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Late Effects on the Urinary Bladder in Patients Treated for Cancer in Childhood: A Report from the Children's Oncology Group

Michael Ritchey, MD[Professor of Urology],
Mayo Clinic College of Medicine Scottsdale, AZ

Fernando Ferrer, MD[Associate Professor of Surgery],
Connecticut Children's Medical Center Hartford, CT

Patricia Shearer, MD, MS[Clinical Associate Professor of Pediatrics Director], and
Cancer Survivor Program University of Florida Shands Cancer Center Gainesville, FL

Sheri L. Spunt, MD[Associate Member][Associate Professor]
Department of Oncology St. Jude Children's Research Hospital, Memphis, TN

Department of Pediatrics University of Tennessee, Memphis, TN

Abstract

Childhood cancer survivors who have had pelvic or central nervous system surgery or have received alkylator-containing chemotherapy or pelvic radiotherapy as part of their cancer therapy may experience urinary bladder late effects. This article reviews the medical literature on long-term bladder complications in survivors of childhood cancer and outlines the Children's Oncology Group Long Term Followup (COG LTFU) Guidelines related to bladder function. An overview of the treatment of bladder late effects and recommended counseling for survivors with these complications are presented.

Keywords

urinary tract; urinary bladder; late effect; child; neoplasm

Over the last several decades, improvements in treatment and supportive care have led to long-term survival rates for childhood cancer that exceed 80%.¹ This success has produced a growing population of childhood cancer survivors who are at risk for a variety of medical complications and functional impairments related to their cancer or its treatment. Among the long-term effects described in childhood cancer survivors are abnormalities of bladder function. Severe impairment of bladder function due to pelvic or central nervous system surgery, pelvic radiotherapy, or alkylating agent chemotherapy may lead to hydronephrosis and/or renal dysfunction, sometimes necessitating reconstructive surgery to prevent renal function deterioration. Less severe bladder functional impairment may produce bothersome symptoms such as urinary frequency, urgency or incontinence that diminish quality of life.

This paper will review how normal bladder function may be altered by pediatric cancer treatment. Methods of identifying patients at risk for bladder dysfunction will be discussed, with particular focus on the risk-based screening guidelines outlined by the Children's

Oncology Group (COG).² Finally, the diagnostic approach for evaluating bladder dysfunction will be outlined, and prevention and/or management of conditions causing bladder dysfunction will be reviewed.

Normal Bladder Function

The bladder has two primary functions: storage of urine and micturition (voiding). Urine storage requires two basic elements. First, maintenance of a low, stable pressure during bladder filling must be achieved. This occurs as a function of the viscoelastic properties of the detrusor muscle and normal neural innervation. Second, continence must be maintained by closure of the bladder base during bladder filling.

There are a number of mechanisms whereby normal bladder function can be altered by cancer treatment. Fibrosis or direct injury to the bladder can affect the viscoelastic properties of the bladder, resulting in decreased compliance and elevated bladder pressure during filling. Sustained high intravesical pressures impede ureteral peristalsis, leading to hydronephrosis and or reflux.³ Nerve damage either centrally or peripherally due to pelvic or central nervous system surgery can also have a deleterious effect on bladder compliance and storage of urine. Control of the external sphincter can also be affected by nerve damage.

Bladder Late Effects Following Treatment for Childhood Cancer

Hemorrhagic Cystitis

Hemorrhagic cystitis (HC) is a condition in which irritation of the lining of the bladder leads to exposure of the submucosal blood vessels and bleeding.¹¹ Chemotherapy including the oxazophorine alkylating agents cyclophosphamide and ifosfamide and radiation therapy to the bladder have been implicated in the development of HC.⁴⁻⁶ Patients who receive both treatment modalities are at the highest risk.⁵ The mediator of bladder injury in HC following chemotherapy is acrolein,^{7, 8} which is a hepatic breakdown product of ifosfamide⁹ and cyclophosphamide¹⁰ that is excreted in the urine. Most HC occurs acutely during cancer therapy; however, it may also become a chronic recurring problem with a timeframe as long as 20 years after completion of therapy.⁴ The incidence of hemorrhagic cystitis after pediatric cancer therapy is difficult to measure with certainty, but has been reported to be 15% in Ewing sarcoma patients treated with cyclophosphamide.⁵

