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# Cannabinoid System Contribution to Control Micturition

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**ABSTRACT**

Cannabinoid compounds, such as those that can be extracted from the Cannabis sativa plant (marijuana), produce a very wide array of central and peripheral effects, some of which may be of importance for the control of lower urinary tract function. Thus, stimulation of cannabinoid receptors, located both in the central nervous system and in different components of the lower urinary tract, has been shown to affect both normal micturition and various disturbances of bladder function. It is clear that systemically administered cannabinoids may be able to become clinically useful; however, a much greater understanding of the mechanisms of cannabinoid receptors in the control of the human lower urinary tract is necessary to facilitate development of novel cannabinoid drugs for the treatment of micturition disorders such as overactive bladder syndrome.

## INTRODUCTION AND REVIEW

*The Endocannabinoid System*

Voiding dysfunction related to neurological lesions is particularly challenging to treat with our current pharmacological armamentarium due to the limited number of drugs that have an efficacy and adverse effect profile sufficient for approval and clinical use. Currently, the most commonly used drugs target the cholinergic (muscarinic acetylcholine receptors) and adrenergic systems (β3-adrenoceptors), or affect both autonomic and somatic nerves (botulinum toxin). As the different pathophysiological processes of lower urinary tract symptoms are under investigation, the understanding of the contribution of other endogenous systems to the control of micturition will expand our therapeutic options.

The endocannabinoid system plays a prominent role in several normal and pathological conditions, and has generated significant interest as a novel target in the academic and pharmaceutical fields. Phytocannabinoids can be extracted from the cannabis plant (marijuana). The main psychoactive compounds are Δ9-tetrahydrocannabinol (Δ9-THC), cannabidiol, and cannabinol. The chemical and pharmacological investigation of these compounds led to the discovery of 2 G-protein coupled cannabinoid (CB) receptors type I ($CB_1$) and type II ($CB_2$). A third receptor has recently been established to be sensitive to CB, called the G-protein coupled receptor 55 (GPR55; for review see [1]). The endocannabinoid system is composed of at least 2 major arachidonate-derived ligands, N-arachidonoylethanolamide (anandamide) and 2-arachidonoylglycerol (2-AG), which mediate their effects by binding to $CB_1$ and $CB_2$ receptors (Figure 1). Both ligands are synthesized postsynaptically on demand and delivered in a retrograde fashion to bind to presynaptically localized CB1 receptors in the central nervous system (CNS) [2]. Activation of presynaptic $CB_1$ receptors in the brain or on primary afferents prevents neurotransmitter release by diminishing calcium conductance and by increasing potassium conductance [3]. They can modulate GABAergic and glutamatergic synapses and postsynaptic transmission of norepinephrine and dopamine. Activation of both receptors inhibits adenylyl cyclase by coupling to the α–subunit of the G protein of the Gi/o family.

In the nervous system, anandamide and 2-arachidonoylglycerol are primarily metabolized by the serine hydrolase enzymes

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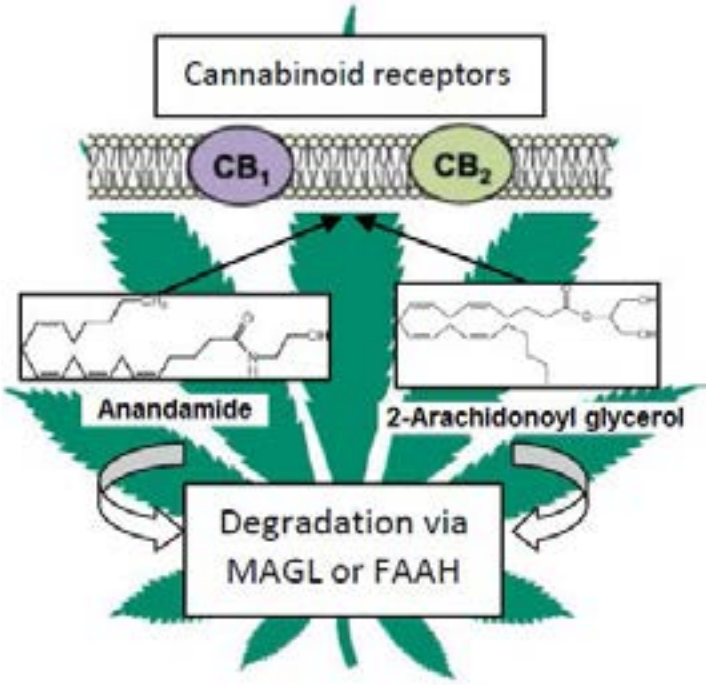
Figure 1. The endocannabinoid system and its metabolism. Anandamide and 2-Arachidonoyl glycerol are synthesized, and act at both cannabinoid receptor type 1 ($CB_1$) and type 2 ($CB_2$). They are then degraded by their respective enzymes FAAH = fatty acid amide hydrolase and MAGL = monoacylglycerollipase.




fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL), respectively [4]. Preventing their degradation with inhibitors of these enzymes can enhance their endogenous actions and avoid the deleterious side effects of direct agonists of CB receptors. Anandamide and other exogenous cannabinoids are known to react with other receptors such as the vanilloid TRPV1 channel [5]. The vanilloid TRPV1 channel is a nonselective cation channel activated by naturally occurring vanilloids, capsaicin, and resiniferatoxin. CB1 receptors are located in a much higher density within than outside the CNS [6]. CB2 receptors are present in peripheral cells such as lymphocytes and macrophages, and in organs such as the spleen and thymus. In the nervous system, they are found on infiltrating immune cells and resident microglia/macrophages. CB2 receptors are located on peripheral nerve terminals [7] but are also present on post-synaptic neurons in several regions of the brain and on non-neuronal cells of the CNS, such as infiltrating immune cells and resident microglia/macrophages [8, 9].

*Cannabinoid Receptors in the Lower Urinary Tract*

Both $CB_1$ and $CB_2$ receptors have been localized in the rat bladder, particularly on the urothelium [10]. In whole human bladders obtained from male organ donors, both $CB_1$ and $CB_2$ receptors were found to be expressed twice as much in the urothelium than in the detrusor, and were localized to the cell membranes. Overall, $CB_1$ receptor expression was higher than that of $CB_2$ receptors [11]. Bakali et al. also demonstrated that both humans and rats expressed $CB_1$ receptors, TRPV1 channels, and FAAH in their bladder [12]. $CB_2$ receptors was found to be expressed in higher densities in rat, monkey, and human bladder mucosa (urothelium and suburothelium) than in the detrusor, and was also co-localized with TRPV1 and calcitonin gene-related protein (CGRP) [13]. In the detrusor wall and $CB_2$ receptor immunoreactive fibers were identified on VAChT-positive nerve fibers [14]. $CB_2$ receptors, but not $CB_1$ receptors, were up-regulated in the bladder after acute and chronic inflammation induced by intravesical acrolein in rats [15]. $CB_1$ receptor immunoreactive fiber density was significantly increased in the suburothelium of the bladder specimen from patients with painful bladder syndrome and idiopathic detrusor overactivity, and correlated with their symptom scores, as compared to control [16]. Bladder $CB_2$ receptors possibly mediated the effects of oral cannabinoid agonists in a placebo-controlled study on multiple sclerosis (MS) patients. $CB_2$ mRNA expression was higher in the bladder of MS patients, and decreased after active treatment [17]. $CB_1$ and $CB_2$ receptors were identified in the spinal cord and dorsal root ganglia of rats, but bladder inflammation did not affect their expression [15]. Spinal cord and dorsal root ganglia $CB_2$ receptor expression was significantly up-regulated in inflammatory and neuropathic pain conditions in rats, and may help mediate analgesic effects [18].

Most studies identify $CB_1$ and $CB_2$ receptors in the bladder urothelium and detrusor along with other related proteins such as FAAH or TRPV1 channels, with variable density across species. The spinal cord also expresses cannabinoid receptors. Pathological processes related with inflammation or pain conditions can cause an up-regulation of these receptors, particularly $CB_2$.

*Cannabinoid in Pain*

Sativex (Δ9-THC with cannabidiol) is now licensed in Canada and in the UK for symptomatic relief of cancer pain and/or the management of neuropathic pain and spasticity in adults with multiple sclerosis. The antinocipeptive action of CB receptors is likely related to their peripheral spinal and supraspinal anatomical location relevant to pain in the brain, spinal dorsal horn, dorsal root ganglia, and peripheral afferent neurons [19]. CB receptor agonists have been extensively investigated in animal studies and in clinical trials, but their therapeutic effect has been limited by their psychoactive components. This has prompted interest in investigating compounds that inhibit

the metabolism of endocannabinoids, or compounds that are peripherally restricted.

*Cannabinoids in Clinical Trials*

The first clinical study of the potential effect of cannabinoids on bladder function was published in 1997. It was a questionnaire-based study where patients with MS using cannabis reported an improvement in urinary symptoms (urinary urgency in 64%, urinary hesitancy in 58.5%, and urinary incontinence in 54.7%) [20]. Whole plant cannabis extract was studied in an open-label trial in patients with advanced MS, and there was a decrease in severe lower urinary tract symptoms, urinary urgency, the number and volume of incontinence episodes, frequency, and nocturia [21]. These findings were followed by a randomized multicenter placebo-controlled clinical trial where oral administration of cannabis extract, Δ9-THC, or placebo was given to patients with MS. Both active compounds significantly decreased urgency incontinence episodes compared to placebo [22]. There are now 3 available medications that activate the CB1/CB2 receptors in the clinic: Cesamet (nabilone), Marinol (dronabinol; Δ9-THC), and Sativex (Δ9-THC with cannabidiol).

*Cannabinoid in Micturition*

The presence and activity of $CB_1$ receptors in the bladder was first suggested by the finding of an inhibition of electrically evoked contractions of the mouse urinary bladder in the presence of a $CB_1$ receptor agonist. In the same study, the selective $CB_1$ receptor antagonist, SR141716, caused parallel rightward shifts in the log concentration-response curves of CP 55,244, WIN 55,212-2 (nonsubtype selective CB receptor agonists), and anandamide (selective for $CB_1$ receptors) for inhibition of electrically evoked bladder contractions [23]. Martin et al. demonstrated some species differences for the effect of $CB_1$ receptor agonists on neuronally evoked bladder contractions, with a higher inhibitory effect in mice than in rats. SR141716 potentiated electrically evoked contractions through an undetermined mechanism [24]. Anandamide application produced slowly developing contractions in muscle strips isolated from the rat urinary bladder. These responses were attenuated by previous capsaicin sensitization [25]. The presence of either anandamide or CP55,940 did not affect carbachol-induced contractions in neither rat, monkey, nor human bladder preparations. However, anandamide increased electrical field stimulation- (EFS) induced contractions, while CP55,940 decreased them at all frequencies [13]. ACEA, a selective $CB_1$ receptor agonist, attenuated the EFS and carbachol-induced contractions of the rat bladder. GP1A, a $CB_2$ receptor agonist, only decreased carbachol-induced contractions in the rat bladder [12]. The application of ajulemic acid, a mixed $CB_1$/$CB_2$ receptor agonist, to rat bladder preparations significantly decreased the CGRP release compared to control, presumably from sensory afferent fibers [10]. Cannabidiol decreased the carbachol-induced contractions in both rat and human bladder preparations, but this effect was only attenuated by the TRPV1 channel antagonists ruthenium red and capsazepine in the rat [26].

CB receptor activation reduced afferent activity in an electrophysiological ex vivo preparation under normal conditions [27]. A nonselective CB receptor agonist was found to decrease afferent activity from inflamed bladders at certain intravesical pressures, an effect that was blocked by a selective $CB_1$ receptor antagonist [28]. These studies consistently show the lack of direct effect of cannabinoid agonists on bladder contractility. However, there are significant conflicting findings between the different CB receptor agonists and their action on carbachol or electrically induced bladder contractions. Cannabinoid receptor activation decreases contractility in vitro, as seen in several studies. The effect of cannabinoid agonists on carbachol-induced contractions has been less convincing, and may be mediated through other receptors, such as the TRPV1 channel.

The effect N-acylethanolamides, anandamide (via CB1 receptors) and palmitoylethanolamide (putative endogenous $CB_2$ receptor agonist), caused analgesia in models of viscero-visceral hyper-reflexia induced by inflammation of the urinary bladder [29,30]. These agents were found to decrease the expression of spinal cord c-fos at L6 following intravesical nerve growth factor (NGF) instillation [31]. Cyclophosphamide injection increased the anandamide content in the rat bladder, while its intravesical instillation increased c-fos expression in the spinal cord and increased the bladder reflex activity, which was blocked by TRPV1 channel antagonists, capsazepine and resiniferatoxin. The authors concluded that anandamide, via TRPV1 channel stimulation, is partly responsible for the bladder hyperactivity and hyperalgesia observed in cystitis [32]. Intraperitoneal administration of GP1a, a highly selective $CB_2$ receptor agonist, decreased the mechanical sensitivity in a mouse model of acrolein-induced cystitis, possibly by preventing phosphorylation of ERK1/2 via MAPK activation [33]. Treatment with a selective $CB_2$ receptor agonist (O-1966) following spinal cord injury improved bladder recovery in rats by modifying the inflammatory response [34]. $CB_2$ receptor agonism appears to decrease viscero-visceral pain caused by bladder inflammation, possibly by modulating afferent signaling in the spinal cord and promoting an anti-inflammatory effect. $CB_2$ receptor activation has an immunomodulatory function that can limit



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the endothelial inflammatory response, chemotaxis, and inflammatory cell adhesion and activation in atherosclerosis and reperfusion injury [35].

Administration of CP55,940 and methanandamide during cystometry in cats decreased micturition volume threshold at all doses but did not change the frequency of spontaneous detrusor contractions [36]. Intravesical anandamide increased threshold pressures and decreased micturition intervals in rats, while CP55,940 increased both threshold pressure and micturition interval [13]. Intra-arterial WIN55,212-2 in rat cystometry significantly increased micturition threshold at all doses, and was particularly enhanced following turpentine-induced bladder inflammation or bilateral hypogastric neurectomy [37]. Cannabinor, a highly selective $CB_2$ receptor agonist, increased micturition intervals and threshold pressures during conscious cystometry [14]. The chronic administration of this compound during 2 weeks following partial urethral obstruction in rats decreased post-void residual and a number of nonvoiding contractions, and increased bladder compliance compared to controls [38]. Stritmatter et al. demonstrated that FAAH is expressed in the bladder of rats, mice, and humans. They also demonstrated that systemic or intravesical administration of a FAAH inhibitor, Oleoyl ethyl amide (OeTA), during awake cystometry significantly increased intercontraction intervals, micturition volume, bladder capacity, and threshold pressure in rats. These effects were abolished with the concomitant use of SR144528, a $CB_2$ receptor antagonist, showing that FAAH inhibition mediated its effect on micturition via $CB_2$ receptors [39]. Selective CB agonists and antagonists have provided valuable information to understand their action in the control of micturition. However, their selectivity and potency are relative and cannot completely obviate their action at other sites. Knockout mouse technology can provide very powerful means of determining gene function in vivo. We assessed the voiding function in $CB_2$ knockout mice by quantitatively measuring urodynamic parameters at baseline and after administering different CB compounds. $CB_2$ knockout mice were found to have lower maximal pressure and basal pressure, and a higher intercontraction interval, bladder capacity, and compliance than control mice. However, no differences were observed in the in vitro responses to carbachol and EFS in bladder strips [40].

Overall, cannabinoid agonists have an inhibitory effect on micturition by increasing threshold pressures and decreasing frequency, possibly through afferent signaling. Anandamide has a more controversial mechanism of action, as it seems to influence micturition differently, demonstrated by in vitro and in vivo studies. The endocannabinoid anandamide is known to also activate TRPV1 channels, potentially via the release of CGRP [41]. Studies have found that a higher concentration of anandamide is required to evoke a TRPV1 channel-mediated release of this neuropeptide compared to that mediated via the $CB_1$ receptor [42].

Although there is a significant body of data demonstrating that cannabinoids affect micturition, there is very little known about the site of action that is primarily responsible for their action. As most cannabinoid agents easily cross the blood-brain barrier because of their lipophilicity, systemic administration cannot determine how much of their voiding effects are due to peripheral or central activation.

Intrathecal administration of compounds provides several applications. It allows the investigation of localized drug delivery of minimal concentration to distinguish their action at the spinal level. Also, restricting the distribution of active concentrations of these compounds to the spinal cord, we are avoiding deleterious psychoactive side effects from brain CB receptor activation. As the micturition reflex involves the spinal cord and ganglia, this approach may allow the development of new management strategies for the treatment of intractable detrusor over activity.

Füllhase et al. studied the effects of OeTA administered intrathecally on normal rats and rats with bladder over activity induced by partial urethral obstruction or intravesical prostaglandin E2. Intrathecal OeTA decreased micturition frequency in normal rats, and also decreased overall bladder pressures in rats with bladder over activity in a dose-dependent fashion, without affecting behavior. The same doses did not affect the cystometric parameters when given systemically. FAAH and $CB_1$ and $CB_2$ receptors were expressed in the rat sacral spinal cord, while $CB_1$ and $CB_2$ receptors were only increased in obstructed rats [43].

## SUMMARY AND CONCLUSION

The role of the endocannabinoid system in the physiology and pharmacology of the lower urinary tract is an expanding field of study. The endocannabinoid system may be involved in the regulation of bladder function, possibly at several levels of the micturition pathway. Cannabinoid receptor agonists have an effect on micturition through a yet unknown mechanism, as demonstrated by clinical trials and in vivo and in vitro animal studies. There are likely interactions with other receptors or channels to ultimately inhibit micturition. Exogenous selective CB receptor agonists and antagonists have provided valuable information, increasing our understanding of the effects of



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cannabinoids in micturition control. However, further studies on both the central nervous and peripheral effects are warranted to increase our knowledge on how both therapeutic and unwanted effects of these agents can be balanced. To avoid CNS-related side effects of cannabinoids, drug approaches with peripheral CB receptor selective compounds, or drugs that target FAAH, may be preferable to harness the potential therapeutic effects of cannabinoids on lower urinary tract disorders.

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# Preventing Catheter-Associated Urinary Tract Infections

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**ABSTRACT**

Catheter-associated urinary tract infections, a worldwide, leading hospital-acquired infection, have substantial impact on patient safety and antibiotic consumption. These urinary catheter-related infections are associated with morbid events, such as delirium, and with longer lengths of stay and higher costs of medical care. It has been estimated that 65 to 70% of CAUTIs may be preventable with recommended evidence-based practices. For this reason, the Centers for Medicare & Medicaid Services no longer reimburses acute care and rehabilitation hospitals for the cost associated with treating these infections, and has a national goal to reduce these infections by 25% in 2014. An expanding body of literature has demonstrated methods for ensuring the practices and processes for decreasing these infections. This article will provide a synopsis of current practices and multimodal prevention strategies for catheter-associated urinary tract infections.

## OVERVIEW

The elimination of hospital-acquired infections (HAIs) is a key aspect of patient safety initiatives in many countries. These infections are primarily caused by instrumentation of the bladder. The United States National Healthcare Safety Network (NHSN) reports that indwelling urinary catheters (IUC) are used in close to two-thirds of patients in the intensive care units, and in about one-fifth of patients on the general medical-surgical units [6]. In hospitalized older medical patients without a specific medical indication, an IUC has been associated with a greater risk of death: 4 times as great during hospitalization and 2 times as great within 90 days after discharge [11]. Saint and colleagues [22] have described inappropriate catheter use as a form of physical restraint as they are associated with discomfort leading to immobility, a cause of pressure ulcers. Catheter-associated urinary tract infections (CAUTI) are costly, making the business case for prevention of these HAIs a key component of a cost-control program [1]. Despite CAUTIs being described as "never events," as in "they never should occur," the cause, an IUC, is still commonly used in the acute care setting.

CAUTIs are considered to be complicated infections, because normal host defense mechanisms are compromised by the presence of a foreign body. Although frequently asymptomatic, up to one-third of patients with catheter-associated bacteriuria will develop symptoms of CAUTI, especially if the catheter remains in place long-term (defined as > 30 days) [14]. The length of time IUCs remain in situ is directly related to increases in CAUTIs. Antimicrobial therapy is only transiently effective if the catheter remains in place.

