheterization and/or medications, the patient can be reassessed with urodynamics including a pressure flow study if a surgical intervention could be beneficial.

The work group recommends that CUR patients be followed over time for both changes in risk and urinary symptoms. Follow-up should include at least a yearly interval history and physical exam, PVR measurements, and assessment of symptoms, preferably with validated QOL questionnaires. Patients can be followed at shorter intervals and if practitioners feel closer surveillance is warranted. Patients with previous high risk factors of altered GFR or upper tract findings on imaging should be also followed with serum electrolytes and renal ultrasound. In the absence of active stone disease, prior findings of hydronephrosis, or newly identified risk high factors, there is no current clinical indication for longitudinal imaging of the kidneys for patients with low-risk CUR. If patients report changes in urinary symptoms, or these are noted on validated questionnaires, the provider should initiate discussion regarding treatment options, risks, and benefits.

INDEX PATIENT EXAMPLES OF CUR CATEGORIES AND ALGORITHM:

1) A 50-year-old man presents for evaluation of urinary frequency, hesitancy, slow stream, and nocturia. A work-up reveals an AUA-SI >15, a 50-g prostate on digital rectal exam, normal urinalysis, and a measured PVR of 350 ml. Timed voiding and fluid management strategies were started with little improvement, and a second PVR obtained six months later demonstrated a PVR of 450 mL. Subsequent renal ultrasound and renal panel showed no abnormalities. (Low Risk/Symptomatic)

The work group would recommend that this symptomatic patient could be offered CIC and/or alpha blocker/DTH antagonist medication to address symptoms impacting on his quality of life. Longitudinal surveillance and effectiveness of the treatments over time can be measured through validated questionnaires. Because of the concurrent risks of an indwelling catheter (e.g., colonization, infections, discomfort, etc.), an indwelling catheter would be an inappropriate choice for this man. Alternatively, a formal evaluation for an additional component of outlet obstruction with a UDS might determine that the patient should consider an outlet procedure as a future alternative.

2) A 77-year-old man with a history of congestive heart failure and intermittent diuretic use has four culture-proven UTIs over the past three months. He reports a long history of bothersome, irritative LUTS, which are confirmed on a urinary-specific questionnaire. Evaluation reveals an approximately 60-g prostate, two separate PVR measurements over six months of >500 mL, and urinalysis positive for leukocyte esterase, nitrites, and crystals. Renal ultrasound shows mild-moderate hydronephrosis and a 3-cm bladder stone. Renal panel shows a eGFR of 60. (High Risk/Symptomatic).

The work group would recommend initiating immediate catheterization to address recurrent UTIs and renal ultrasound findings. Either intermittent catheterization or a short course of an indwelling catheter can be used to determine impact of draining bladder on upper tract findings. Consider evaluation for a possible outlet procedure and lithotripsy, if medically cleared for an anesthetic. Should he fail medical clearance, he could perform CIC or consider suprapubic tube with longitudinal surveillance for both signs and symptoms of further decompensation of his upper tract changes and QOL.

3) A 75-year-old female with no urologic symptoms, prior urologic history, or neurologic comorbidity presents to the emergency room with hip pain after a fall. A CT scan shows a distended bladder with no hydronephrosis. Physical exam shows mild vaginal vault prolapse. Subsequent post void ultrasounds confirm a persistent PVR of 400 mL. No further abnormalities are noted on the renal panel, and the patient reports no current or past urinary symptoms and no symptoms of vaginal vault prolapse. After completing rehabilitation, the patient reports no urinary symptoms or UTIs but continues to have a PVR >400 mL on re-evaluation eight months later. (Low Risk/Asymptomatic)

The work group would recommend longitudinal surveillance for this low-risk individual.