Radiation-induced HC may be either acute or chronic, the latter due to endarteritis that leads to tissue hypoxia, ischemia and necrosis.¹² Radiation doses >30 Gy to the whole bladder or >60 Gy to a portion of the bladder are risk factors for development of HC [Table I]. Radiomimetic chemotherapeutic agents such as the anti-tumor antibiotics dactinomycin and doxorubicin in combination with radiation may contribute additional risk.^{4,6,13}

Hemorrhagic cystitis is usually painless, although patients may report urinary urgency, frequency, dysuria, suprapubic pain and occasional bladder spasms. The amount of blood loss is variable, but life-threatening hemorrhage can occur. Infection with adenovirus or BK virus may contribute to the risk of HC.¹⁴

A number of treatments for prevention of treatment-induced HC have been tried. Vigorous hydration, catheter drainage and continuous bladder irrigation may decrease symptoms during therapy. Two drugs that bind to acrolein and limit its damage are N-acetylcysteine (Mucomyst) and 2-mercaptoethane sodium sulfonate (Mesna).^{7,8} The incidence of HC is decreased in patients whom receive mesna during cyclophosphamide therapy.¹⁵ Mesna administration is now the standard of care for most pediatric cancer protocols utilizing high dose cyclophosphamide.

Bladder Fibrosis and Direct Bladder Injury

Long-term bladder fibrosis and contracture has been reported in patients previously treated for HC related to oxazaphosphorine-alkylating agents. Jerkins et al reported bladder contracture in 3 of 23 patients presenting with HC following treatment of childhood cancer. All had received cyclophosphamide and 18 had also undergone radiation treatment.¹⁶

The effects of radiation therapy on bladder function can be acute and/or chronic. A number of investigators have examined the late effects of radiation therapy on bladder function utilizing an animal model.¹⁷⁻²² Changes in bladder function with diminished bladder compliance are noted between days 170 and 245 after irradiation and correlates with radiation dosage.¹⁷ These late changes are attributed to fibrosis as a consequence of collagen deposition in the bladder wall. Unlike acute injury, these changes are not reversible. Cumulative radiation dose >45 Gy to the whole bladder poses the highest risk for bladder toxicity [Table I].²³⁻²⁴

Yeung et al evaluated 11 children with pelvic rhabdomyosarcoma, of whom 7 had involvement of the bladder or prostate.²⁵ After mean follow-up of 6.6 years, all 7 of the irradiated children had enuresis, an abnormal bladder capacity, and/or an abnormal voiding pattern. In four children, urodynamic studies demonstrated a reduced functional bladder capacity.

Cancer surgery involving the lower genitourinary tract has the potential to impair normal function of the bladder and normal voiding mechanisms. Myogenic/neurologic impairment may occur due to transection of bladder muscle and nerves during surgery to remove the bladder or adjacent pelvic tumors.²⁶⁻²⁸ Partial cystectomy can affect bladder function by reducing the bladder volume.^{24, 29} The greater the amount of bladder resected, the more likely bladder volume and function will be compromised. Hays et al. reviewed the outcomes of 40 patients treated for primary bladder rhabdomyosarcoma.²⁴ Partial cystectomy was performed in 33 of the 40 patients. The extent of partial cystectomy ranged from 15% to 80% of the bladder mucosal surface. All 40 patients received chemotherapy and many received cyclophosphamide in conjunction with radiation therapy. Information regarding bladder function was obtained by patient survey. Nine of the 19 irradiated patients had symptoms suggesting a small or contracted bladder. Further analysis of this group suggested that patients receiving greater than 40 Gy radiation had a higher incidence of bladder symptoms. All three patients receiving greater than 50 Gy had bladder complications.

Neurogenic Bladder

Any cancer therapy that results in injury to the innervation of the bladder can have deleterious effects on bladder function resulting in impaired bladder storage, inability to void and/or incontinence. Neural innervation to the bladder can be affected at several levels: brain, spinal cord, and peripheral nerves. These areas can be affected by tumor growth alone, or surgery and radiation used to treat the tumor. The effect on bladder function is dependent on the level of injury.

Brain tumors and their treatment can produce centrally-mediated bladder dysfunction. This is usually manifested by urinary incontinence. There is loss of inhibition of the bladder and the patient is unable to prevent voiding. This may be associated with detrusor overactivity or uninhibited bladder contractions.³⁰ Lesions above the pons do not affect the voiding reflex. This results in less impact on the upper urinary tract than is commonly seen with spinal cord problems.