Meddings and Saint [17] describe a conceptual model to outline the "lifecycle" of an IUC (Figure 1). Each part of the cycle describes an actionable target that begins with catheter placement (1), continues when the catheter remains in-situ (2), can stop when the catheter is removed (3), but in many patients resumes if another IUC is re-inserted. These authors note there is an opportunity for an intervention at each stage of the cycle. In addition to the length of the time the IUC is in place, there

**KEYWORDS**: catheter associated urinary tract infections, indwelling urinary catheter, prevention, evidence-based guidelines, bladder bundle

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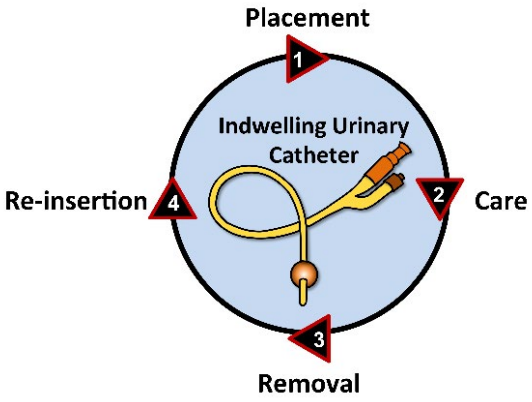
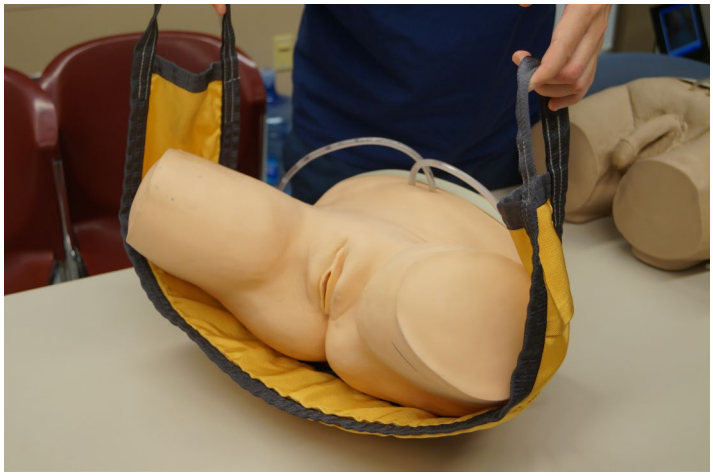
Figure 1. Indwelling urinary catheter cycle.




Adapted from: Meddings J. Saint S. (2011) Disrupting the life cycle of the urinary catheter. *Clin Infect Dis*. Jun;52(11):1291-3

Figure 2. Insertion use of lifts.

Figure 3. Insertion use of lifts.



are other risk factors for development of a CAUTI, including improper catheter insertion techniques, female gender, older age, compromised immune system, and comorbid conditions (e.g., diabetes, renal dysfunction). Other contributing factors to the development of a CAUTI are non-evidence-based (EB) nursing care practices for managing catheters. Procedures such as meatal cleansing with antiseptics, unsecured catheters, catheter irrigation, disconnecting the catheter from the drainage tubing, and others, are routinely performed by nurses, are not supported by EB research and, in many cases, have been shown to contribute to the development of a CAUTI. The fact that nurses are not following specific practices to prevent CAUTIs was shown in a survey about prevention of hospital-acquired UTIs and other device-associated infections distributed to both nonfederal and federal U.S. hospitals [21].

*CAUTI Prevention Guideline*

The latest guideline, which was revised by the CDC Healthcare Infection Control Practices Advisory Committee (HICPAC), is the Guideline for Prevention of CAUTIs [10], and it provides updated recommendations on catheter use and maintenance to prevent UTIs. Recommendations in this guideline were also included in the International Clinical Practice Guidelines of the Infectious Diseases Society of America [12]. The HICPAC CAUTI guideline was developed through a systematic review of the best available evidence and includes new research and technological advancements for the prevention of CAUTIs (Table 1). The guideline emphasizes quality improvement initiatives and provides suggestions for implementation. HICPAC has estimated that up to 69% of hospital-acquired CAUTIs may be prevented by implementation of an EB prevention program. Although patients who have IUCs in place long term will most certainly develop a CAUTI, evidence suggests that certain interventions can reduce the incidence of CAUTI in patients who have IUCs in place for short-term duration, and certain catheter-care strategies can prevent infections. The cornerstone of any CAUTI prevention program would be to remove the IUC as soon as possible. In addition, components identified that can decrease IUC use and prevent hospital-acquired CAUTIs include: instituting hospital-wide administrative interventions, implementing quality improvement programs, educating physician and nursing staff on indications, and evidence-based nursing care of the IUC to prevent infection [18]. What is

Table 1. Synopsis of Best Practice for Prevention of CAUTIs in acute care hospitals (adapted from Gould et al. 2010 and Hooton et al. 2010).

| Basic Principles | Practice Recommendations |
|---|---|
| Proper Urinary Catheter Maintenance | • Following aseptic insertion of the urinary catheter, maintain a closed drainage system<br>• Maintain unobstructed urine flow |
| Performance Measures | • Compliance with educational programs<br>• Calculate percent of personnel who have proper training<br>• Compliance with documentation of catheter insertion and removal dates<br>• Conduct random audits of selected units and calculate compliance rate |
| Consider Using Alternatives to IUC | • Intermittent catheterization for urinary retention<br>• External catheters for men with urinary incontinence |
| Proper Techniques for Urinary Catheter Insertion | • Hand hygiene immediately before and after insertion or any manipulation of the catheter and system<br>• Catheter insertion using aseptic technique and sterile equipment<br>• Minimize urethral trauma during insertion, use generous amounts of sterile lubricant<br>• Position female patients to ensure clear visualization of the urinary meatus; in men, the penis should be held in a new vertical position during insertion<br>• Catheter securement<br>• Maintain a closed drainage system and unobstructed urine flow<br>• Consider IUC systems with pre-connected, sealed catheter-tubing junctions, and avoid disconnecting the IUC from the drainage bag |
| Recommended Techniques for Catheter Maintenance | • Cleanse the periurethral area with bathing or showering and do not use antiseptics in this area<br>• Empty the collecting bag regularly, at least every 4 to 6 hours or when urine in the drainage bag reaches 400 mL to avoid migration of bacteria up the lumen of the catheter system<br>• Use a separate, clean collecting container for each patient; avoid splashing, and prevent contact of the drainage spigot with the non-sterile collecting container<br>• Keep drainage devices on opposite sides of the bed and keep drainage devices in semi-private rooms on opposite sides of the room. |
| Catheter Changing and Reinsertion | • Changing IUC or drainage bags at routine, fixed intervals is not recommended<br>• Change IUCs and drainage bags based on clinical indications (e.g., infection, obstruction, or closed system is compromised) |
| Management of Obstruction | • Catheter irrigation is not recommended unless obstructed by blood clots<br>• If obstruction is anticipated, closed continuous irrigation is suggested to prevent obstruction<br>• Consider use of a portable ultrasound device to evaluate possible obstruction |

missing is the lack of integration of EB research with clinical expertise to minimize IUC use and prevent infections. Conway and colleagues [5] noted that EB practice and adoption of policies to prevent CAUTI was lacking in intensive care units (ICUs) studied, as only 42% of ICUs reporting having written policies in place for at least 1 of 4 prevention practices: use of portable bladder ultrasound scanners, condom catheters for men with urinary incontinence, reminders, or stop orders.

*Implementing Practices to Prevent CAUTIs*

There is EB research that suggests that certain interventions can reduce the incidence of CAUTIs in patients managed by short-term IUC. They include staff education about catheter management, combined with regular monitoring of CAUTI incidence, a hospital-wide program to ensure catheterization only when indicated, and prompt removal of IUC. One of the first strategies that hospitals should employ to prevent CAUTIs is the development of an appropriate infrastructure that includes



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Figure 4. Male insertion of IUC catheter.

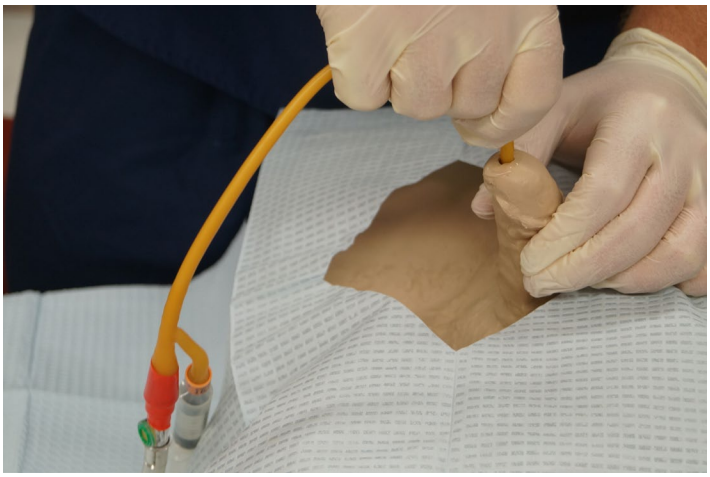

Figure 5. IUC catheter.

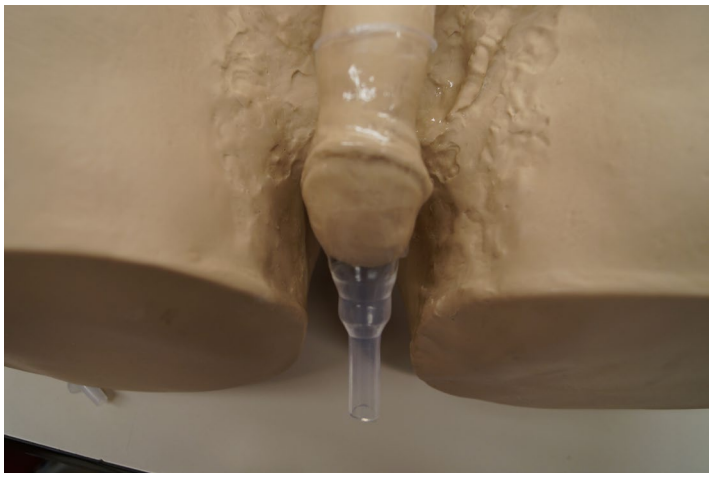

Table 2. IUC indications (Adapted from Gould et al. 2010).

**Appropriate indications for an IUC include:**

- Acute urinary retention/bladder outlet obstruction
- Need for accurate I and O if critically ill
- Assist in healing of open sacral/perineal wound in incontinent patients
- To improve comfort in end-of-life care, if needed
- Perioperative use in selected surgical procedures
- Urologic/other surgeries on contiguous structures of GU tract
- Anticipated prolonged duration of surgery (should be removed in PACU)
- Operative patients with urinary incontinence
- Need for intraoperative hemodynamic monitoring

**Inappropriate uses of IUCs include:**

- As a substitute for nursing care of the patient with incontinence
- As a means of obtaining urine for culture or other diagnostic tests when the patient can voluntarily void
- For prolonged postoperative duration without appropriate indications (e.g., structural repair of urethra or contiguous structures, prolonged effect of epidural anesthesia, etc.)

some type of surveillance. Urinary catheters should be used only if necessary and should be removed as soon as practical. Table 2 outlines appropriate and inappropriate IUC use.

Some studies have indicated that early removal of IUCs can reduce UTI rates by up to 40%. To achieve this, nurse-directed IUC removal protocols on prevention of CAUTIs have shown positive outcomes. Fakih et al. [9] reported on the effect of nurse-led multidisciplinary rounds on 10 medical-surgical units on reduction in the unnecessary use of IUCs. The group reviewed the patients' records to determine appropriate indication for the IUC and if it was not found, the patient's nurse was asked to contact the physician to request discontinuation. In this study, more than two-thirds of IUCs with no indication for placement did not have a clear reason for placement. So through a simple monitoring intervention, unnecessary catheter use was reduced by 10%. Wenger [25] described a 3-pronged approach that included education, testing new and better catheter products, and ending with a nurse-driven protocol for catheter removal. This hospital's leadership gave nurses the authority to remove IUC through the use of a protocol of specific criteria defining medical necessity. Parry et al. [19] showed that aggressive implementation of the nurse-directed catheter removal protocol was associated with lower catheter use rates and reduced infection rates. Some acute care hospitals have created "catheter champions," a group of nurses who are a daily resource to all medical and nursing staff for any catheter-related problems that arise. Developing protocols that describe steps to take following catheter removal, so as to

Table 3.The ABCDE Bundle for Prevention of CAUTIs (Adapted from Saint et al. 2009).

| | Recommendation | Considerations |
|---|---|---|
| **A** | Adherence to general infection control principles (e.g., hand hygiene, surveillance and feedback, aseptic insertion, proper maintenance, education) is important | To ensure aseptic insertion, clinician should consider positioning of the patient to allow adequate visualization of the perineum (Figure 2 and Figure 3); correct position of the male penis to prevent urethral trauma during insertion (Figure 4) |
| **B** | Bladder ultrasound may avoid unnecessary catheter use | Development and implementation of an algorithm to guide hospital staff on steps to follow after IUC removal will prevent unnecessary IUC reinsertion |
| **C** | Condom catheters or other alternatives to an IUC, such as intermittent catheterization or incontinence products, should be considered in appropriate patients | External male catheters and pouches (Figure 5 and Figure 6) are an alternative for male patients who have urinary incontinence and they will contain urine leakage and protect the skin from breakdown |
| **D** | Do not use the IUC unless medically appropriate | Follow the HICPAC guidelines for appropriate catheter insertion and removal found in Table 2 |
| **E** | Early removal of the catheter using a reminder or nurse-initiated removal protocol | Monitor CAUTI rates and Device Days |

deter the reinsertion of a catheter, may be necessary.

Staff should develop policies that detail criteria for IUC indications and inappropriate use (Table 2). As part of surveillance, the hospital should provide and implement written guidelines for catheter use, insertion, and maintenance [14].

*Stop Orders for Catheter Removal*

The most important strategies for prevention of CAUTIs is to avoid insertion of an IUC and, if necessary, limit the duration to as short a time as possible. Given that the rate of infection is closely related to the duration of catheterization, the high frequency of inappropriate catheterization, and the finding that physicians are often unaware of catheter presence, it is possible that an automatic urinary catheter "stop order" or reminder would be useful. Such an innovative system-wide administrative intervention, similar to an antibiotic stop order, would ideally remind physicians that their patient has an indwelling catheter, which in turn might help reduce inappropriate catheterization [18]. In 2008, Saint noted that only 9% of hospitals reported using an IUC stop order or reminder. Meddings et al. [13] note that a stop order requires action, as they prompt the clinician, usually a bedside nurse, to remove the catheter by default after a certain time period (e.g., with 24 hours). Fakih et al. [8] evaluated the effect of 3 interventions over a 5-year period. The interventions included:

- a nurse-driven multidisciplinary effort for early IUC removal,
- an intervention in an emergency department to promote appropriate placement, and

Figure 6. Retracted penis pouch.

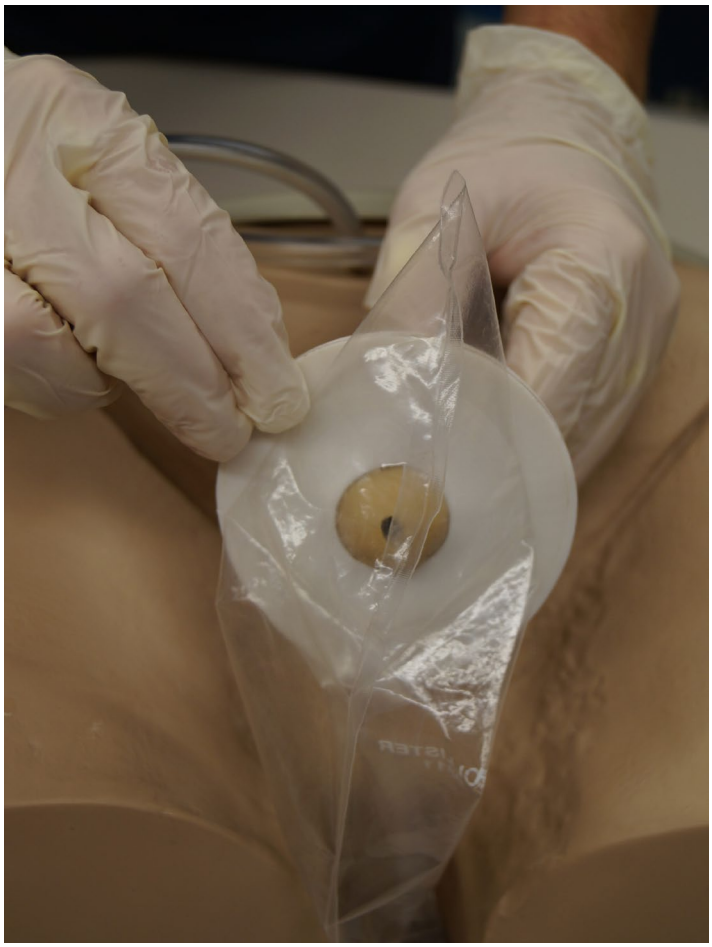

Table 4. Resources for CAUTI prevention.

- Agency for Healthcare Research and Quality: http://1.usa.gov/pypoll
- Association for Professionals in Infection Control and Epidemiology: http://bit.ly/Yv8gHS
- Centers for Disease Control and Prevention, Healthcare Infection Control Practices Advisory Committee: http://1.usa.gov/13i71zs http://1.usa.gov/ZvdLW1
- Institute for Healthcare Improvement: http://bit.ly/Xo4PTM
- Joint Commission: http://bit.ly/q2YLuX
- Society for Healthcare Epidemiology of America: http://bit.ly/14psW3J

- twice-weekly assessment of IUC prevalence with periodic feedback on performance for non-intensive care units.

These researchers found that once given the responsibility for IUCs, bedside nurses become "champions" for catheter removal, and supporting bedside nurses with alternatives (e.g., condom catheter) can reduce IUC use. However, although the implementation of this automatic order is becoming more popular [2] and are part of CAUTI prevention programs, Loeb et al. [15] noted that stop orders for IUC safely reduced duration of inappropriate urinary catheterization in hospitalized patients but did not reduce UTIs.

*Use of a "Bladder Bundle"*

Saint [20] noted that there is no "magic bullet" for CAUTI prevention. However, in 2009, he described a "bundle" of best practices for IUC and labeled them the "Bladder Bundles." A bundle is a set of EB practices that are designed to be implemented together to optimize treatment, prevent or reduce complications, and improve outcome [3]. The Bladder Bundle is the mnemonic ABCDE described by Saint et al. [21] in their discussion on translating CAUTI prevention research into practice via a bladder bundle. These bundles are a simplified list of the key points (Table 3) of the HIPAC EB clinical practice guideline, and are educational interventions around appropriate IUC use and clinical skill in IUC placement, use of non-invasive technology to determine bladder volume, and protocols to aid clinical decision-making for IUC use and removal [13]. Others have used this bundle. Krien et al. [13] noted bladder bundle implementation involved educating health-care workers about appropriate indications, establishing a process for regular catheter assessment and removal, use of a nursing-based discontinuation protocol, and collecting data for monitoring IUC use and indication. Venkatram and colleagues [24] reported on successful implementation of the UTI bundle in medical IUCs, which resulted in an almost 90% reduction of IUC-related UTIs. Fakih and colleagues [7] reported on a statewide initiative in Michigan that used bladder bundles to decrease inappropriate IUC use. This EB research needs to be adopted by acute care hospitals.

## CONCLUSION

Indwelling urinary catheters are a significant source of all hospital infections. The best prevention is to remove the catheter as soon as possible. Strong surveillance programs, nurse-directed protocols, automatic removal orders, and the use of a bundle can control catheter-related infections. Evidence-based research and guidelines, professional organizations, and federal agencies (Table 4) are assisting clinicians in managing these problematic devices.

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# Accuracy of Computed Tomography for Identifying Locally Advanced Disease in Patients with Muscle-Invasive Bladder Cancer

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**ABSTRACT**

**Introduction**: To retrospectively evaluate the utility of computed tomography (CT) scanning in identifying patients with locally advanced bladder cancer.