4) An 80-year-old man with a distant history of transurethral resection of the prostate (TURP) and chronically elevated PVR but no bothersome urinary symptoms is found to have a markedly elevated serum potassium and eGFR of 20 mL/min during a routine medical exam. Renal ultrasound reveals severe bilateral hydroureteronephrosis and a PVR of 1,800 mL. (High Risk/Asymptomatic)

The work group accepts that this patient has CUR, albeit in the absence of two separate PVRs over 6 months. His PVR is consistent with longstanding bladder decompensation. Due to the profound upper tract changes with azotemia, a short course of an indwelling catheter is recommended to determine the reversibility of the severe metabolic changes associated with his decompensated CUR. Should this patient have significant improvement of his azotemia and be able to be compliant with intermittent catheterization, he should be converted to CIC and followed longitudinally for both safety and QOL concerns. Urodynamic and cystoscopic evaluation can be performed after stabilization to identify cause and potential interventions.

CURRENT MANAGEMENT FOR CUR

Once the threshold for intervention for CUR has been met (Table 3), multiple options are available for treatment. After treatment, the clinical indication metric that triggered the intervention should be followed to ensure that it improves or at least does not progress. Medications, self-catheterization, indwelling catheters, and surgical interventions are all possible options for treatment of CUR with varying degrees of efficacy.

Medication:

Medications used to treat outlet obstruction caused by the prostate in men, particularly alpha-blockers and 5-alpha-reductase inhibitors,[37] are generally indicated for older men with CUR and benign prostates. These are well described in the AUA BPH guidelines, but it is important to note that patients with acute urinary retention are more likely to pass a trial of void if started on alpha-blockers.[38] Primary bladder neck obstruction associated with CUR can be treated in both genders with alpha-blockers; however, the use of alpha-blockers in women with more global CUR without defined BOO appears to have marginal or no benefit.[39]

Bethanechol, a cholinergic agonist, has been used to improve bladder contractility in patients with non-obstructive CUR. Although occasionally patients show marginal improvement in PVR when administered bethanechol,[40] the medication has a significant the adverse event (AE) profile. Common AEs associated with bethanechol include drowsiness, nausea, abdominal pain, and headache. Less common but more severe side effects include bronchospasm and hypotension.[41]. The CUR White Paper Work Group does not recommend this medication for routine treatment of CUR, based on the potential adverse events and lack of efficacy.

Catheterization:

Unless anatomic obstruction prohibits catheterization, a regimen of intermittent catheterization is a reasonable option for treatment of symptomatic CUR. However, there are no standards regarding optimal catheterization interval or the types of catheters to use. Per a Cochrane review examining 31 trials, there is no convincing evidence that the incidence of UTI during intermittent catheterization is affected by use of aseptic or clean technique, coated or uncoated catheters, self-catheterization or catheterization by others, or by any other strategy.[42] The consensus of the CUR White Paper work group is that clean intermittent catheterization (CIC) should be performed frequently enough to effectively target reduction of risk and symptoms and should be tailored for the individual treatment plan. Practitioners should discuss the possibility of UTI and urethra trauma with patients before initiating treatment.

If an indwelling catheter is needed for long-term care, it is the CUR work group's recommendation that a suprapubic catheter is preferable to a urethral catheter. Patients using a suprapubic catheter should have the tube changed at least every four weeks and be monitored for UTI and progressive urinary incontinence. Patients being managed with a urethral catheter should have regular physical exams to identify urethral erosion. Similar to a suprapubic catheter, a urethral catheter should be exchanged at least monthly.

Surgical Treatments of CUR:

Surgical management of CUR is dictated by the etiology of CUR. In men, obstructive causes are either due to an enlarged prostate, bladder neck obstruction, or urethral stricture disease. Multiple surgical techniques are available for the treatment of LUTS/BPH and are detailed in many comprehensive reviews.[37] Each modality has specific risks, benefits, and likely target populations who can benefit from treatment. Urethral strictures in men can be treated by a variety of

endoscopic or open surgical means with varying degrees of success primarily based on location, etiology of stricture, and length of the stricture.[43]

Chronic BOO in women can be iatrogenic and it most often associated with a prior mid-urethral sling placement. CUR due to this etiology can be treated with simple sling incision,[44,45] with the understanding that some women could suffer from recurrent urinary incontinence after the sling is divided. Other treatable causes of BOO in women are high-grade pelvic organ prolapse causing BOO and primary BOO. Multiple options are available to correct pelvic organ prolapse including pessary placement, vaginal, laparoscopic, or abdominal repairs. Older case studies suggest that these modalities are effective.[46,47] . Primary bladder neck obstruction in women can also be surgically treated with transurethral incision of the bladder neck.[48]