**Methods**: We performed an Institutional Review Board-approved review of 858 patients that underwent radical cystectomy (RC) from 2000 to 2008 at our institution. We selected patients with muscle-invasive bladder cancer (MIBC) who underwent up-front RC without neoadjuvant chemotherapy and who were assessed by preoperative CT scan. We limited this analysis to 48 CT scans obtained prior to transurethral resection. All CT scans were blinded and retrospectively re-read by a dedicated genitourinary radiologist (CSN) to identify tumor location, the presence of wall thickening, and evidence of extravesical disease (stranding or nodularity) or lymph node metastases. These radiologic findings were compared with pathologic findings.

**Results**: Pretransurethral resection CT scans were able to accurately identify tumor location in 66.7% of patients (sensitivity = 88.9%, specificity = 33.3%) while lymph node assessment was accurate in 58.3% (sensitivity = 75%, specificity = 62.5%). However, only 16.7% of patients with pathologic T3b disease were actually identified on CT as having radiologic evidence of extravesical disease. Specific radiologic signs suggestive of local disease extension, such as wall thickening, stranding, and nodularity correlated poorly with true pathologic T3b disease.

**Conclusion**: CT scanning has limits in its ability to accurately identify extravesical disease and lymph node spread in patients with MIBC. Investigations into additional or alternative means of clinical staging for bladder cancer patients are incredibly crucial.

## INTRODUCTION

CThe survival of patients with bladder cancer varies greatly based on the stage of their disease [1]. Unfortunately, physicians are notoriously poor at staging patients with invasive disease [2-8]. It remains critically important to be able to identify those patients with locally advanced disease (such as extravesical extension of tumors or clinically node-positive disease) in order to appropriately prognosticate survival and to identify patients who would gain the most benefit from up-front chemotherapy.

Current staging of bladder tumors is based on visual assessment of the tumor on cystoscopy, pathologic assessment via transurethral resection (TUR) specimens, exam under anesthesia (EUA) to assess for evidence of a 3-dimensional mass, and computed tomography (CT) imaging. Both older and newer studies have reported that CT imaging is limited by its poor accuracy in detecting local tumor extension and lymph node metastases [9,10]. Here we sought to further evaluate the ability of CT imaging to identify locally advanced disease in a rather homogeneous population of patients with cT2 bladder

**KEYWORDS**: Urinary bladder neoplasms, X-ray computed tomography, neoplasm staging

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cancer by comparing a blinded review of preoperative imaging to pathologic features.

## METHODS

Using an Institutional Review Board-approved protocol, we queried our prospectively collected database and identified 858 consecutive patients who underwent radical cystectomy (RC) for urothelial carcinoma of the bladder from January 2000 to December 2008. We isolated patients designated having cT2N0M0 disease following their TUR and EUA; those patients with a palpable 3-dimensional mass on EUA and those who received chemotherapy prior to surgery were excluded in order to study a homogeneous cohort. Patients who underwent imaging immediately following TUR (< 30 days) were also excluded in order to avoid bias from confounding extravesical inflammation or extravasation commonly seen after resection.

All CT images were then de-identified and reviewed by a dedicated genitourinary radiologist (CSN), who was blinded to the pathologic features and clinical outcome. The CT images were acquired from various institutions, using a variety of helical and multidetector scanners, and thus there was no uniform protocol that was used. Axial CT images of 2.5 mm to 10 mm sections were reviewed. Endpoints of interest included tumor location, radiographic suspicion of locally advanced disease, and individual radiographic signs potentially predictive of extravesical disease or lymph node metastases.

The presence or absence and location of focal bladder wall thickening greater than that of the adjacent bladder wall, intraluminal bladder wall nodules/nodularity, and/or focal post-contrast enhancement of the bladder wall was documented, and the bladder location recorded and taken to represent the site of tumor(s). Local extension of disease was considered if there was stranding and/or nodularity in the adjacent perivesical fat. For this study, pelvic lymph nodes were considered to be positive for disease if ≥ 0.5 cm in the short axis.

We then compared the radiologic impression and findings to the pathologic results. Summary statistics were used to describe demographical and clinical characteristics of the study population. Basic statistical measures were used to decipher the accuracy of CT imaging in detecting locally advanced bladder cancer.

## RESULTS

Using our stringent selection criteria for this study, we identified 48 patients with complete clinical and pathologic data who also had a pre-TUR CT scan available for review. For these patients, the median time from CT to TUR was only 3 days and from TUR to RC was 42. Despite this selection, 45.8% of our cT2 patients were found to be upstaged to pT3 disease pathologically and 16.7% were node positive (Table 1).

Table 1. Comparison of preoperative radiographic impression to pathologic outcome.

| Pathologic Stage (Number) | < rT3b | ≥ rT3b | Equivocal |
|---|---|---|---|
| pT0 (5) | 4 | | 1 |
| pTis (7) | 4 | 1 | 2 |
| pTa (3) | 3 | | |
| pT1 (5) | 3 | 1 | 1 |
| pT2 (6) | 4 | 1 | 1 |
| pT3a (8) | 5 | 2 | 1 |
| pT3b (12) | 9 | 2 | 1 |
| pT4a (2) | 0 | | 2 |

| Pathologic Stage (Number) | rN0 | rN+ |
|---|---|---|
| pN0 (40) | 29 | 11 |
| pN+ (8) | 4 | 4 |

None of the patients were originally thought to have CT findings consistent with advanced disease, but for the purposes of this study the CT scans were re-evaluated for radiologic findings consistent with extravesical disease (i.e., ≥ rT3b) or nodal metastases (rN+). The repeat radiographic impressions indicated that 14.6% of patients had rT3b disease and 31.3% rN+ (Table 1). However, only 2 of 12 patients (16.7%) with pathologic T3b disease were correctly identified as having radiologic signs suspicious for extravesical disease. Furthermore, 5 of 7 patients (71.4%) thought to have rT3b disease and 11 of 15 (73.3%) thought to have rN+ disease were overstaged. Finally, 12 of 29 patients (41.4%) thought to have organ-confined disease (< rT3b and rN0) were understaged.

EUA is an underutilized but important part of the staging evaluation for muscle-invasive bladder cancer (MIBC). However, the accuracy of EUA can vary based on tumor location and body habitus, with poor sensitivity in obese patients. Here we found that EUA was unable to identify macroscopic tumor extension in 12 of the 48 patients (25%). However, tumor location was accurately identified by CT in 66.7% of patients (sensitivity = 88.9%, specificity = 33.3%), and lymph node assessment was correct in 58.3% (sensitivity = 75%, specificity = 62.5%) (Table 2).

We then evaluated the correlation of extravesical extension with bladder wall thickening, extravesical stranding, and

Table 2. Predictive ability of imaging to identify tumor and node location.

| | Tumor Location (%) | Node Location (%) |
|---|---|---|
| Sensitivity | 88.9 | 75 |
| Specificity | 33.3 | 62.5 |
| Negative predictive value | 16.7 | 92.6 |
| Positive predictive value | 95.2 | 28.6 |
| Accuracy | 66.7 | 58.3 |

Table 3. Predictive ability of specific radiographic signs to identify extravesical disease.

| | Bladder wall thickening (%) | Extravesical stranding (%) | Extravesical nodularity (%) | Combined (%) |
|---|---|---|---|---|
| Sensitivity | 91.7 | 66.7 | 16.7 | 100 |
| Specificity | 22.2 | 41.7 | 86.1 | 13.9 |
| Negative predictive value | 88.9 | 78.9 | 75.6 | 100 |
| Positive predictive value | 28.2 | 27.6 | 28.6 | 27.9 |
| Accuracy | 39.6 | 47.9 | 87.5 | 35.4 |

extravesical nodularity as individual variables. As shown in Table 3, these criteria were not sufficient to accurately identify extravesical disease as only 28.2, 27.6, and 28.6% of patients with pT3b disease were found to have these radiographic findings, respectively. Furthermore, 28 patients had at least pT2 disease; among these, 11 of 23 (47.8%) with bladder wall thickening, 8 of 19 (42.1%) with extravesical stranding, and 2 of 5 (40%) with extravesical nodularity had extravesical disease.

## DISCUSSION

Accurate clinical staging is essential for the appropriate selection of therapy for all cancers, and it is especially pertinent to bladder cancer given that current staging paradigms result in pathologic upstaging (extravesical disease extension or lymph node positivity) ranging from 36 to 73% following radical cystectomy [3-6]. It is partly due to this limitation in clinical staging that many experts recommend the use of neoadjuvant chemotherapy (NAC) to all patients with MIBC [11-14]. Most, however, will agree that the true benefit of NAC is in patients who harbor occult nodal metastases and/or have tumors that extend beyond the confines of the bladder. Thus, the hope is that refinements in technology allow CT imaging to better delineate cases of locally advanced disease and therefore increase utilization of preoperative chemotherapy. At our cancer center, we have reported on the use of clinical parameters to risk-stratify these patients—namely, the presence of lymphovascular invasion on TUR specimens, hydroureteronephrosis, variant histologic subtypes, and suspicion for extravesical disease on EUA—in an attempt to identify patients judged to be at the highest risk and who would likely benefit from NAC [15].

Despite CT imaging demonstrating a respectable positive predictive value for identifying tumor extension into perivesical fat, it displayed a dismal specificity. Thus CT imaging adds minimal benefit for local tumor staging, which highlights the importance of incorporating EUA into the staging regimen to help identify locally advanced tumors. Nevertheless, CT imaging was able to exclude lymph node metastases in most patients (negative predictive value of 92.6%), indicating that it remains an important part of this aspect of staging.

Ideally, one would like to use preoperative cross-sectional imaging as the primary modality to accurately stage the extent of local tumor invasion and patterns of lymph node spread or distant metastases (bony or visceral). However, accuracy of CT for bladder cancer staging has been reported to be at best 50% with at least a 25% rate of understaging [9,10]. Since some of these series included patients that were treated prior to 2000, and CT scanning technology has advanced since then, we decided to re-evaluate the utility of CT scanning (from 2000 until now) in the hands of a dedicated genitourinary radiologist blinded to patient outcomes and pathologic features. Unfortunately, we have corroborated prior studies showing that cross sectional imaging with CT scans remains unreliable in identifying the presence of extravesical disease. Moreover, we found no reliable radiologic signs that consistently identified the extravesical extent of disease. Finally, identification of small-volume lymph node metastases is barely adequate with today's CT scans.

Our study cohort consisted of our most recent 12 years of patient data. However, our findings are primarily limited by the heterogeneity in the available CT imaging quality and technique. Some of our CT images were derived from scanning techniques as far back as 2000. Furthermore, only axial CT images were reviewed since the majority of scans were obtained from routine staging protocols rather than any kind of specialized or research thin-cut section protocols with the possibility of 3-D reformations. Nevertheless, we specifically did not exclude CT studies from other institutions in order to replicate real world

results.

We do recognize that the number of patients selected for this re-review can be considered small. However, we used strict criteria to avoid the biases of a post-TUR CT scan, and it is possible that we have not been able to demonstrate an improvement in staging due to the small number of CT scans reviewed; however, it is likely that inclusion of post-TUR scans would only lower the accuracy of CT scanning due to procedure-introduced artifacts.

Ultimately, CT imaging is not yet sensitive enough to distinguish between organ-confined and extravesical bladder cancer. Moreover, CT is especially difficult to interpret in the post-biopsy or transurethral setting secondary to inflammatory changes. Magnetic resonance imaging has been proposed as a better cross-sectional imaging modality to stage patients given the high tissue contrast with contrast enhancement and diffusion-weighted imaging. Unfortunately, studies have been unable to prove the significant clinical benefit of magnetic resonance over CT that justifies its use [16-20]. These limitations in cross-sectional imaging highlight our desperate need for better patient stratification, whether it is through molecular analyses of tumor characteristics on TUR specimens, circulating tumor cells, or molecular imaging.

## CONCLUSION

CT scanning has limits in its ability to properly identify extravesical disease or lymph node spread in patients with MIBC. Investigations into additional or alternative means of clinical staging for bladder cancer patients are incredibly crucial.

## ACKNOWLEDGEMENTS

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# Alpha-Adrenergic Blockers with or without Deflazacort for the Expulsion of a Lower Ureteric Calculus ≤ 10 mm: A Comparative Study

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**ABSTRACT**

**Introduction**: A lower ureteric calculus is one of the most commonly encountered conditions in daily urological practice. There are various options for management of lower ureteric calculus, which includes watchful waiting, extracorporeal shock wave lithotripsy (ESWL), and ureteroscopic lithotripsy (URSL). The aim of our study was to evaluate the efficacy of following drugs in the expulsion of a lower ureteric calculus ≤ 10 mm. The drugs used are (1) tamsulosin, (2) naftopidil, (3) tamsulosin and deflazacort, and (4) naftopidil and deflazacort.

**Methods**: A prospective study was carried out in the Department of Urology from August 2012 to January 2013. A total of 150 patients were enrolled and were randomized into 5 equal groups of 30: A (control), B (naftopidil), C (tamsulosin), D (naftopidil and deflazacort), and E (tamsulosin and deflazacort). Complete hemograms; blood urea; serum creatinine; urine routine examination and culture and sensitivity; X-ray of the kidney, ureter, and bladder (KUB); and/or ultrasonography were done in all cases. Cases were followed up to 30 days or upon spontaneous passage of the calculus, whichever was earlier. X-ray KUB and/or ultrasonography were done to confirm the passage of the stone.

**Results**: The expulsion rate for a calculus ≤ 10 mm was statistically significant in all the groups in comparison to the control group. The mean days of expulsion and use of analgesics was also low in all the groups compared to control. Amongst all groups, the stone expulsion rate was highest, and episodes of pain and mean days of expulsion were lowest for the D group.

**Conclusion**: It is concluded that alpha-adrenergic blockers facilitate the expulsion of lower ureteric stones ≤ 10 mm and decreases the episodes of colic, which is further improved by the addition of deflazacort. Naftopidil plus deflazacort gives the best results in regards to stone expulsion rates, mean days of expulsion, and episodes of colic.

## INTRODUCTION

A lower ureteric calculus is one of the most commonly encountered conditions in daily urological practice. There are various options for the management of lower ureteric calculus, which includes watchful waiting, extracorporeal shock wave lithotripsy (ESWL), and ureteroscopic lithotripsy (URSL). Though URSL is the gold standard for management of lower ureteric calculi, it is invasive, requires anesthesia, and facilities are not available everywhere in developing countries like India. The

**KEYWORDS**: Lower ureteric calculus, medical expulsive therapy, alpha-adrenergic blocker

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size of the calculus remains the main deciding factor for the type of intervention.

There are various studies that show positive results with medical expulsive therapy (MET) for lower ureteric calculi in relation to expulsion rates and duration. The various drugs that are used for MET for lower ureteric calculi are α-adrenergic antagonists and calcium channel blockers. There are 3 types of α-blockers; namely α1a, α1b, and α1d, of which α1a and α1d are present in high densities in the lower ureter. Both α-antagonists and calcium channel blockers inhibit the contraction of ureteral muscle responsible for ureteral spasms while allowing antegrade stone propagation. Ureteric stones cause inflammatory changes in the ureteric wall and that submucosal edema in and around the stone, which worsens the ureteric obstruction. This submucosal edema can be reduced by corticosteroids like deflazacort. We did a prospective study to look for the efficacy of α-adrenergic blockers (tamsulosin and naftopidil) with or without deflazacort for the expulsion of distal ureteric calculi ≤ 10 mm. The aim of our study was to evaluate the efficacy of the following drugs in the expulsion of lower ureteric calculi ≤ 10 mm.

- Tamsulosin
- Naftopidil
- Tamsulosin and deflazacort
- Naftopidil and deflazacort

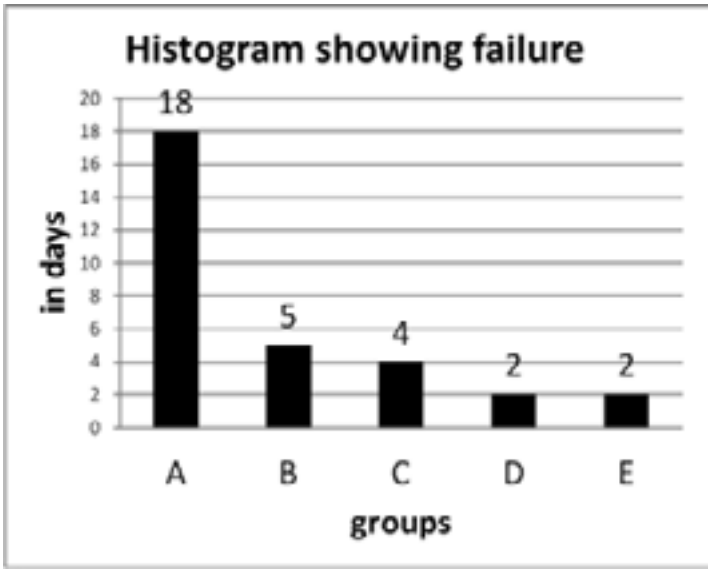
## METHODS

A prospective study was carried out in the Department of Urology, from August 2012 to January 2013. A total of 150 patients were enrolled and were randomized into 5 equal groups of 30:

- A – control: high fluid intake along with drotaverine (80 mg) whenever required
- B – naftopidil: naftopidil (50 mg) once daily at bedtime
- C – tamsulosin: tab. tamsulosin (0.4 mg) once daily at bedtime
- D – naftopidil and deflazacort: naftopidil (50 mg) and deflazacort (6 mg) at bedtime
- E – tamsulosin and deflazacort: tamsulosin (0.4 mg) and deflazacort (6 mg) at bedtime

The above-mentioned drugs were given for a maximum period of 30 days or until the spontaneous passage of a stone (whichever was first). Complete hemograms; blood urea; serum creatinine; urine routine examination and culture and sensitivity; X-ray of the kidney, ureter, and bladder (KUB); and/or ultrasonography were done in all cases. Patients with symptomatic unilateral, solitary lower ureteral calculi proved either on a skiagram or sonography of the KUB. Calculus size ≤ 10 mm (in the major axis) were included in the study. Patients with active urinary tract infection, acute/chronic renal failure, history of urinary tract surgery, uncorrected distal obstruction, marked hydronephrosis, and patients < 18 years old were excluded. Ethical committee clearance was taken for the study.

Figure 1. A histogram showing failure rate.




During follow-up, patients were asked to pass urine in a stone collector. Follow-up was done with a USG KUB after 2 and 4 weeks. Successful MET was considered when a stone was not seen in USG/X-ray KUB. Failure was considered if 1) the patient failed to pass the stone at the end of 30 days, or 2) uncontrolled pain and/or uroseptic fever led to hospitalization during the study period.

## RESULTS

The study included 150 patients with an age range of 19 to 57 years (mean = 32.81). The male and female ratio was 2.6:1 (109:41). The smallest stone size was 3.7 mm and the largest was 10 mm. Mean stone size < 5 mm was 4.7 mm, and 5 to 10 mm was 7.37.

The stone expulsion rates in groups A, B, C, D, and E was 40%, 83%, 86%, 93%, and 93%, respectively (Table 1). Groups B, C, D, and E showed statistically significant stone expulsion rates as compared to group A, as determined by a statistical test of proportion (P value for B = 7.65 x 10 to 7, C = 1.355 x 10 and 7, D = 1.6 x 10 and 9, and E = 1.6 x 10 to 9). However, there was no difference between C and D and between C and E (P value = 0.4014). Similarly, there was no difference between D and E (P value = 0.50). Also there was no difference between B and C (P value = 0.4497) and there was no difference among B, D, or E (P value = 0.3522).

The mean duration of stone expulsion in groups A, B, C, D,

and E was 12.42 days, 11.8 days, 12.27 days, 6.4 days, and 9.92 days, respectively (Table 1). Group D showed a statistically significant mean duration of expulsion compared to group A (P value of 0.0031) as determined by student t test. There was no statistically significant mean duration of expulsion in groups B, C, and E compared to group A (P value for group B = 0.351, C = 0.466, and E = 0.063), as determined by student t test. The difference between the means of groups B and D was found to be significant with P value = 0.000354, and also the difference between the means of groups C and D was found to be significant with P value = 0.000443, as determined by student t test.

The patients with episodes of pain in group A, B, C, D, and E was 22 (73.3%), 19 (63.3%), 15 (50%), 10 (33.3%), and 13 (43.3%), respectively (Table 1). There was a statistically significant advantage in groups C, D, and E compared to group A (P value in group C = 0.002, D = 4.009 x 10 to 7, and E = 0.0001), as determined by a statistical test of proportion.
The failure rate in groups A, B, C, D, and E was 18 (60%), 5 (16.6%), 4 (13.3%), 2 (6.6%), and 2 (6.6%) (Figure 1).

One patient from group A required hospitalization because of severe abdominal pain and fever, and he was considered a failure. The patients who were not stone free with MET were successfully managed by ureteroscopic lithotripsy.

Table 1. Showing the stone expulsion rates ,mean duration of expulsion, and episodes of pain in all the groups.

| Groups | Stone expulsion rate (%) | Mean duration of expulsion (in days) | Patients having pain (%) |
|---|---|---|---|
| A | 12 (40%) | 12.42 | 22 (73.3%) |
| B | 25 (83%) | 11.8 | 19 (63.3%) |
| C | 26 (86%) | 12.27 | 15 (50%) |
| D | 28 (93%) | 6.4 | 10 (33.3%) |
| E | 28 (93%) | 9.92 | 13 (43.3%) |

## DISCUSSION

For lower ureteric stones, the spectrum of treatment options includes watchful waiting, ESWL, ureterolithotomy, and URSL. URSL is considered to be the gold standard for lower ureteric stones, but it is not risk free, requires general anesthesia, is expensive [1], and facilities are not widely available in developing countries like India. To have a treatment modality that is safe, noninvasive, and effective, non-complicated lower ureteric stones need time. According to the European Association of Urology Guidelines on Urolithiasis for 2013, medical expulsive therapy is recommended for any ureteric calculus < 10 mm if active stone removal is not indicated and alpha-blockers are used for MET.

Three different types of adrenergic receptors are identified: $\alpha$1a, $\alpha$1b, and $\alpha$1d [2]. The distribution of adrenergic receptors throughout the inner and outer smooth muscles of the ureter is highest for $\alpha$1d, followed by $\alpha$-1a and $\alpha$1b [3]. Blocking these $\alpha$-adrenergic receptors inhibits basal smooth muscle tone and hyperperistaltic uncoordinated frequency while maintaining tonic propulsive contractions [4]. Calculi in the ureter induce uncoordinated ureteric contractions, which interfere with calculi expulsion. Muscle relaxation with maintenance of normal antegrade peristaltic activity will facilitate expulsion of a stone. The ureteric calculus stimulates inflammatory changes in periuretric tissues with submucosal edema hampering further calculi expulsion [5]. Hence, the drugs that can block these $\alpha$

-adrenergic receptors in the distal ureter or those that can reduce the edema in and around the ureteric calculi can facilitate calculi expulsion. Such drugs include $\alpha$-adrenergic receptor blockers and anti-inflammatory drugs like corticosteroids. A number of randomized clinical trials (RCTs) have tested these drugs, and the resulting findings have almost always been interpreted and proclaimed as proof of efficacy [6].

Griwan et al. reported a calculus expulsion rate of 90% using tamsulosin [7]. They also found a statistically significant decreased number of pain episodes in the tamsulosin group compared to the control group. Al-Ansari found statistically significant stone expulsion rates (82%) in the tamsulosin group compared to the control group (61%) [8]. In our study, the calculus expulsion rate in lower ureteric calculi was 86% and a statistically significant decrease in the number of pain episodes in the tamsulosin arm (50%) compared to control arm (73.3%). Deliveliotis et al. found decreased stent-related urinary symptoms and pain with alfuzosin in patients who opted for conservative management for ureteric calculi with an indwelling DJ stent [9].

Porpiglia et al. studied the efficacy of tamsulosin and deflazacort for the expulsion of lower ureteric calculi less than or equal to 1 cm, and found statistically significant increased calculi expulsion rates, decreased calculi expulsion duration, and decreased pain episodes compared to control [10]. In our study, we also found a statistically significant increased calculi expulsion rate, decreased calculi expulsion duration, and decreased pain episodes compared to control.

Xizhao Sun et al. found statistically significant calculi expulsion rates with naftopidil (90%) compared to the control group (26.6%) [11]. In our study, we found a statistically significant calculi expulsion rate in the naftopidil group (83%) compared

to the control group (40%).

In our study, the naftopidil plus deflazacort group had a statistically significant advantage over the control group with stone expulsion rates, the mean duration of expulsion, and decreased pain episodes.

## CONCLUSION

Medical expulsive therapy should be considered for uncomplicated distal ureteral calculi less than or equal to 1 cm as the first line of treatment. Alpha-adrenergic blockers have been found to increase and hasten stone expulsion rates, reduce mean days to stone expulsion, and decreases pain episodes. The addition of deflazacort further hastens the calculus expulsion rates, reduces mean days to stone expulsion, and decreases pain episodes. In our study, we got the best results with naftopidil plus deflazacort. However, larger prospective randomized controlled trials will provide more information into the effectiveness of MET for uncomplicated lower ureteric calculi.

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# Tubeless, Stentless Percutaneous Nephrolithotomy: An Initial Study

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**ABSTRACT**

**Objective**: To study the ability of rendering our patients tube and stent free after percutaneous nephrolithotomy (PNL).

**Patients and Methods**: Between February 2011 and March 2012, 38 patients (40 units) with 20 to 60 mm (mean: 31.17) renal stones underwent tubeless stentless PNL. The sample consisted of 28 males and 10 females, and their ages ranged between 17 and 65 years (mean: 33.7). Twenty-two cases were in the right kidney while 18 were in the left, and the stones were bilateral in 2. Most of the stones were in the renal pelvis and lower calyx and removed through the lower calyx subcostal with a single puncture. After ensuring that the patient was almost stone free, no nephrostomy was left and the ureteric catheter was removed within 30 minutes.

**Results**: Operative time ranged between 15 and 80 mins (mean: 42.34) and no blood transfusion was needed. The mean reduction in hemoglobin level was 1.52 gm (range: 0.3 to 4.8) and the hospital stay ranged between 12 to 36 hours (mean: 17.7). The success rate was 100% while the stone free rate was 95%. Analgesia was needed in 20% of cases. There were no intraoperative complications while postoperative complications occurred in 3 patients (7.9%) in the form of leakage, perirenal collection, and secondary hemorrhage.

**Conclusion**: Tubeless, stentless PNL is safe with acceptable complications, provided patients are stone free with no or minimal extravasations, have acceptable bleeding, and there is a single puncture. It decreases hospital stay, postoperative pain, and the need for analgesia, and subsequently lowered work abstinence. A further study with a larger sample is needed.

## INTRODUCTION

In recent years, percutaneous nephrolithotomy (PNL) has replaced open surgery in treating renal stones. Nephrostomy tubes with different diameters were the standard postoperative method for drainage, aiming at tamponade bleeding [1,2]. However, postoperative pain and prolonged hospital stays proved to be outcomes [3,4]. Hence it was recently replaced by either the double-J stent or externalized ureteric catheter [1,5], which was known as tubeless PNL. Further advancement in PNL is omitting both the nephrostomy tube and ureteric catheter or double-J stent; this is known as totally tubeless PNL [3,6].

## PATIENTS AND METHODS

Between February 2011 and March 2012, 38 patients (40 units) out of 350 patients admitted to our department for PNL and underwent tubeless stentless percutaneous nephrolithotomy

**KEYWORDS**: Stentless, tubeless, PNL

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(TSPNL). The files were retrospectively reviewed in order to study the outcome.

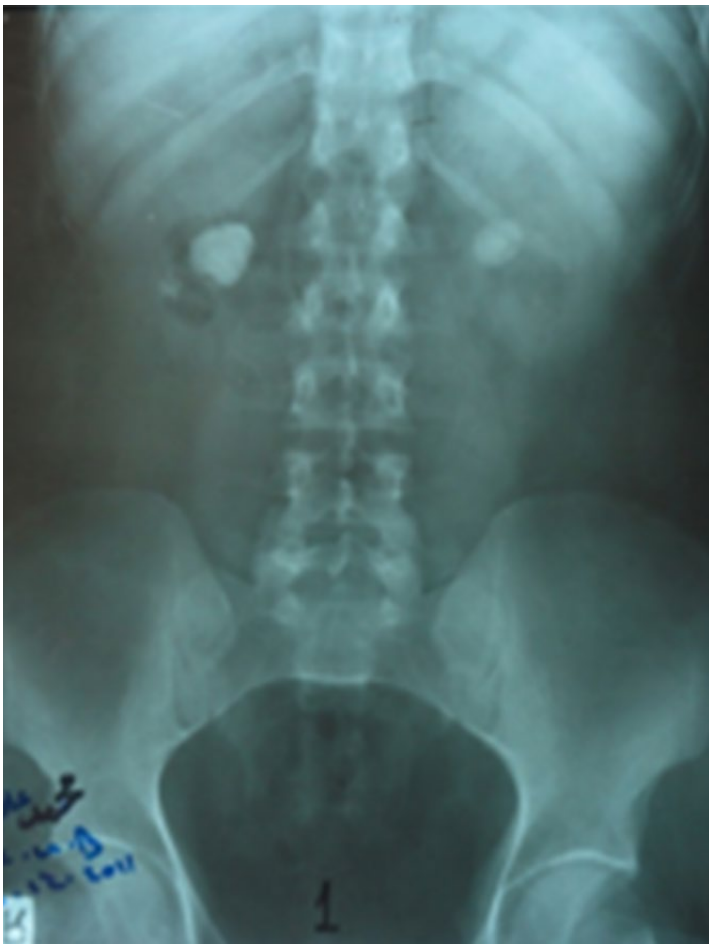
After obtaining approval from the medical committee and written consent from the patient, we made a decision to enroll him/her for TSPNL. Our inclusion criteria were: the patient must be stone free with acceptable bleeding, no or minimal extravasation, and a single puncture.

Under general anesthesia, a ureteric catheter of 6 Fr was inserted with a 14 Fr Foley urethral catheter. Thirty-six patients were treated in the prone position while 2 patients were treated in the supine position (the standard method). Our method of tract dilatation used the one-shot dilatation method through insertion of a 30 Fr Amplatz dilator over the central Alken, and then sliding a 34 Fr Amplatz sheath over. Bilateral PNL was done in 2 patients, 1 simultaneously and the second was staged. Toward the end of the procedure, we examined the pelvicalyceal system by nephroscope and by fluoroscopy guidance to be sure that the patient was stone free. Retrograde pyelography was done so there was no or minimal extravasation, the Amplatz sheath was removed (tubeless), and the wound was stitched using o/silk. The ureteric catheters were removed within 30 minutes, and 1 hour later the Foley catheter was also removed. The patients were transferred to the ward and observed for pain and analgesic need. Hemoglobin (Hb), kidney, ureter, and bladder X-rays (KUB), and abdominal ultrasound during the first postoperative day were routinely done.

## RESULTS

The stone burden was 20 to 60 mm (mean: 31.17) in the greatest diameter. Operative time was between 15 to 80 mins (mean: 42.34). There were 2 patients who had bilateral kidney stones; in one, both sides were treated simultaneously (Figure 1a, Figure 1b, Figure 2) while the other one was staged. No patient needed a blood transfusion and the Hb drop ranged between 0.3 to 4.8 gm (mean: 1.65). Eight patients (20%) needed analgesia in the form of 75 mg of declofenac (once in 5, twice in 1), 50 mg of tramadol in 2, and the rest (80%) did not need any. Hospital stay was 12 to 24 hours (mean: 17.4) with only 1 patient needing 36 hours due to urine leakage. The success rate was 100% while the stone-free rate was 95%, as 2 patients had residual 4 mm lower calyceal stones. Postoperative complications occurred in 3 patients (7.9%): 1 developed mild retroperitoneal collection and was treated conservatively; another developed leakage stopped by double-J stent insertion; and the third developed bleeding 5 days after discharge, was readmitted, and was given 2 units of blood with embolization.

Figure 1a. Preoperative KUB.



## DISCUSSION

The technique of PNL has been steadily refined and improved since its development in the 1970s. During this process of evolution, there was a tendency to drain the kidney percutaneously in the belief that this was the safest option while also allowing a second-look procedure [6]. Omitting a nephrostomy tube was established without serious complications. Lastly, avoiding ureteric stenting with a double-J stent, or externalized ureteric catheter, is the most recent improvement in the PNL technique in selected patients [7]. As ureteric stenting is associated with significant symptoms, it has been necessary to devise validated stent symptom scores for use in trials [8]. Also, the necessity for performing a cystoscopy for removal with potential for further morbidity can be avoided by the use of an externalized ureteric catheter [9].

There was no significant postoperative ureteral obstruction. This is attributed to the careful selection of patients with minimal or no residual stone load. Also, the potential for clot colic is probably not as likely as might be expected, because it's well established that urine has a thrombolytic effect due to the presence of urokinase [10].

Figure 1b. Preoperative IVP.

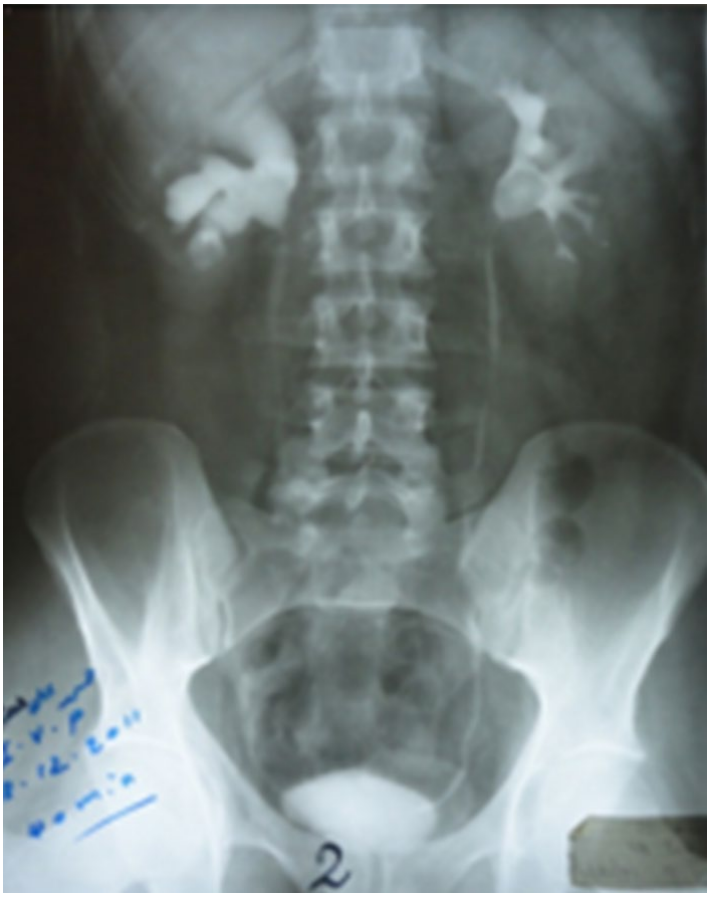
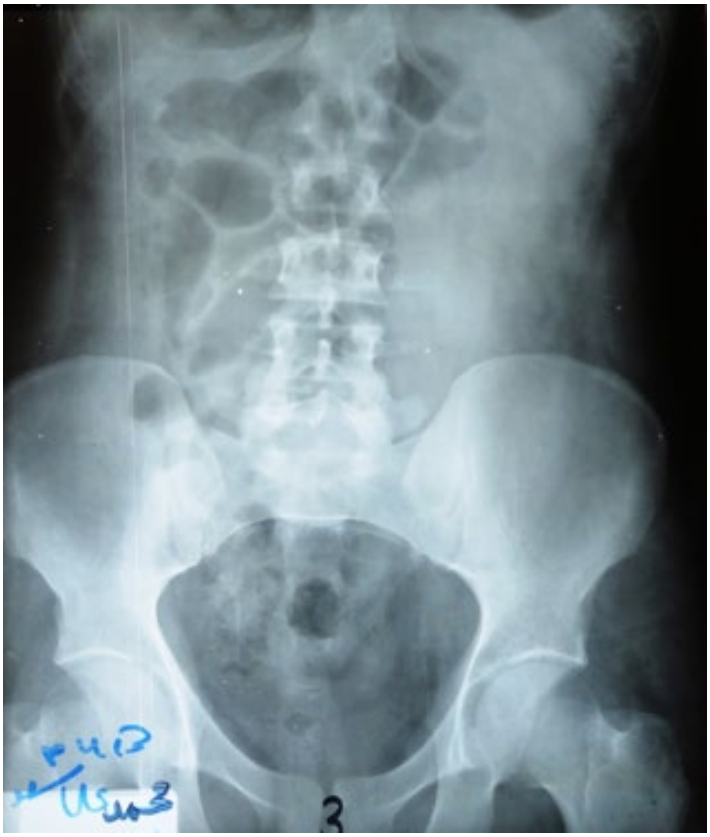


Figure 2. Postoperative KUB..



Gupta et al. performed totally tubeless PNL on 96 patients, with symptomatic lower calyceal stones < 1 cm that were resistant to extracorporeal shockwave lithotripsy [11]. All patients were stone free with minimal morbidity and shorter hospital stays.
Istanbulluoglu et al. compared totally tubeless PNL with standard PNL, with a mean stone burden of 448.93 and 453.35, respectively, and found that totally tubeless PNL can be performed safely in selected patients when there is no major bleeding or perforation of the collecting system, no residual stone fragments, or congenital anomalies. Analgesia requirement and hospital stay are significantly less than with the standard method [12]. A limited number of tubeless PNL in children were reported [13], with only 1 study with a limited number of cases of totally tubeless in preschool children, which was performed by Oztrurk et al. They stated that the maneuver is safe and effective with no significant difference between it and the standard method in terms of analgesia hospital stay [14]. The stone size was 15.24 mm.

From our point of view there was a tendency to make PNL a day case as the hospital stay was less than 24 hours in most cases (mean: 17.4). Also, the stone size was 2 to 6 cm (mean: 3.41), which means that the stone burden was increased in comparison to previous studies [4,11,14].

Few minor complications occurred and were managed conservatively; apart from serious bleeding that occurred in 1 patient who needed readmission and was treated by embolization. Analgesia was needed in only 20% of patients and blood transfusion was needed in 1 case.

## CONCLUSION

Stentless, tubeless PNL is a useful option to consider. It has

the advantages of decreased postoperative pain, analgesia need, and hospital stay; decreased cost; and less missed work. It should be restricted to patients who are stone free with acceptable bleeding, and a single puncture without or with minimal extravasation. Further studies with a larger sample may decrease these limitations.

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# Obstructive Effect of a Urethral Catheter During Voiding: Myth or Reality?

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**ABSTRACT**

**Introduction**: Whether or not the presence of a urethral catheter can provoke an obstructive effect during voiding remains a controversial subject. Using the Valentini–Besson–Nelson (VBN) mathematical micturition model, the purpose of this study was to compare the geometric effect of the urethral catheter in regards to the effect of other mechanical parameters likely to influence the voiding phase during a urodynamic study.

**Methods**: The VBN mathematical micturition model was used to compute theoretical voidings. Starting from defined voiding conditions ($Q°_{max}$) such as $V_{ini}$ = 300 mL, no catheter, normal detrusor contractility, and no urethral compression, we searched for relationships between changes in $Q_{max}$ and the studied parameters: catheter diameter (F), detrusor contractility (k), and urethral compression (urac).

**Results**: A linearized approximation was obtained for both genders. The geometric obstruction due to the catheter was almost negligible for nonobstructed individuals compared with the volume effect up to a 6 Fr catheter size. Large decreases in $Q_{max}$ resulted from impaired detrusor contractility or urethral compression. Higher effects resulted from concomitant decrease in detrusor contractility and urethral compression. Geometric effect of the catheter could lead to overestimation of bladder outlet obstruction in men.

**Conclusion**: A decrease in $Q_{max}$ during voiding cystometrogram was found to be more often related to causes other than the catheter size, which, based on the VBN model, appeared to have a weak (almost negligible for nonobstructed individuals) effect, especially for small sizes (≤ 6 Fr).