CUR due to decreased bladder contractility can also be treated surgically, albeit with less certainty. Outlet procedures may be an option for men with benign prostates and decreased bladder contractility who do not want catheterization, and some data support efficacy. [49] Patients with a history of radical prostatectomy and evidence of CUR should be evaluated with cystoscopy to rule out iatrogenic causes of obstruction. [50]

Sacral neuromodulation is approved by the FDA for the treatment of non-obstructive urinary retention in men or women and can be used in patients with decreased bladder contractility. A recent meta-analysis of 14 studies confirmed the efficacy of sacral neuromodulation for non-obstructive urinary retention noting a mean decrease in PVR of 236 mL.[51]

Experimental surgical techniques for treating CUR associated with neurogenic dysfunction such as nerve re-routing and latissmus dorsi myoplasty have limited long-term data in a highly selected population.[52,53]. Similarly, reductive techniques such as bladder diverticulectomy and reduction

cystoplasty remain the subject of small case reports.[54-56]. The CUR White Paper group does not recommend these treatments for routine CUR patients.

IDENTIFICATION OF OUTCOME MEASURES FOR CUR

As there has previously been no agreement on a shared definition of CUR, there is a lack of high-quality evidence for outcomes of interest for treatments of patients with this condition.[2] The work group recommends that four primary CUR outcomes, if applicable to the population and intervention, should be assessed in patients with CUR:

1. Symptoms improvement, as measured by quality questionnaires
2. Risk reduction, as defined by resolution of hydronephrosis, renal failure, recurrent UTI, urosepsis, and secondary complications from overflow incontinence
3. Successful trail of voiding without catheterization
4. Stability of symptoms and risk over time

As the medical risks associated with CUR are not defined, longitudinal assessment of these patients should consider other medical conditions that may impact outcomes. As such, a full medical history and physical examination, including cognition and functional ADLs, as well as other pelvic functions, should be undertaken at diagnosis and during follow up. For example, while the incidence of UTIs is increased in diabetic patients, it is unknown if this patient population has a higher incidence of high risk of poor outcomes from associated CUR. Similarly unknown are the risks posed by CUR in patients with immunosuppression.

Standardized outcome measures for CUR treatments may help stimulate comparative treatments and identify a best practice related to specific patient types. Accordingly, the work group

recommends longitudinal studies to assess the validity for these outcomes measures and help understand the prevalence of low-risk patients becoming high-risk over time.

KNOWLEDGE GAPS/OPPORTUNITIES

Despite the significant potential risk attributed to CUR, much remains uncertain with regards to definition, causation, and optimal interventions.[3] Further, epidemiologic studies are often conducted in general populations that cannot be easily generalized to clinical practice.[57,58]. To help begin a conversation about this important subject, the work group provided a standardized working definition for CUR, a treatment algorithm, and proposed CUR treatment outcome measures. The work group recognizes the limitations with this definition and acknowledges that the volume of elevated PVR that defines CUR should be based on empiric data. Future studies may demonstrate that a CUR definition may differ by gender and other influential risk factors. Similarly, a CUR definition may also be based on the likelihood of response to therapies that reduce the underlying mechanism such as BOO. More studies are needed to change the work group's current proposed definition into an evidenced-based categorization. Subsequent changes to the treatment algorithm and outcome measures would then follow.

These points represent compelling opportunities for future investigations. The following research gaps that are worthy of further resources have been identified:

1) A multi-institutional cohort study including both men and women using a standardized definition of CUR will allow urologists to better understand the natural history, identify risk factors, and procure necessary samples for the development of biomarkers and new interventions. This would also allow for the case-specific use of UDS to determine if UDS characteristics are predictive of outcomes.