## INTRODUCTION

Invasive urodynamic studies using transurethral catheterization are commonly performed to evaluate bladder outlet obstruction (BOO) in males and to predict voiding dysfunction after anti-incontinence procedures in females. A controversial subject is the potential obstructive effect from the mere presence of the catheter during voiding, which could lead to a false interpretation of these investigations.

A nondebatable effect of the catheter comes from its geometric presence, which reduces the lumen and the urethral cross-section through which urine travels during voiding. The main consequences of this effect are a decreased flow rate and a longer flow time. That geometric effect is difficult to distinguish from other mechanical effects, which can influence the maximum flow ($Q_{max}$) such as the initial bladder volume ($V_{ini}$), or the role of urethral compression, which in the early stage

**KEYWORDS**: Catheter, flow rate, mathematical modeling, urodynamics

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of an obstructive process can induce a significant hypertrophy of the bladder wall, resulting in stronger detrusor contraction. Additional factors can influence voiding, including the fact that patients are voiding in an unusual environment, which can lead to abnormal nervous excitations mainly due to anxiety in this perceived stressful situation.

Therefore, to reach reliable conclusions on the obstructive effect of the urethral catheter, studies should be conducted on patients with the same kind of lower urinary tract dysfunction (LUTD) and for similar initial bladder volumes.

Although many studies on this subject have been published, no reliable conclusions have been proposed thus far. An obstructive effect of both 5 Fr and 10 Fr catheters has been reported in men with benign prostatic enlargement (BPE) [1], but conversely no significant effect of an 8 Fr catheter was noted in men with lower urinary tract symptoms (LUTS) [2]. In women, publications are even more limited, but controversial, and show opposite findings as follows: significant obstructive effect of a 6 Fr [3], of a 7 Fr catheter in healthy women [4], of different sized catheters [5,6], or 7 Fr [7] in women with LUTS, a positive effect with a 7 Fr catheter [8], and no effect of a 4 Fr catheter [9] or of 2 5 Fr catheters [10].

For other parameters such as voided volume and its effect on increasing $Q_{max}$, more data is available [11,12].

Thus, for both genders, evaluation of the changes in maximum flow rate induced by a urethral catheter remains an unresolved issue. And in men this is a very relevant question since pressure flow studies are the gold standards to determine whether or not BOO is present. Now, if there is an impact from the presence and size of the urethral catheter on maximum flow rate ($Q_{max}$) and consequently on detrusor pressure ($p_{det}$), one should wonder about the consequences of such impact on the categorization of BOO using the Abrams-Griffiths number (A-G) or ICS provisional nomogram [13] (3 classes according to the BOO index (BOOI) [14]) which do not take into account the catheter effect.

To try to address this unsettled debate, we applied the VBN mathematical model of micturition, which allows simulations of the possible scenarios likely to influence $Q_{max}$, including catheter size, initial bladder volume, detrusor contractility, and urethral compression.

## METHODS

The VBN mathematical micturition model [15,16] was used to investigate the effect of catheter size during voiding and to tease out its role against other influential parameters of voiding, such as bladder volume, degree of detrusor contractility, and urethral obstruction secondary to outer urethral compression.

In the VBN model, the detrusor contractility (or detrusor force) is characterized by the VBN parameter k (k = 1 for normal detrusor) (no unit) and is independent of gender. Because the anatomy of the urethra differs in men and women, outer urethral obstruction is characterized for each gender by specific parameters: $\gamma$ for female and pucp (prostatic urethral counter pressure) for male (unit cm $H_2O$) ($\gamma$ = pucp = 0 for normal subject).

Reference, nonintricate, and intricate cases were defined. Reference case was defined as normal detrusor contractility (k = 1), normal urethra (no compression, no constriction), normal nervous excitations of the detrusor and sphincter, and no abdominal straining. Nonintricate cases implied nonreference values of detrusor contractility, urethral parameters, simplicity of nervous excitations, and no predominant abdominal straining [17]. Intricate cases implied abnormal nervous excitations, predominant abdominal straining, and interrupted flow curves. Only reference and nonintricate cases were considered in this study.

Computations for nonintricate cases needed only 5 simple entries: gender (mainly due to the anatomic differences in urethra between female and male), catheter size and initial bladder volume, detrusor contractility, and urethral condition.

Simulations were made without a catheter and for a range of catheter sizes frequently utilized during urodynamic studies (UDS): 3.5, 5, 6, 7, and 8 Fr; initial bladder volume range was 100 to 600 mL (the urodynamic parameters during the voiding phase depend on the initial bladder volume). Comparisons were made between the computed $Q_{max}$ in various conditions.

Starting from defined voiding conditions ($Q°_{max}$) such as $V_{ini}$ = 300 mL, no catheter, normal detrusor contractility (k = 1), and no urethral compression (g = pucp = 0), we searched for relationships between changes in $Q_{max}$ and the studied parameters: catheter diameter (F), detrusor contractility (k), and urethral compression (named urac): $Q°_{max}$=37.0 mL/s for women and 29.1 mL/s for men.

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The VBN model gave the value of $Q_{max}$ in any case. In this paper, the global change $\Delta Q_{max}$ was fitted by a sum of independent terms, each of them related to a studied parameter X:

$$Q_{max} = Q°_{max} + \Delta_V Q_{max} + \Delta_F Q_{max} + \Delta_k Q_{max} + \Delta_{urac} Q_{max}$$

For each term we searched for the best fitting power law $\Delta_X Q_{max} = \alpha_X * \Delta X^n$. The contribution of each parameter was evaluated, the sum of the contributions was made, and the result compared to the computation in order to evaluate the precision.

For men, A-G was evaluated from computed $p_{det.Qmax}$ and $Q_{max}$ in various conditions.

## RESULTS

Characteristic curves $Q_{max} = f(V_{ini}, F, k)$ were obtained using the VBN software for women and men (examples are given in Figure 1 for women and Figure 2 for men). From these curves, the global change in $Q_{max}$ was obtained and the coefficients a and n identified for each studied parameter.

*Step by step evaluation of the contribution of the parameters*

***Volume effect*** (no catheter, normal detrusor contractility, no urethral compression)
The relationship Q(V) has been previously evaluated [10-11]:
$Q_{max} = Q°_{max} + \alpha_V * \Delta V^{1/2}$
with $\alpha_V$ = 1.417 for women and 0.956 for men, and n = ½ for both genders.
***Catheter size*** (normal detrusor contractility, no urethral compression)
$Q_{max} = Q°_{max} + \alpha_V * \Delta V^{1/2} + \alpha_F * \Delta F^n$
with $\alpha_{cath}$ = -0.0625 for women and -0.132 for men, and n = 2 for women and 1.8 for men.
***Detrusor contractility*** (no urethral compression)
$Q_{max} = Q°_{max} + \alpha_V * DV^{1/2} + \alpha_F * \Delta F^n + \alpha_k * \Delta k$
with $\alpha_k$ = 21.32 for women and 11.90 for men, and n = 1 for both genders.
***Urethral compression***
$Q_{max} = Q°_{max} + \alpha_V * \Delta V^{1/2} + \alpha_F * \Delta F^n + \alpha_k * \Delta k + \alpha_{urac} * \Delta urac$
with $\alpha_{urac}$ = -0.57 for women and -0.60 for men, and n = 1 for both genders.

Figure 1. Effect of various parameters on Qmax for women (initial bladder volume range from 0 to 600 mL, catheter size from 0 to 8 Fr. A) Reference case (k = 1; urac = 0). B) Effect of impaired detrusor contractility (k = 0.6; urac = 0). C) Concomitant effect of detrusor contractility and urethral compression (k = 0.45; urac = 15 cm $H_2O$).

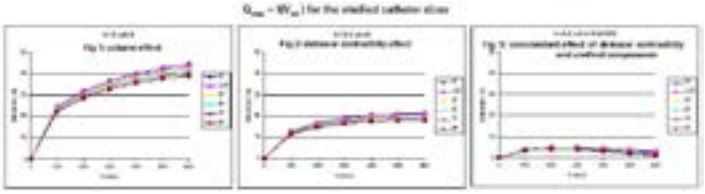
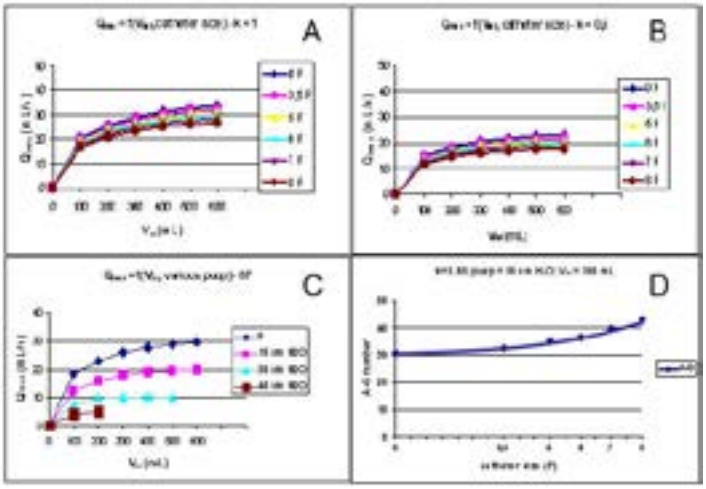


Figure 2. Effect of various parameters on Qmax for men (initial bladder volume range from 0 to 600 mL). A) Reference case, catheter size from 0 to 8 Fr. B) Effect of impaired detrusor contractility (k = 0.5), catheter size from 0 to 8 Fr. C) Effect of urethral compression and a 6 Fr catheter. D) Change in A-G number due to catheter size (k = 0.85, urac = 30 cm $H_2O$).




*Evaluation of change in $Q_{max}$ due to each parameter assuming the linearized equation (Table 1)*

***Volume effect*** (no catheter, normal detrusor contractility, no urethral compression)

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Table 1. Comparisons of maximum flow rate for initial bladder volume Vini = 300 mL between VBN computation and the value deduced from the linearized equation. One can observe that discrepancies occur for mechanical conditions involving impaired detrusor and urethral compression.

| $V_{ini}$ = 300 mL | Women: $Q°_{max}$ = 37.0 mL/s | | Men: $Q°_{max}$ = 29.1 mL/s | |
|---|---|---|---|---|
| Mechanical condition(s) | Computation | Linearized equation | Computation | Linearized equation |
| 6 Fr | 34.8 mL/s | 34.75 mL/s | 25.9 mL/s | 25.8 mL/s |
| k = 0.5 | 25.3 mL/s | 25.35 mL/s | 20.5 mL/s | 20.5 mL/s |
| urac = 15 cm $H_2O$ | 28 mL/s | 28.2 mL/s | 20.1 mL/s | 20.1 mL/s |
| 6 Fr, k = 0.5 | 24.7 mL/s | 24.3 mL/s | 18 mL/s | 17.2 mL/s |
| 6 Fr, urac = 15 cm $H_2O$ | 26.9 mL/s | 26.0 mL/s | 17.9 mL/s | 16.9 mL/s |
| k = 0.5, urac = 15 cm $H_2O$ | 14.5 mL/s | 17.5 mL/s | 9.8 mL/s | 12.5 mL/s |
| 6 Fr, k = 0.5, urac = 15 cm $H_2O$ | 13.9 mL/s | 15.3 mL/s | 8.5 mL/s | 8.2 mL/s |

Table 2. Evaluation of the geometric effect of the urethral catheter on A-G number (or BOOI) in reference case (normal detrusor contractility, normal urethra (no compression, no constriction), normal nervous excitations of detrusor and sphincter, and no abdominal straining).

| Catheter size (Fr) | 0 | 3.5 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|
| $Q_{max}$ (mL/s) | 29.1 | 27.9 | 26.8 | 25.9 | 24.8 | 23.5 |
| $p_{det.Qmax}$ (cm $H_2O$) | 30 | 31 | 32 | 32.5 | 33 | 34 |
| $\Delta Q_{max}$ (mL/s) | 0 | -1.2 | -2.3 | -3.2 | -4.3 | -5.6 |
| $\Delta p_{det.Qmax}$ (cm $H_2O$) | 0 | 1 | 1.9 | 2.6 | 3.3 | 4 |
| $\Delta$(A-G) | 0 | 3.4 | 6.5 | 9 | 11.9 | 15.2 |

In the usual range of initial bladder volume, an increase in volume led to an increase of $Q_{max}$. An increase from 200 mL to 400 mL led to $\Delta Q_{max}$ = +8.3 mL/s for women and $\Delta Q_{max}$ = +5.6 mL/s for men.

***Catheter size*** (normal detrusor contractility, no urethral compression)

The effect of a 6 Fr catheter was $\Delta Q_{max}$ = -2.25 mL/s for women and $\Delta Q_{max}$ = -3.32 mL/s for men.

For an increase of bladder volume from 200 to 400 mL, the volume effect was always higher than the catheter effect for women, while for men that condition was only observed for catheter sizes smaller than 8 Fr.

***Detrusor contractility*** (no urethral compression)

A large decrease in $Q_{max}$ resulted from a decrease in detrusor contractility for both genders. For example, for $V_{ini}$ = 300 mL, a decrease in detrusor contractility k from 1 to 0.5 led to $DQ_{max}$ = -10.5 mL/s for women and $\Delta Q_{max}$ = -8.6 mL/s for men.

***Urethral compression***

A large decrease in $Q_{max}$ resulted from an increase in urethral compression for both genders. For example, for $V_{ini}$ = 300 mL, a urethral compression of 15 cm $H_2O$ led to $\Delta Q_{max}$ = -8.8 mL/s for women and $\Delta Q_{max}$ = -9.0 mL/s for men.

Note that k and urac can compensate if $\alpha_{urac}$*$\Delta$urac = $\alpha_k$*$\Delta$k as in the first stage of BPE; i.e., when the detrusor force can compensate for urethral obstruction.

*Comparison of the values of $Q_{max}$ obtained from computation and linear equation (Table 1)*

Results are given in Table 1.

*Effect of the geometric effect of the catheter on A-G and BOOI*

A-G or BOOI (and provisional ICS nomogram) do not take into account the catheter effect and therefore both $p_{det.Qmax}$ and $Q_{max}$ values are all attributed to a urethral compression from BPE.

In fact, the contribution of the catheter should be evaluated. The following are formulas taking into account the obstructive effect of the catheter on both $p_{det.Qmax}$ and $Q_{max}$:

$\Delta Q_{max} = 0.132*F^{1.8}$, $\Delta p_{det.Qmax} = 0.714*DQ_{max}$ and $\Delta$A-G = $\Delta p_{det.Qmax} + 2*\Delta Q_{max} = 0.358*F^{1.8}$

For example, for a male subject without BOO ($V_{ini}$ = 300 mL, k=1, no urac, and different catheter sizes) the use of the above formulas led to the results given in Table 2. The geometric effect of the catheter introduced an uncertainty in the evaluation of BOO (ICS limits of A-G are from < 20 unobstructed to > 40 obstructed): DA-G = + 9 (6F) and + 15.2 (8F).

In another example shown in Figure 2D, one can see the geometric effect of the catheter on the evaluation of A-G for

a man with BPE ($V_{ini}$ = 300 mL, moderate impaired detrusor contractility k = 0.85 and urethral compression of 30 cm $H_20$).

## DISCUSSION

For a given initial bladder volume, the observed $Q_{max}$ during intubated flow is often lower than the $Q_{max}$ during free uroflow. Sometimes the decrease is higher than the expected decrease secondary to the geometric effect of the catheter. In fact, several mechanical effects (such as detrusor contractility, urethral compression, and geometric effect of the catheter) may combine together and functionally affect and modify $Q_{max}$. Thus, a reliable evaluation of the catheter effect remains difficult. In this study, only mechanical conditions and the possible "urethral reflex" were analyzed due to the foreign material in place [18], and abnormal nervous excitation of detrusor and sphincter are not considered.

Mathematical modeling is a very useful tool to allow simulations of such intricate conditions. For standard voiding, the initial conditions are as follows: $V_{ini}$ = 300 mL; k = 1; urac = 0; no catheter; and thus, one can use an approximation such that the various effects are additive. The coefficients a and n related to each effect have been evaluated. It is clear that this approximation is not reliable when the bladder volume is close to zero or when a patient is nearing retention. In these 2 extreme conditions, the linearized approximation gives only qualitative results.

This manuscript presents comparative orders of magnitude for the different effects. Increases in initial volume leading to increased $Q_{max}$ and the geometric obstruction due to the catheter are almost negligible compared with the volume effect until reaching a 6 Fr catheter size for both genders. On the other hand, strong decreases in $Q_{max}$ are observed with impaired detrusor contractility or urethral compression, with the highest effect when concomitant decreases in detrusor contractility and urethral compression are present.

In a BPE patient needing an evaluation of BOO, the geometric effect of the catheter induces an uncertainty on the obstruction status according to A-G numbers (or BOOI), which may underestimate the degree of obstruction. In their study, Klausner et al. [19] have demonstrated that there was a category migration in the Abrams-Griffiths nomogram, with a change from 5 Fr to 10 Fr catheters, and they concluded, "this category migration might potentially result in unnecessary therapeutic action." Another condition to take into account is in the first stage of BPE when hypertrophy of the bladder wall maintains adequate contractile function; in that situation, the decrease in $Q_{max}$ due to urethral obstruction can be partially or totally compensated by the increase in detrusor contractility. Consequently, $Q_{max}$ is mainly affected by $V_{ini}$ and/or the presence of the urethral catheter.

Finally, it is important to note that any obstruction (including the catheter effect) increases the voiding time. It has been demonstrated [20] that such conditions lead to high residual volumes due to an early closure of the sphincter.

## CONCLUSION

The main reason for a decrease in $Q_{max}$ during an intubated flow is low detrusor contractility with or without compressive urethral obstruction. If the decrease in $Q_{max}$ can be due to the presence of the catheter, we found that in this study, using the VBN model, that effect remained negligible for the usual catheter sizes selected for urodynamic testing compared to other causes of $Q_{max}$ decrease.

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# A Large Calculus in Crossed Renal Ectopia without Fusion: A Case Report

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**ABSTRACT**

Crossed renal ectopia is a congenital malformation that occurs either in fused or non-fused form. Only 10% are of the non-fused variety. Most cases remain undiagnosed because they remain asymptomatic. We report a case of crossed left-to-right renal ectopia with stones and successful management.

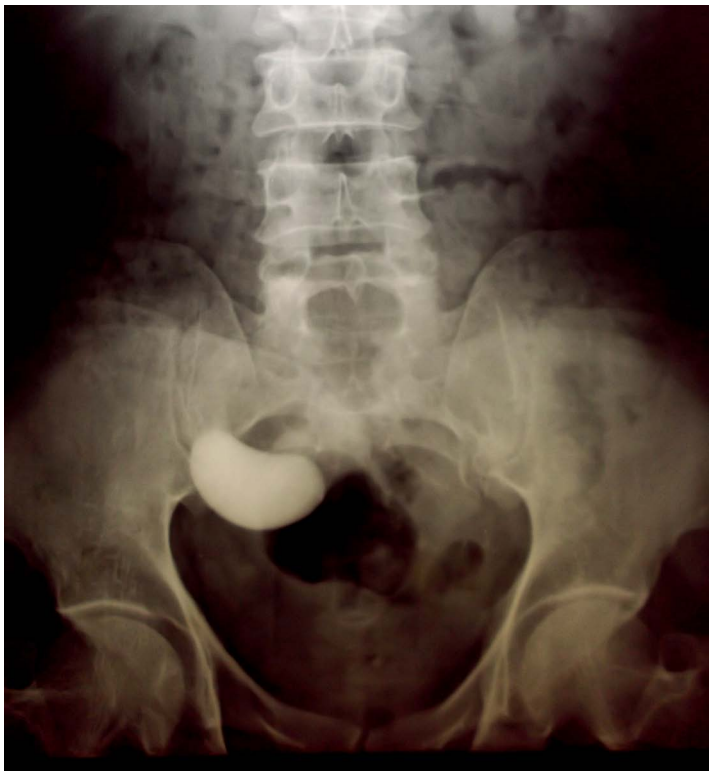
## INTRODUCTION

Crossed renal ectopia is a congenital malformation that occurs either in fused or non-fused form. Only 10% are of the non-fused variety. Most cases remain undiagnosed because they remain asymptomatic [1]. We report a case of crossed left-to-right renal ectopia with stones and successful management.

## CASE REPORT

A 50-year-old male presented with complaints of right lower abdominal pain for 2 years. The pain was dull and intermittent. There was no history of hematuria, graveluria, increased urinary frequency, or urgency. There was a palpable lump in the right lower abdomen. Urinalysis revealed microscopic hematuria, while the urine culture was sterile. His hematological and biochemical profiles were normal. The abdominal ultrasound revealed a large calculus about 4 cm x 4 cm in the left-to-right crossed ectopic kidney, casting a posterior acoustic shadow. The right kidney was malrotated. A plain abdominal X-ray showed a large radio-opaque shadow over the lower border of the right side of the ala of the sacrum (Figure 1). Intravenous urography revealed a normally functioning, malrotated orthotopic right kidney with a non-dilated pelvicalyceal system. The left-to-right crossed ectopic kidney showed a large calculus with a dilated pelvicalyceal system (Figure 2). Computed tomography showed a left-to-right crossed ectopic kidney with dilated pelvicalyceal

Figure 1. Plain abdominal X-ray showing a heart-shaped radio-opaque shadow over the lower border of right side of the ala of the sacrum.



**KEYWORDS**: Crossed ectopia, kidney without fusion, calculus

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system and malrotated orthotopic kidney (Figure 3 and Figure 4). A micturating cystourethrogram showed no reflux. Cystoscopy showed normal bilateral ureteric orifices.

Bilateral ureteric catheterization was done. Right pyelolithotomy was done in the supine position with a 300 tilt using an extraperitoneal approach. The overlying fascia was opened with sharp dissection, and peripelvic dissection was carried out. The ureter of the orthotopic right kidney was present just lateral to the pelvis of the crossed ectopic kidney. A liberal pyelolithotomy was done. A stone (4 cm x 4 cm x 2 cm) was delivered with little manipulation (Figure 5 and Figure 6). A DJ stent was placed in the left-to-right cross-ectopic ureter (Figure 7). The postoperative period was uneventful.

## DISCUSSION

Simple renal ectopia refers to a kidney that is located on the proper side of the abdomen but is abnormal in position. Crossed

Figure 2. Intravenous urography revealed malrotated orthotopic right kidney and crossed ectopic kidney with hydronephrosis.

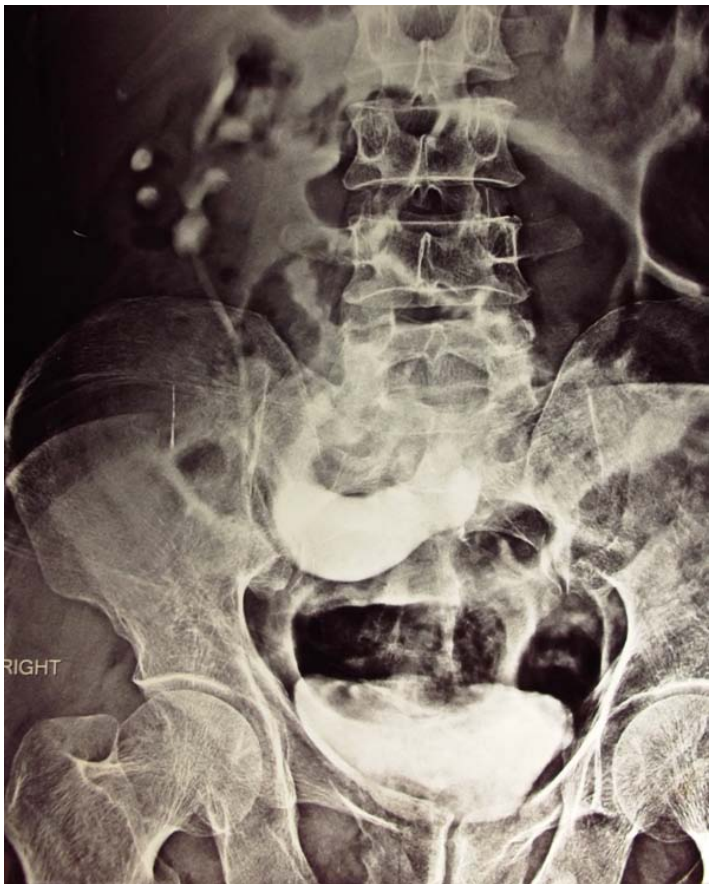



Figure 4. Computed tomography showed a left-to-right crossed ectopic kidney.

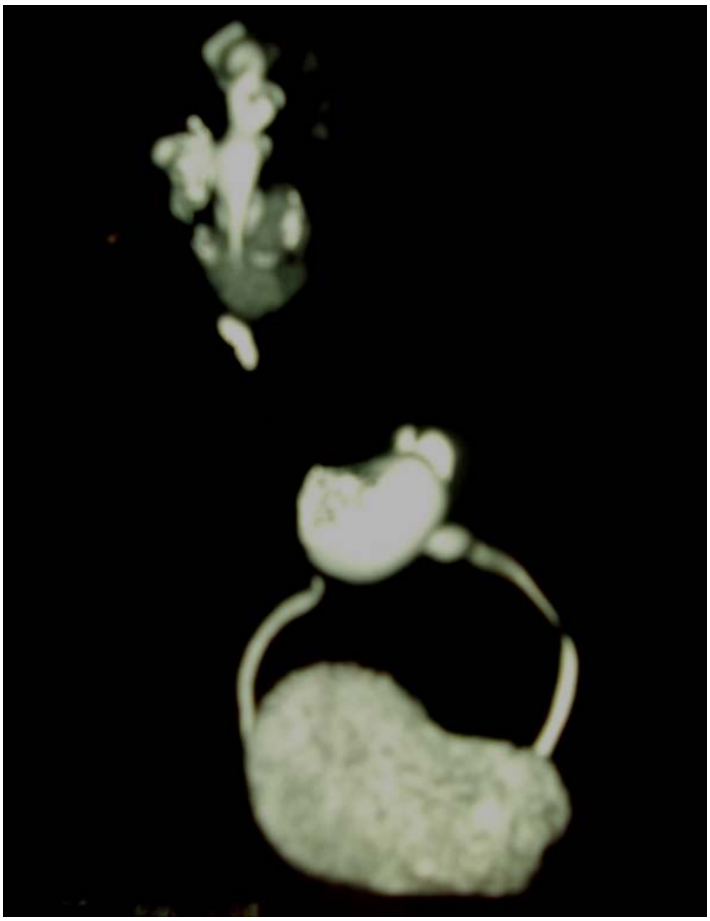


Figure 3. Computed tomography showed a left-to-right crossed ectopic kidney with a dilated pelvicalyceal system.

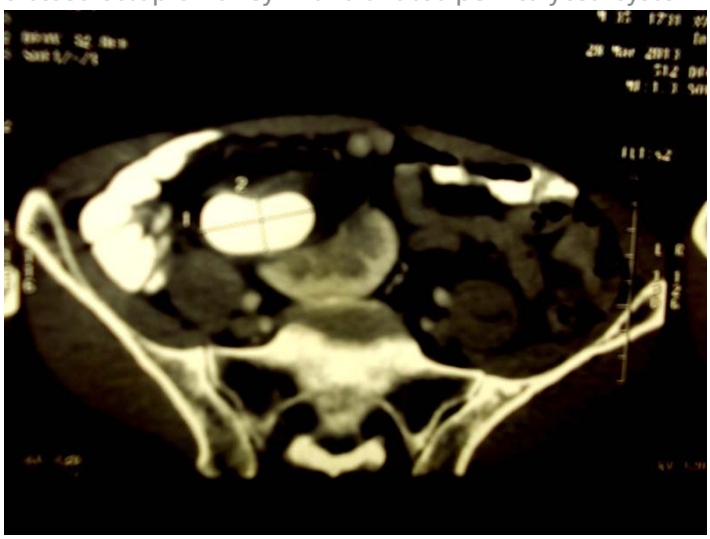


Figure 5. Operative photograph showed a heart-shaped calculus.

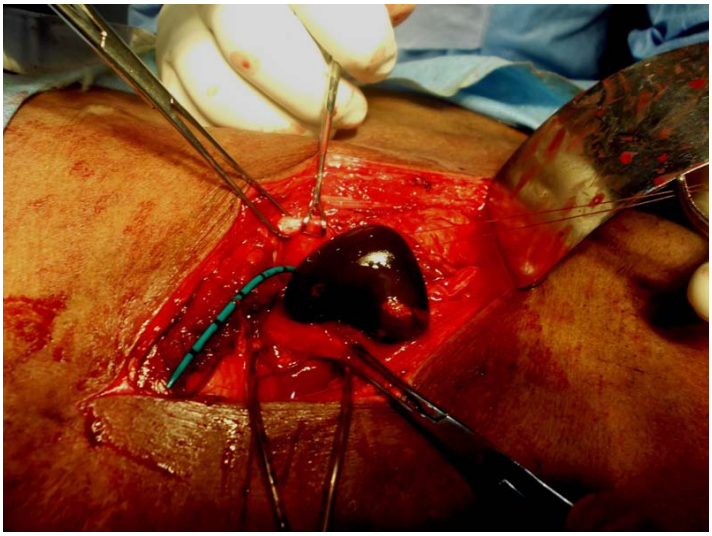


Figure 6. A heart-shaped stone.


renal ectopia on the other hand refers to a kidney that has crossed from left to right or vice versa and was first described by Pamalorus in 1954 [2,3].

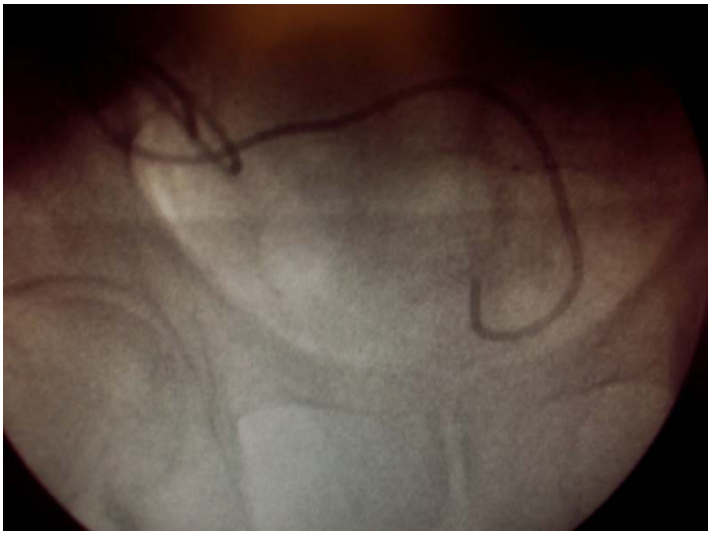
Fusion anomalies of the kidney were first categorized by Wilmer, but McDonald and McClellan re-fixed and expanded this classification to include crossed ectopia with fusion, crossed ectopia without fusion, solitary crossed ectopia, and bilaterally crossed ectopia [4].

A total of 62 patients with crossed ectopia without fusion have been reported [5]. This constitutes 10% of all crossed ectopic kidneys. The anomaly occurs more commonly in males, with a ratio of 2:1, and left-to-right ectopia is 3 times more common than right-to-left ectopia. The un-fused variety has been reported as 1 in 75,000 autopsies [6].

The cause of crossed renal ectopia is not known. Wilmer suggested that crossover occurs because of pressure from abnormally placed umbilical arteries that present cephalad migration of the renal unit, which then follows the path of least resistance of the opposite side. Genetic influence may play a role because familial inheritance of crossed renal ectopia has been reported [7].

The ectopic kidney is inferior, with either a diagonal or horizontal position with an anteriorly placed renal pelvis. A variable but definitive distance usually separates the 2 kidneys and each one is surrounded by its own Gerota's fascia. In every case of crossed renal ectopia without fusion, the ureter from the normal kidney enters the bladder on the same side,

Figure 7. The postoperative photograph showed a DJ stent in situ.



whereas that of the ectopic kidney enters the bladder on the contralateral side [8].

Most cases of crossed renal ectopia are asymptomatic and noted incidentally during autopsy, screening tests, or during investigation for unrelated causes [1,6]. Urinary tract disease such as vesicoureteral reflux, urinary tract infections, ureteroceles, renal calculi, and renovascular hypertension can coexist with ectopic kidneys, which are likely to be complicated by ureteropelvic junction obstruction because of their frequent abnormal shape, malrotation, and aberrant vasculature [9].

Other congenital anomalies may accompany crossed renal ectopia such as unilateral agenesis of the fallopian tubes and ovaries, skeletal abnormalities, an imperforate anus, and cardiopulmonary anomalies [9]. There was no congenital anomaly in our patient.

The diagnosis is made by ultrasonography and intravenous urography. An ultrasound can detect concomitant urinary pathology and cystic changes [10]. Anatomic delineation is best achieved by intravenous urography. Besides function, it can give an idea about ureteric displacement [11]

Other imaging modalities such as retrograde and intraoperative antegrade ureterography, renal cortical scintigraphy using 99m Tc-dinercaptosuccinic acid scans, computed tomography, and magnetic resonance imaging have been shown to be useful in the diagnosis of renal ectopia and ectopic ureters [12]. Generally, no treatment is needed for an ectopic kidney if renal function is normal and no complication such as urethral tract infection, stones, or obstruction are found. Even in the absence of these, patients need to be followed up closely [3].

Calculi in renal ectopia could be managed with shock wave lithotripsy (SWL), ureteroscopy, percutaneous nephrolithotomy, laparoscopic-guided percutaneous nephrolithotomy, laparoscopic pyelolithotomy, and open pyelolithotomy [13-17].

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# Bladder Diverticulum with Stone and Transitional Cell Carcinoma: A Case Report

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**ABSTRACT**

The incidence of bladder diverticulum is approximately 1.7% in children and 6% in adults. Dysplasia, leukoplakia, and squamous metaplasia and stone formation may develop in diverticulum and sometimes with malignant changes. The most common histological subtype of diverticulum tumors is transitional cell carcinoma (TCC). Herein we report 2 such cases of transitional cell carcinoma arising in diverticulum of the urinary bladder, one of which was associated with diverticular stones.

## INTRODUCTION

Bladder diverticulum is herniation of the bladder mucosa through bladder wall musculature (detrusor muscle). The incidence of bladder diverticulum is approximately 1.7% in children and 6% in adults [1]. Dysplasia, leukoplakia, and squamous metaplasia develop in approximately 80% of diverticulum. Chronic infection and inflammation, secondary to urinary stasis, were responsible for this situation [2].

Bladder tumors arising inside a diverticulum are uncommon, with a reported incidence ranging from 0.8 to 10%. The most common histological subtype of diverticulum tumors are transitional cell carcinoma (TCC) and squamous cell carcinoma (SCC), constituting 70 to 80% and 20 to 25% of all tumors, respectively [3]. TCC together with SCC is reported in 2% of all tumors while adenocarcinoma constitutes the other 2% of these diverticular tumors.

## CASE REPORT

*Case Number 1*

A 55 year-old male patient presented with lower urinary tract symptoms (LUTS) for 1 year. He had no history of hematuria. His urinalysis showed 0 to 2 pus cells but no red blood cells (RBC). No growth was present in the urine culture. Kidney, ureter, and bladder X-rays (KUB) were suggestive of a radio-opaque shadow in the left ureter line at the level of L-5 vertebrae (Figure 1). But the ultrasonography (USG) was suggestive of stones within a large bladder diverticulum with a thickened and irregular bladder wall while the prostate was normal in volume. Cystoscopy suggested the diverticulum in the left lateral wall of the bladder and it was covered with necrotic calcified tissue, along with a stone and a papilliferous growth surrounding it. Transurethral biopsy was performed, which showed low-grade, non-invasive urothelial tumors on histopathological examination.

Since the metastatic workup was negative for any local regional or distant metastasis, partial cystectomy was done and patient had an uneventful recovery. Final histopathology suggested low-grade TCC with a surgical margin free from tumor invasion. At the 1-year of follow-up with a cystoscopy check, the patient is tumor free.

*Case Number 2*

A 72 year-old-male patient presented with hematuria. Urinalysis showed RBC 15-20/HPF, 5 to 6 pus cells, and the culture was

**KEYWORDS**: Bladder diverticulum, stone, transitional cell carcinoma

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Figure 1. An opacity that is approximately 2 cm in its longest axis.

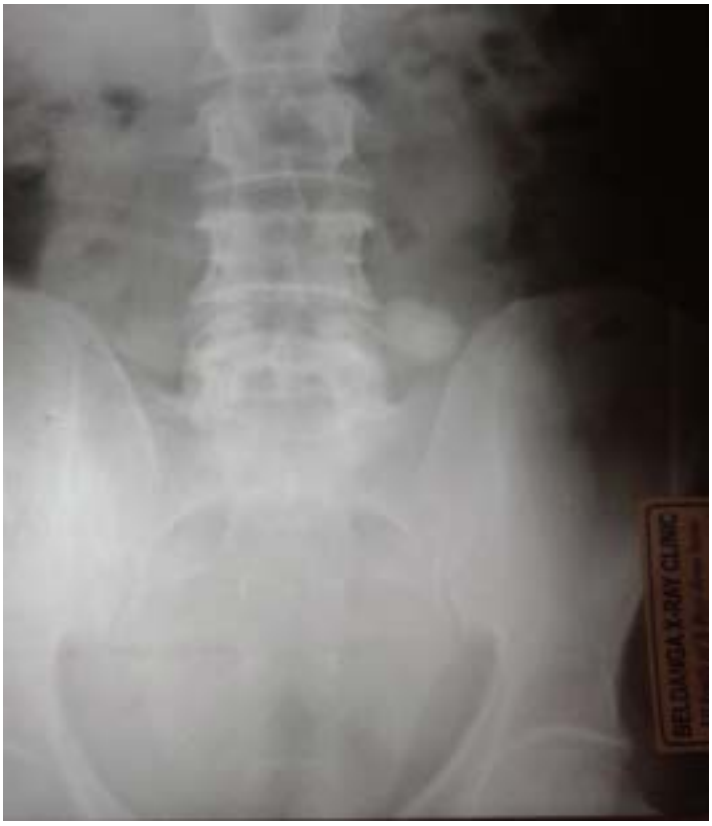


Figure 2. USG shows a big diverticulum in the left lateral wall.

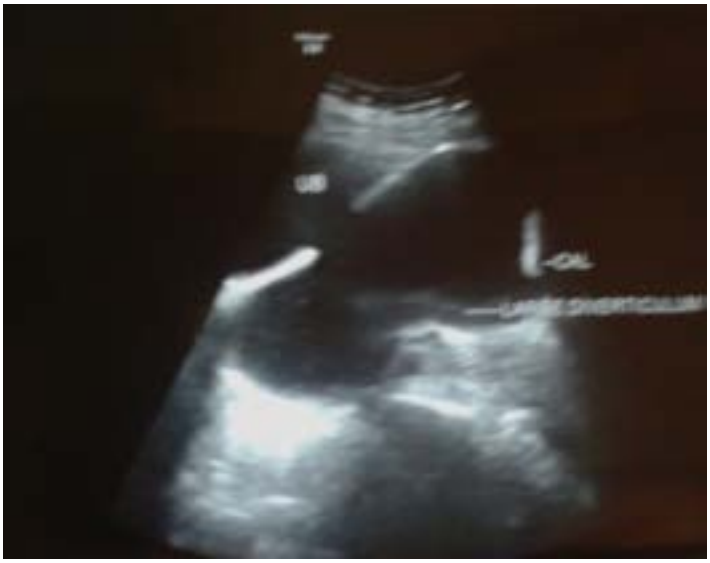
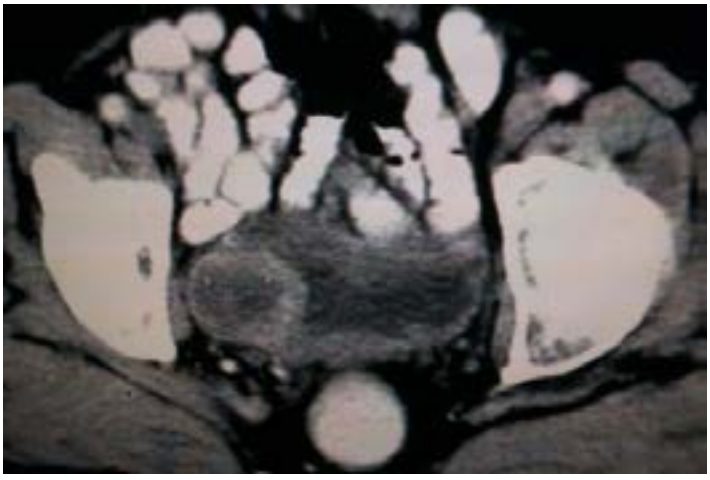


Figure 2. USG shows a big diverticulum in the left lateral wall.



positive for E. coli. The USG suggested a large diverticulum in the right lateral wall of the bladder along with a tumor. A computed tomography (CT) scan showed a large diverticulum with a tumor (2 cm x 3.5 cm) within it with no enlarged lymph nodes (Figure 3). Transurethral resection (TUR) biopsy was done and it suggested muscle invasive TCC. Radical cystectomy with an ileal conduit was done, and the histopathology suggested muscle invasive TCC. At the 6-month follow-up, the patient is doing well.