2) Identification of molecular markers of the decompensated bladder would allow urologists to understand CUR at a more detailed physiologic level. This would aid in the ability to pinpoint where the system is failing. Biomarkers, so commonplace in the cancer realm, are virtually nonexistent in benign urology. If an underlying physiology at the cellular level is the ultimate cause of CUR, then measurement of shed cells, proteins, and genetic traces such as RNA may not only determine causality but predict future outcomes. In the laboratory, better animal models that develop elevated residual urine and CUR mimicking the human condition are necessary.
3) Investigations for pharmacological and neurological interventions that can reawaken decompensated bladder detrusor tissue would aid many individuals who are otherwise destined for permanent catheterization.

CONCLUSION

The AUA CUR White Paper work group defines CUR as an elevated PVR of >300 mL that persists for at least six months and is documented on two or more separate occasions. The work group proposes that CUR be stratified by identifiable high risk factors and by degree of symptoms with appropriate follow-up and treatment based on these stratifications. Many therapeutic options are available for CUR, and it is proposed that four outcome measures be incorporated into future CUR treatment studies: assessment of symptoms, reduction of risk, ability to void without catheterization, and stability of symptoms/risk over time. Defining CUR will hopefully open comparative research to understanding and treating this challenging condition.

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Table 1: Conditions Commonly Associated with Non-Neurologic CUR

Outlet obstruction	Poor bladder contractility
• Benign prostatic obstruction	• Long standing outlet obstruction
• Long Term Use of Medications 1. Antihistamine 2. Alpha Adrenergic agonists 3. Antipsychotics	• Long Term Use of Medication 1. Anticholinergic/Antispasmotic 2. Tricyclic Antidepressants 3. Beta adrenergic agonists 4. Calcium channel blockers 5. Non-steroidal anti-inflammatory 6. Opioids 7. Benzodiazepines 8. Antipsychotics
• Urethral or bladder neck stricture	• Diabetes Mellitus
• Urethral stones, tumors, valves	• Constipation
• High-grade pelvic floor prolapse	• Frailty[13]
• Urethral diverticula in women	• Idopathic
• Prior anti-incontinence procedure	
• Prior vaginal vault prolapse repair	
• Primary bladder neck obstruction in men and women	
• Dysfunctional Voiding	

Table 2: Indications of "high-risk" chronic urinary retention

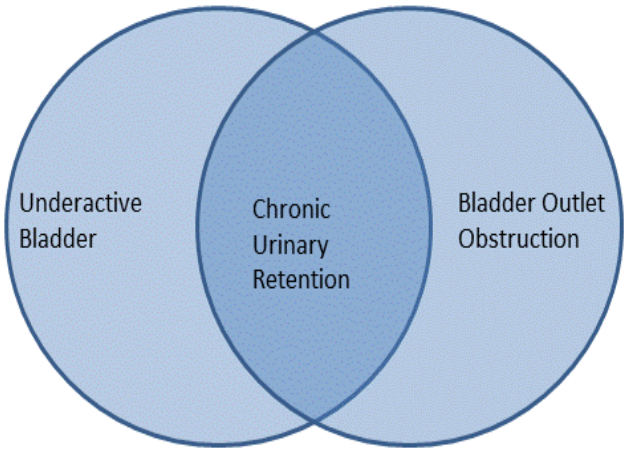
Radiologic findings • Hydronephrosis • Hydroureter
Laboratory findings • Stage 3 chronic kidney disease (eGFR 30 to 59 mL/min/1.73 m^2) • Recurrent, symptomatic, culture-proven UTI • Culture-proven systemic urosepsis
Signs and symptoms • Urinary incontinence associated with perineal skin changes • Urinary incontinence associated with sacral decubitus ulcers

Table 3. Summarizes treatment recommendations for CUR stratified by symptoms and risk.

	Low Risk	High Risk*
Asymptomatic	Do not treat	1) Drain bladder, reassess risk 2) Treat CUR if associated with risk
Symptomatic	Discuss symptom-specific treatment options	1) Drain bladder, reassess risk 2) Treat CUR if associated with risk 3) Discuss symptom-specific treatment options

*See Table 2 for definition of high risk

Figure 1. Overlap of CUR with clinical syndromes of UAB and BOO



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