## DISCUSSION

Mucosal herniations through areas of congenital or acquired weakness in the muscular bladder wall are called diverticulum. Congenital bladder diverticulae are usually asymptomatic and usually detected incidentally during investigation for recurrent urinary tract infection, hematuria, or bladder emptying disorder. While acquired bladder diverticulae almost always occur secondary to intravesical obstruction [1]. It was previously thought that bladder tumors originating within a diverticulum were uncommon. However, according to the current study, neoplastic changes were present in half of cases (36/71; 51%), including both noninvasive (16/36; 44%) and invasive (20/36; 56%) carcinoma. Patients with invasive carcinoma in diverticulum have an increased frequency of less common bladder cancer subtypes. Bladder tumors in a diverticulum are a diagnostic and therapeutic problem. Yagci et al. pointed out that the neoplasms originating from a bladder diverticulum

are characterized by early transmural invasion and have a tendency for higher histopathological grades [4]. Cheng et al. corroborated this result and indicated that neoplasms originating in a bladder diverticulum are characterized by a high incidence of local recurrence [5]. Lack of muscle fibers in the diverticulum makes it difficult to stage the tumor. Therefore, the tumor invades earlier and more readily than in a normal bladder wall because the bladder contains thick muscle.

The initial examination of patients with vesical diverticular tumors often consists of excretory urography and cystourethroscopy. The most common radiographic finding of a diverticular tumor is an intraluminal-filling defect, and these are best visualized in postmicturition films of excretory urography or cystography series. They may also appear as the foci of mucosal irregularity, an incompletely filled diverticulum, or nonvisualization of a previously identified diverticulum. Still, with these techniques, diverticular neoplasms may remain underdiagnosed due to nonopacification owing to the narrowed neck of diverticulum. In comparison, in recent years, cross-sectional imaging studies like CT and MRI are being used more commonly with greater accuracy for the diagnosis and staging of such intradiverticular tumors. A CT scan shows a focal on diffuse thickening of the diverticular wall while early peridiverticular tumor extension is seen as obscuration of the pelvic fat planes surrounding the neoplasm. Multiplanar imaging and excellent soft-tissue contrast resolution of MRI facilitate accurate delineation of the primary neoplasm, determination of intramural invasion, and extravesical tumor extension [6].

The transurethral approach for the treatment of diverticular tumors is often difficult and inappropriate due to the narrow diverticular neck, thin submucosal layers, and fear of bladder perforation with complete resection. Hence, pathologic staging following transurethral resection is difficult and often inaccurate [1]. Therefore, some authors advocate a very aggressive surgical approach involving open exploration and partial or radical cystectomy without prior transurethral resection [7]. A multimodal aggressive approach, including surgery, radiation, and chemotherapy, has been suggested by Garzotto et al. The authors claimed that a downstaged tumor by preoperative irradiation had a better survival than for those with no downstaging [8]. However, others have advocated a selective individualized approach, taking into account the clinical stage and pathologic grade of the tumor [3]. Low-grade, low-stage tumors may be successfully treated with diverticulectomy alone; however, the ability to reliably predict stage and grade preoperatively is limited, and this should be undertaken only with extreme caution and with adequate counseling and follow-up [1]. Whatever the approach, close surveillance is always warranted.

## CONCLUSION

When imaging demonstrates bladder-filling defects, the differential diagnosis should include malignant and benign neoplasms, blood clots, edema in the wall due to an adjacent stone, ureterocele, an enlarged prostate, muscular wall hypertrophy, postoperative changes, endometriosis, and fungus balls. Neoplasia and stones may develop in a bladder diverticulum. Until now, only a few case reports of bladder diverticulum with stones and TCC have been reported. We should be vigilant in this regard, and diverticulum should be managed before complications develop.

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# Colovesical Fistulae Due to Diverticular Disease of a Sigmoid Colon: A Case Report

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**ABSTRACT**

A colovesical fistula is the most common type of fistula associated with diverticular disease of the colon. Diverticular disease accounts for 65-75% of vesicoenteric fistulae. We present a case of a 56-year-old male who presented with pneumaturia and fecaluria, and was found to have colovesical fistulae. A micturating cytourethrogram and CECT scan of the abdomen confirmed the diagnosis. Primary repair of the bladder with excision of fistulae and resection anastomosis of the colon was done in a single stage. At the 6-month follow-up, the patient was doing well and was symptom free.

## INTRODUCTION

A 56-year-old male presented to us with a history of dysuria, fecaluria, and pneumaturia for 3 weeks. There was no history of lower urinary tract symptoms, hematuria, hematochezia, abdominal pain, or weight loss. There were no associated illnesses. On physical examination, the abdomen was soft and nontender. The digital rectal examination revealed no abnormality. The blood examination revealed leukocytosis. A micturating cytourethrogram revealed a colovesical fistula and a contrast-enhanced computed tomography (CECT) of the abdomen revealed the fistula tract between the sigmoid colon and bladder. Cystoscopy revealed inflamed bladder mucosa in the left lateral wall; however, no definite fistula opening could be identified. Sigmoidoscopy revealed multiple diverticulae in the sigmoid colon along with an inflamed indurated opening of the fistula. The patient was put on intravenous antibiotics for 10 days and a leucocyte count was repeated. The leucocyte count was normal. The patient was planned for an elective laparotomy. General anesthesia with endotracheal intubation was administered and the abdomen opened via midline incision. The sigmoid colon was found adhered to the left lateral wall of the bladder along with a fistulous communication. Excision of the fistula tract, cystotomy, and resection of the involved sigmoid colon was done. The bladder was closed in 2 layers and end-to-end anastomosis of the sigmoid colon was done. An omental flap was interposed between the bladder and the bowel. The patient recovered well in the postoperative period. At the 6-month follow-up, the patient was doing well with no symptoms. A CECT of the abdomen revealed no evidence of recurrence of fistulae.

## DISCUSSION

Colovesical fistulae occur most commonly in the setting of diverticulitis (65-75% of cases) [1]. Other causes include Crohn disease, malignancy, infection, trauma, foreign bodies, and radiation [2]. The peak incidence of colovesical fistulae is between 65 to 75 years of age. Approximately 2% of patients with diverticulitis may experience a colovesical fistula. Symptoms of vesicoenteric fistulae may originate from the urinary or gastrointestinal tract; however, in general, lower urinary tract symptoms are more common at presentation [3]. Lower urinary tract symptoms include pneumaturia, frequency, urgency, suprapubic pain, recurrent urinary tract infection, and hematuria. Pneumaturia is considered the most common presenting symptom noted in 50 to 70% of cases. Gastrointestinal symptoms may include fecaluria and tenesmus.

**KEYWORDS**: Colovesical fistula, diverticulitis, sigmoid colon

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The classic presentation of vesicoenteric fistulae is described as Gouverneur syndrome and consists of suprapubic pain, urinary frequency, dysuria, and tenesmus. Recurrent UTIs or cystitis refractory to antibiotic therapy may suggest a colovesical fistula [4]. Cystoscopy, CECT of the abdomen, and radiographic studies can all independently diagnose fistulae [5,6].

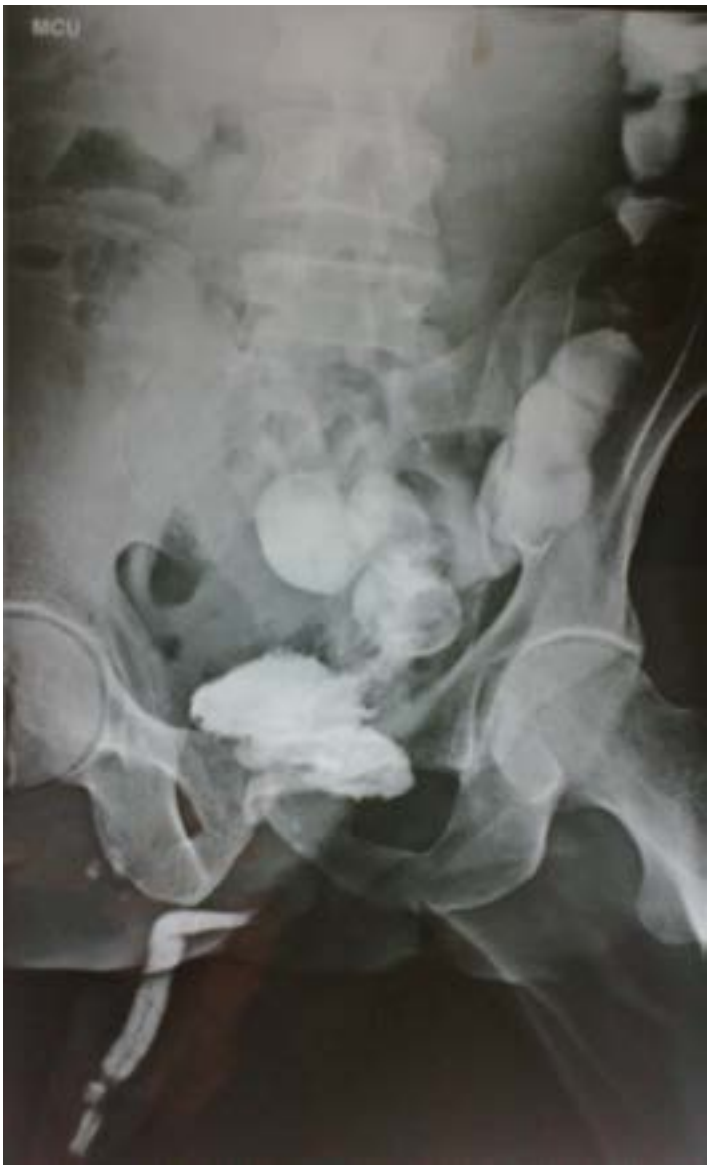
Cystoscopy has the highest diagnostic yield and some abnormality is noted in greater than 90% of patients. The findings on cystoscopy are often nonspecific and include localized erythema and papillary or bullous change. Cystoscopy in our case showed inflamed bladder mucosa in the left lateral wall. However, a definite fistula opening could not be identified. A CECT is the imaging modality of choice. The triad of findings that are suspicious of colovesical fistula include bladder-wall thickening adjacent to a loop of thickened colon, air in the bladder, and the presence of colonic diverticulae. Ultrasonography has been reported to be useful in the diagnosis of colovesical fistulae. A characteristic "beak" sign may be noted [7-10]. Although commonly used barium enemas are less likely to diagnose a fistula. The Bourne test can be a useful adjunct in the evaluation of colovesical fistulae. The first voided urine following a nondiagnostic barium enema is centrifuged and examined radiographically. Oral administration of activated charcoal particles may be used to confirm colovesical fistulae, as they will appear in urine as black particles. We believe the Bourne test can be an inexpensive test to diagnose colovesicle fistulae akin to the "poppy seed" test [3].

Colovesicle fistulae may be managed medically or surgically. In nontoxic, minimally symptomatic with nonmalignant causes of colovesicle fistulae, a trial of medical therapy, including intravenous total parenteral nutrition, bowel rest, and antibiotics may be warrented. In our case the patient presented with an elevated leucocyte count; therefore, medical therapy was not considered. The goal of operative management is to separate and close the involved organs. Excision of the fistula and closure of involved organs is performed. A single or multistage procedure may be needed depending on the condition of tissues and surrounding inflammation. Multistage procedures consist of diversion of the fecal steam by a proximal diverting colostomy with colostomy closure at a later date when fistula closure has been demonstrated. Laparoscopic closure of colovesicle fistulae has been described, albeit with a high rate of conversion to open repair [11,12].

## CONCLUSION

Colovesical fistulae remain a complex and distressing problem for a patient, and individualization of patient care is paramount in their management. Furthermore, long-term studies are needed to address this issue.

Figure 1. A micturating cysto-urethrogram (MCU) showing a colovesical fistula.

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# Spontaneous Dissolution Mid-Shaft of a Double-J Ureteric Stent

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**ABSTRACT**

A vanishing shaft of a double-J uretric stent is a rare complication of a "forgotten" ureteric stent. A retained "forgotten" ureteric stent is not only disastrous for the patient but also comes with severe medicolegal implications for the treating urologist. Herein we report such a case with its subsequent management.

## INTRODUCTION

Polyurethane double-J stents are widely used in modern urological practice. "Forgotten" indwelling stents can result in complications such as encrustation, pyelonephritis, recurrent obstruction, stent migration, and breakage, but the disappearance of the ureteric part of the stent is very rare. We present such a case of forgotten indwelling stent with spontaneous dissolution mid-shaft, and its management.

## CASE HISTORY

A 43-year-old male presented with complaints of lower urinary tract symptoms; predominantly frequency and dysuria. He had a past history of right open ureterolithotomy 13 years back and was subsequently lost for follow-up. His renal biochemical parameters were normal. Urinalysis showed pyuria and microscopic hematuria. A urine culture showed proteus growth. An ultrasound showed a normal left kidney/ureter with right renal pelvic and bladder calculi without any hydronephrosis. On a kidney, ureter, and bladder X-ray (KUB) (Figure 1) there was the appearance of the upper and lower part of an indwelling ureteral stent in the right renal pelvis and bladder area with stone formation, and an absence of any shadow in the ureteric area. On intravenous urography, the bilateral renal units functioned normally. Computed tomography, though relevant, was not done. Culture specific antibiotics were administered. The lower fragment of the stent was removed by cystolithotripsy, and the upper fragment of the stent was removed by right-sided percutaneous nephrolithotomy (PCNL). No nephrostomy tube was placed but a new ureteral stent was given, which was removed after 3 weeks. Postoperative recovery was uneventful.

## DISCUSSION

Forgotten ureteral stents are observed in urologic practice because of poor compliance by the patient or failure of the physician to adequately counsel the patient. Though encrustation and breakage of a stent is commonly reported, disappearance mid-shaft is rarely reported [1]. On a literature search, only 1 such case has been reported to date [1]. El-Faqih and colleagues demonstrated that the rate of complication for polyurethane stents indwelling for less than 6 weeks was 9.6%, whereas the rate increased to 47.5% for stents left for 6 to 12 weeks, and even increased to 76.3% for stents left more than 12 weeks [2]. Kumar and colleagues supported the findings. They found that stents had fragmented into multiple pieces over a mean indwelling time of only 14 weeks [3].

Various mechanisms have been proposed to explain ureteral stent fragmentation. When the stent is exposed to different factors in the urine and the urothelium for a long time, it may lead to a loss of strength, elasticity, and flexibility of

**KEYWORDS**: DJ stent, forgotten

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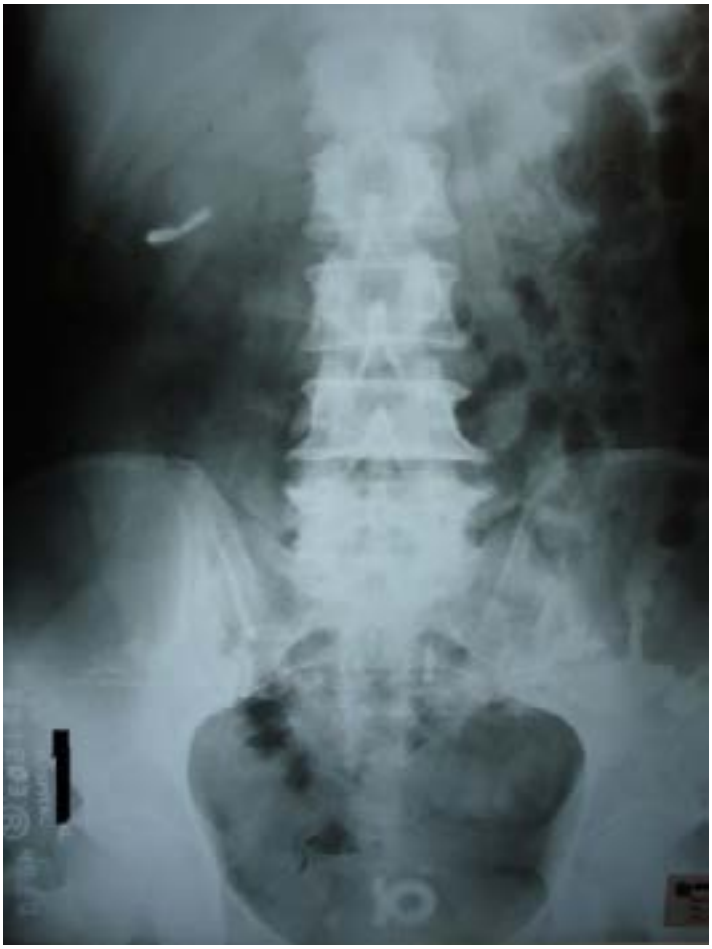
the stent [3], and the degradation of stent polymers leads to loss of tensile strength and hardening of the stent. The tensile elongation (maximal elongation at the break point), known to be a sensitive indicator of the aging process of plastic materials, has been shown to diminish with prolonged deployment. In most cases of fractured stents, many leukocytes in the urine with or without infection were identified; this leads to depolymerization of biomaterials [4]. Polyurethane stents are especially prone to encrustation; this may be due to their higher tensile strength that contributes to their rigidity, which may encourage stasis with periluminal and endoluminal encrustation [5]. Encrustations are often composed of calcium oxalate, which is enhanced by rough surfaces, catheter holes, and edges (major characteristics of polyurethane stents) [5]. Due to encrustations, both ends of the stent may retain in situ and the central shaft may be degraded and may vanish due to a hostile urine environment caused by infections [1]. Irrespective of the material, with the passage of time, all stents are prone to ageing due to encrustation and the loss of tensile strength, resulting in stent fracture, breakage, and even stenturia [6]. Inspection of such stents has shown that these fracture lines generally pass across the stent side holes [3]. Ureteric peristaltic movement, resulting in mid-shaft vanishing with retained upper and lower ends, may enhance spontaneous dissolution of the mid-shaft.

In our case, the upper fragment was removed via PCNL, and the lower fragment was removed via a cystourethroscopic approach. Great care should be taken to prevent any urethral trauma while removing an encrusted, calcified fragment. If a periurethral approach is considered unsafe, then one should not hesitate to perform percutaneous cystoscopic removal of the fragment.

Figure 1. Plain X-ray KUB showing the upper and lower fragments.



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# Posterior Urethral Valve with a Bladder Stone: A Case Report

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*Submitted September 12, 2013 - Accepted for Publication October 24, 2013*

**ABSTRACT**

A posterior urethral (PU) valve and a bladder stone both may cause obstructive voiding symptoms. There are very few patients of a PU valve associated with bladder stones. We are presenting this case because of the rarity of its occurrence and for its unique way of management.

## INTRODUCTION

A posterior urethral (PU) valve and a bladder stone both may cause obstructive voiding symptoms. There are very few patients of a PU valve associated with bladder stones. We are presenting this case because of the rarity of its occurrence and for its unique way of management.

## CASE REPORT

A 4-year-old child presented with complaints of difficulties in voiding, interrupted urinary stream, severe dysuria, straining to pass urine, and hematuria off and on for the last 2 years. The antenatal and postnatal period of the child was uneventful. Developmental milestones were normal. Physical examination revealed no abnormalities. The patient was worked up with routine examinations of blood and urine, serum creatinine, plain abdominal X-ray, ultrasonography of the whole abdomen, uroflowmetry, and retrograde urethrography and micturating cystourethrohraphy. Blood examination showed mild anemia with normal serum creatinine. Urinalysis showed 5 to 10 WBC/HPF, plain abdominal X-ray showed bladder stones, and uroflowmetry revealed obstructed voiding. Ultrasonography showed a normal upper tract with bladder stones and dilated posterior urethra. Retrograde urethrography and micturating cystourethrography showed a posterior urethral valve with bladder stones. Cystoscopy revealed a type I posterior urethral valve with bladder stone.

Under general anesthesia, with full cardiac monitoring, the pediatric cystoscope introduced into the urethra in the lithotomy position. The posterior urethral valve fulgurated. A 10 Fr Nelaton catheter was introduced via the urethra and fixed to the prepuce. The bladder was distended with continuous instillation of normal saline with a Toomy syringe through the Nelaton catheter. A suprapubic cystostomy was done. A nephroscope was introduced through the cannula of the suprapubic trocar and cannula set. The bladder stone was grasped longitudinally and extracted. The suprapubic catheter clamped on the eighth day and the urethral catheter removed. The patient voided with a good stream. On the tenth day, a suprapubic cystostomy catheter was removed. Suprapubic leakage seized after 2 days. Six months of follow-up with uroflowmetry, serum creatinine, and routine examination of urine revealed no abnormalities.

## DISCUSSION

A posterior urethral valve is a common congenital anomaly in infants. The patient is usually present as neonates with bladder outflow obstruction, poor urinary stream, and urinary tract infection [1]. Stones in the bladder are an uncommon presentation in the tropics, especially in children. Its rarity makes the index of suspicion low. The patient's presentation may be mistaken for urinary tract infection because of the presence of frequency and dysuria [2]. A posterior urethral valve may rarely be diagnosed during a later phase of childhood, adolescence, and even adulthood [3]. Posterior

**KEYWORDS**: Posterior urethral valve, bladder, stone

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urethral valves and vesical calculi are, individually, among the most common causes of obstructive lower urinary complaints in children. Posterior urethral valves lead to stasis of the urine and bladder dysfunction, which can lead to calculi formation [4]. The patient is usually presenting with bed-wetting, urinary frequency, dribbling, hematuria, and acute urinary retention [1]. The presentation of vesical calculi is frequency and hematuria, and in the developing world it is a common problem seen in children. Congenital anomalies of the urinary tract can be associated with vesical calculi [5].

In the last decade, most of the children with posterior urethral valves are diagnosed early in life, even prenatally, due to an increased use of ultrasound imaging. This may well be the reason why bladder stones in this group of children are so rarely encountered. A plain X-ray of the abdomen can easily diagnose it but 10% of calculi are missed on radiology due to radiolucency. In some cases, sonography may miss calculi. There are very few reports of an association between a posterior urethral valve and calculi. Although bladder outflow obstruction is predisposed to calculi formation, there is only one report in English literature of vesicolithiasis associated with a posterior urethral valve [1,6]. And recent textbooks do not include vesical stones as a presentation or as complications of a posterior urethral valve [7].

Because of symptoms due to vesical calculi, posterior urethral valves may be missed. Therefore, clinical symptoms are varied and overlapping [8]. Routinely, patients presenting with poor flow and dysuria undergo a plain abdominal X-ray, ultrasound, and cystoscopy. We used a nephroscope and suprapubic cystostomy with a trocar cannula to manage the vesical stone in a minimally invasive way. Cannula of the trocar maintained the suprapubic cystostomy tract, and continuous bladder filling by putting normal saline through the Nelaton catheter with a Toomy syringe under pressure prevented the bladder from collapsing. Grasping the stone longitudinally made it possible to extract the stone from the tract easily. Cystoscopic treatment was avoided to prevent urethral injury and subsequent stricture, as the stone was large.

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# Priapism, An Unusual Sequalae of Malignant Melanoma of the Rectum: A Case Report

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*Submitted September 20, 2013 - Accepted for Publication October 24, 2013*

**ABSTRACT**

The penis is an uncommon site of metastasis, and about 300 cases have been reported worldwide. In order of frequency the primary sites of metastatic penile tumors are the urinary bladder (34.7%), prostate (29.8%), rectum and sigmoid colon (15.7%), and kidney (6.5%). Nearly 50 cases of penile metastasis with varied clinical features from rectal or sigmoid malignancy have been reported. Sagar et al. reported the second case of metastatic malignant melanoma secondary to the penis in 1992. Three and two-thirds of all penile metastasis are metachronus, and about 90% of the reported cases of penile metastasis are part of widespread disease.

We report a case of painful penile metastasis as a manifestation of malignant melanoma of the rectum, which was a disseminated disease.

## INTRODUCTION

The penis is an uncommon site of metastasis, and about 300 cases have been reported worldwide [1]. In order of frequency the primary sites of metastatic penile tumors are the urinary bladder (34.7%), prostate (29.8%), rectum and sigmoid colon (15.7%), and kidney (6.5%). Nearly 50 cases of penile metastasis with varied clinical features from rectal or sigmoid malignancy have been reported [1,2]. Sagar et al. reported the second case of metastatic malignant melanoma secondary to the penis in 1992. Three and two-thirds of all penile metastasis are metachronus, and about 90% of the reported cases of penile metastasis are part of widespread disease [4].

We report a case of painful penile metastasis as a manifestation of malignant melanoma of the rectum, which was a disseminated disease (Figure 1).

## CASE REPORT

A 67-year-old Kashmiri male was complaining of a painful persistent erection for 2 weeks with an inability to pass urine for 1 day. On examination, the patient was pale and emaciated with a palpable lower abdominal midline swelling, confirmed to be a full urinary bladder due to an acute retention of urine. Bilateral inguinal lymphadenopathy was present, the shaft of the penis was tender to the touch, and there were multiple hard nodules at the base of the phallus (Figure 2, Figure 3, and Figure 4).

Suprapubic cystostomy was contemplated to relieve the patient of urine retention. Comprehensive review of the records of the patient revealed that the patient was a diagnosed case of malignant melanoma of the rectum with widespread metastasis to the liver and lungs about 8 months back (Figure 5). The patient had refused to receive chemo radiotherapy for the same.

**KEYWORDS**: Malignant melanoma, rectum, metastasis, priapism

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Figure 1. Rectal polyp histopathology picture revealing ulcerating malignant melanoma; vertical growth phase.

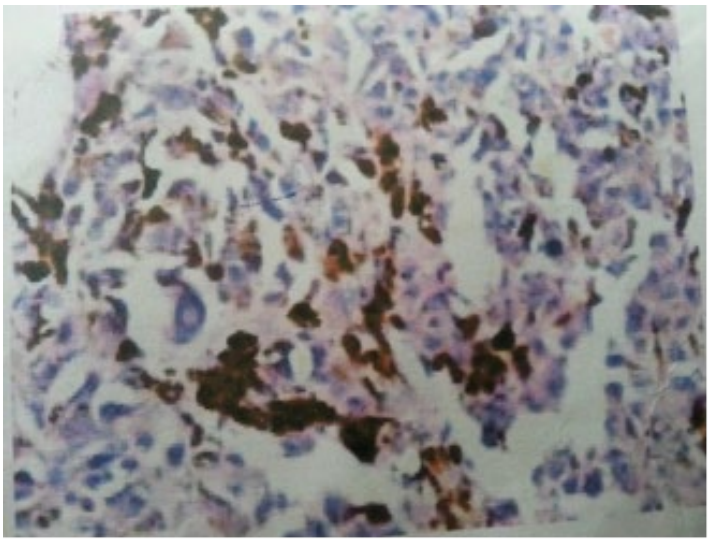
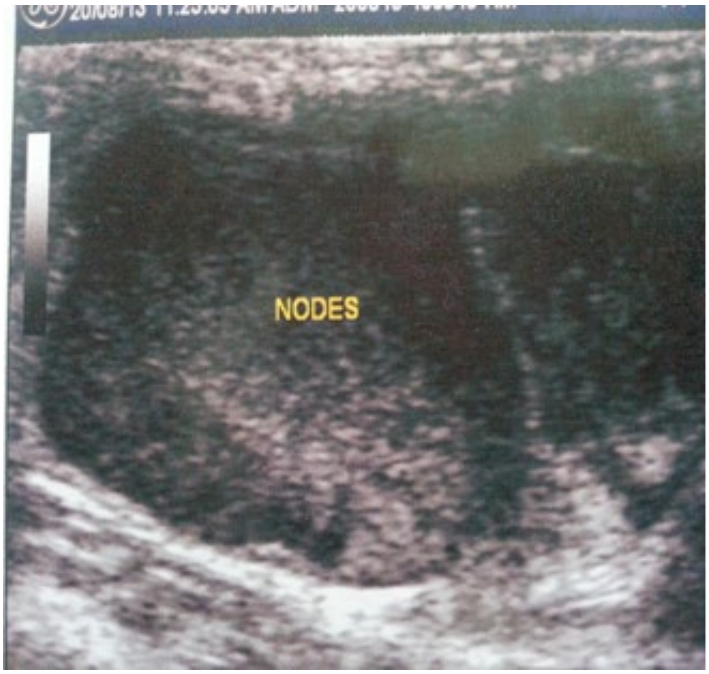
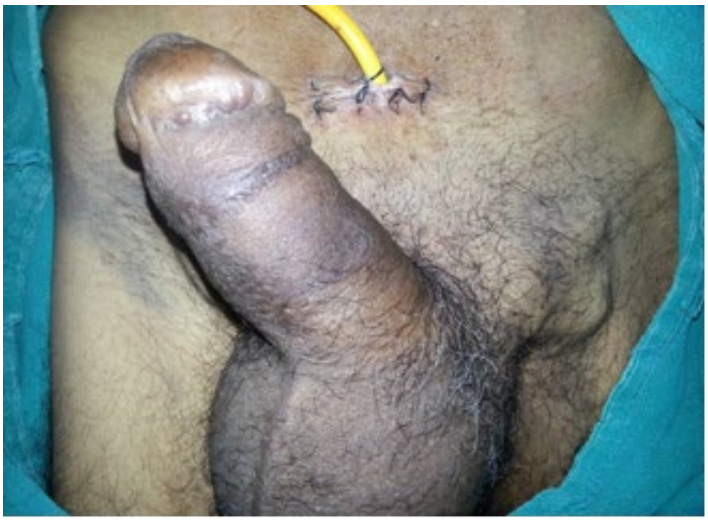


Figure 2. A USG revealing enlarged inguinal lymph nodes.




The penile color Doppler showed lymphatic stasis with bilateral inguinal lymphadenopathy and multiple small nodules at the base of the penis. Fine-needle aspiration cytology of the lymph nodes and the penile nodules was done and the features were consistent with metastatic deposits of malignant melanoma. In view of the advanced nature of the disease and the poor performance score of the patient, no surgical intervention was done, and instead the patient was registered with the medical oncology department where he refused to go for any further treatment. The patient expired within 1 month due to septicemia.

Figure 3. An erect penis with inguinal lymphadenopathy and suprapubic cystostomy in situ.



## DISCUSSION

The penis is a rare site for metastasis despite rich vascularization. Various mechanisms for penile metastasis have been suggested. These include retrograde venous spread, retrograde lymphatic spread, arterial embolism, and local direct extension [4]. Retrograde lymphatic spread into the penile lymphatic channels after obstruction of inguinal and hypogastric nodes seem to be the most plausible theory in our case.

Presenting signs and symptoms in the order of frequency are malignant priapism (40%), urinary retention, penile nodules, ulceration, perineal pain, edema, dysuria and hematuria [1].

Eighty percent of the cases are due to advanced stages of initial neoplasm and generally have a very poor prognosis [5]. The most frequent primary tumor corresponded to the genitourinary area and makes up approximately 70% of the total cases [6]. Twenty-two percent of all the metastasis to the penis originates in the gastrointestinal tract, particularly the sigmoid colon and the rectum (16%) [5].

Figure 4. A bulge at the base of the penis due to the metastatic deposits.

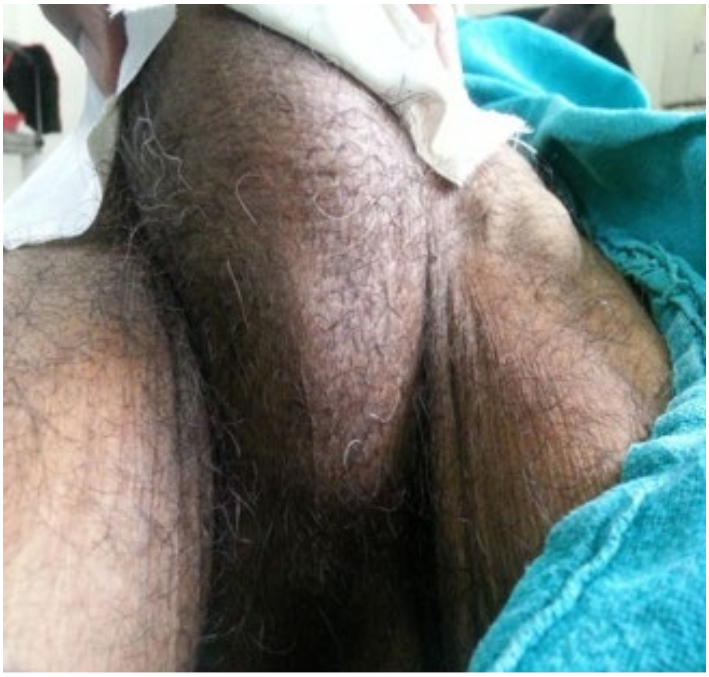
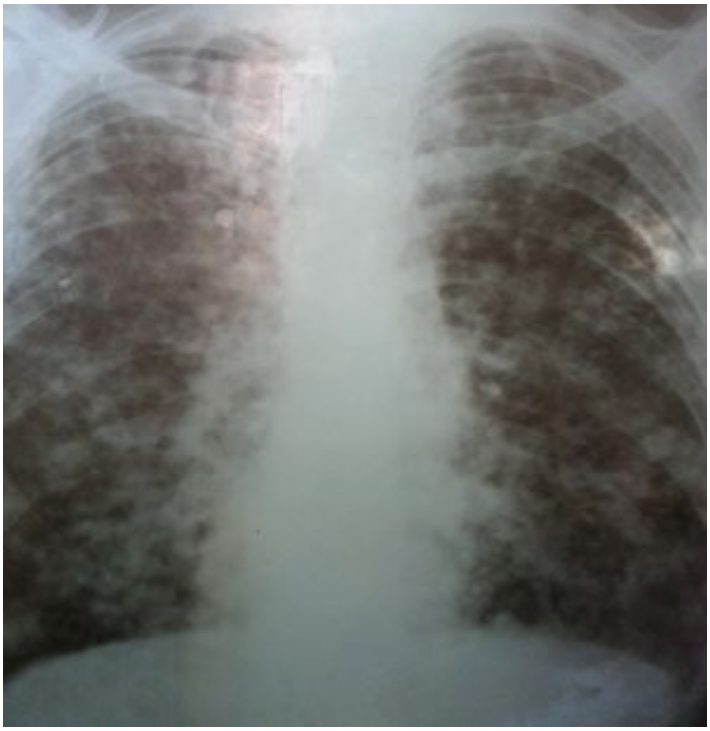


Figure 5. A chest X-ray showing lung metastasis.



Management of penile metastasis is mainly palliative, as it usually represents a part of advanced disease. Management is influenced by the size of the primary extent of the metastatic spread, the general condition of the patient, and also prognostic features of the primary tumor. Treatment varies widely depending on case characteristics, and options are chemotherapy, radiotherapy, cavernosum/spongiosum short circuit, urinary tract diversion through cystostomy, and partial or total phallectomy [8]. Prognosis is invariably poor, with a 5 to 22 month survival rate for colorectal tumors [9].

To the best of our knowledge this is the first ever case of malignant melanoma arising from gastrointestinal tract metastasizing to the penis and presenting as priapism.

## CONCLUSION

Metastasis to the penis from a tumor of the rectum is very rare, with about 50 cases reported to date, none of them being malignant melanoma histologically. We report the first such case. The prognosis is very poor and proper treatment modality needs to be charted out.

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# Transvaginal Excision of Intravesical Mesh Erosion

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*Submitted September 27, 2013 - Accepted for Publication October 17, 2013*

**ABSTRACT**

**Introduction and Objectives**: Transvaginal mesh has been used in the management of a multitude of female urologic conditions; most commonly vaginal prolapse and stress urinary incontinence. However, in the event of a complication related to the use of such mesh, there is scant literature on its safe and efficacious removal. We present a technique for transvaginal removal of vesicular mesh erosion.

**Methods**: The patient is placed in lithotomy position and cystoscopy is performed. Once bilateral ureteral catheters are in place, a Foley catheter is placed. Using a midline transvaginal approach, hydrodissection is performed. Allis clamps are used to grasp the vaginal epithelium, and vaginal flaps are developed. The sling is identified and the midline it is transected. A combination of sharp and blunt dissection is used to free the sling. The sling is dissected to the most lateral extent possible. Once the intravesical mesh is encountered, the entirety of the offending mesh is excised. Once the mesh has been removed, attention is then turned to the resultant cystotomy. The bladder is then closed in multiple layers. A urethral catheter is left indwelling postoperatively.

**Results**: The patient is discharged when ambulatory and tolerating a regular diet. A voiding cystourethrogram (VCUG) is obtained in 1 to 2 weeks and if urinary extravasation is not seen, the urethral catheter is removed.

**Conclusion**: Despite the use of mesh slings for stress urinary incontinence and pelvic organ prolapse, literature describing operative techniques to remove slings in the setting of urinary tract erosion is lacking. The described technique avoids significant manipulation of the urinary tract and further disruption of the periurethral and perivesical fascia while ensuring a watertight closure.

## INTRODUCTION AND OBJECTIVES

Transvaginal mesh has been used in the management of a multitude of female urologic conditions; most commonly vaginal prolapse and stress urinary incontinence. However, in the event of a complication related to the use of such mesh, there is scant literature on its safe and efficacious removal. We present a technique for transvaginal removal of vesicular mesh erosion.

## METHODS

The patient is placed in lithotomy position and cystoscopy is performed to identify the location of the mesh and to place ureteral catheters to aid in the identification of the ureters during the dissection of the offending mesh. Once bilateral ureteral catheters are in place, a Foley catheter is placed and gentle traction is placed on the catheter to aid in identification of the bladder neck by palpating the Foley balloon. Subsequently, using a midline transvaginal approach, hydrodissection is performed using injectable saline to infiltrate the length of

**KEYWORDS**: Mesh erosion, transvaginal surgery, mesh complication

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the intended incision. Allis clamps are used to grasp the vaginal epithelium once incised, and vaginal flaps are developed in order to expose periurethral and perivesical fascia. Once the sling is identified in the midline it is transected, creating 2 arms. With traction on the edge of the transected sling, a combination of sharp and blunt dissection is used to free the sling from the medial to the lateral, working from known to unknown. The sling is dissected to the most lateral extent possible taking care to identify the location of the intravesical mesh. Once the intravesical mesh is encountered, the entirety of the offending mesh is excised, taking care to leave no eroded mesh in the bladder as a nidus for future infections or stones. Stay sutures can be placed upon encountering the intravesical portion of the mesh if there is concern the repair will be difficult to visualize. Once the mesh has been removed bilaterally at its most lateral aspect, attention is then turned to the resultant cystotomy. The bladder is then closed in multiple layers using delayed synthetic absorbable sutures, and stay sutures, if present, are removed. A urethral catheter is left indwelling postoperatively.

## RESULTS

The patient is discharged when ambulatory and tolerating a regular diet. A voiding cystourethrogram (VCUG) is obtained in 1 to 2 weeks and if urinary extravasation is not seen, the urethral catheter is removed.

## CONCLUSIONS

Despite the use of mesh slings for stress urinary incontinence and pelvic organ prolapse, literature describing operative techniques to remove slings in the setting of urinary tract erosion is lacking. The described technique avoids significant manipulation of the urinary tract and further disruption of the periurethral and perivesical fascia while ensuring a watertight closure.