Spinal cord injury (SCI) may occur from direct compression of the cord by tumor.³¹ Resection of tumor and radiation may also injure the cord. SCI can be complete or

incomplete. In complete disruption of the spinal cord, the bladder and external sphincter are disconnected from central control and inhibition.³² This decentralization of the bladder results in detrusor overactivity and poor storage of urine. Acutely, there may be a period of spinal shock, during which there is detrusor underactivity or areflexia and impairment of bladder emptying. Once bladder contractility returns, there is discoordination between the bladder and the external sphincter leading to high voiding pressures. If untreated, the elevated bladder pressures lead to deterioration of renal function.³³

Peripheral nerve damage from extensive pelvic surgery^{27, 28} can cause impaired bladder contractility. Bladder storage will be affected if there is complete denervation, much like that noted with SCI. Damage to the nerves can occur during resection of pelvic tumors, and even as a consequence of lesser, non-extirpative surgery such as ureteral reimplantation.³³ High doses of radiotherapy (>50 Gy) to the lumbar or sacral spine or to the cauda equina may also cause nerve damage that results in neurogenic bladder.³⁴

Secondary Malignancy of the Bladder

Another late effect of cancer therapy is the development of secondary malignancies. Prior exposure to cyclophosphamide for both benign and malignant conditions³⁵⁻³⁹ has been reported to be associated with bladder carcinoma. Cyclophosphamide has also been implicated in the development of leiomyosarcoma of the bladder.⁴⁰⁻⁴¹ The risk of bladder cancer after cyclophosphamide is dose dependent. Travis et al found an excess risk of bladder cancer following high dose cyclophosphamide exposure in older patients with **non-Hodgkin lymphoma**.³⁹ However, a dose relationship of cyclophosphamide and bladder cancer in pediatric cancer survivors has not been established. A recent report from the Childhood Cancer Survivor Study found only 5 cases of secondary bladder cancer among 13,136 patients.⁴² These occurred following treatment of **non-Hodgkin lymphoma** (1 patient), leukemia (2 patients) and soft tissue sarcoma (2 patients). There is one reported case of transitional cell carcinoma of the bladder developing after treatment of **Hodgkin lymphoma** with nitrogen mustard and pelvic radiotherapy.⁴³ Mutations in p53 have been reported in 50% of bladder cancer,⁴⁴ but the mutations have a different spectrum when induced by cyclophosphamide.⁴⁵ Khan et al reported that the mutation spectrum matches the phosphoramidate mustard adduction sequences detected by a repetitive primer extension assay.⁴⁵

Gross hematuria is the most common presentation of bladder carcinoma but some tumors are detected incidentally on imaging evaluation for other problems. Most of these tumors are of low grade and stage and can be managed endoscopically. The risk of recurrence is higher in patients whose bladder carcinoma develops after cyclophosphamide.³⁵

The COG LTFU Guidelines for Bladder Complications

The COG LTFU guidelines are risk-based, exposure-related recommendations for the identification and management of late effects due to therapies utilized in the treatment of childhood cancer, and are designed for asymptomatic survivors presenting for routine medical follow-up two or more years after completion of cancer therapy. More extensive evaluation is warranted for survivors with symptoms suggesting illness or organ dysfunction. Patient education materials called “Health Links” accompany the guidelines; both the guidelines and Health Links can be downloaded from <http://www.survivorshipguidelines.org>. The methods used to develop the guidelines is explained in more detail in the Supplemental Appendix and Supplemental Table.⁴⁶

The COG LTFU guidelines related to bladder dysfunction are outlined in Table I. The guidelines specify the particular bladder complications that may result from childhood

cancer therapy, along with the particular risk factors that have been linked to each condition. The screening recommendations for bladder late effects are limited to an annual history and urinalysis in survivors with potentially bladder-toxic therapeutic exposures.

Evaluation of Bladder Function

Evaluation of bladder function begins with a careful history with an emphasis on voiding. The examiner should elicit information regarding voiding pattern (number of voids per day), character of the urinary stream (caliber and force), evidence of straining to void or intermittency of the stream, and degree of incontinence. For young survivors, parents may not be able to provide specific information regarding their child's voiding history.⁴⁷ The best means to obtain these data is for the family to complete a voiding diary and questionnaire at home over several days [Table II].⁴⁸ The family can prospectively record the time and amount of each void, frequency of incontinent episodes and the relationship to time of voiding, and evidence of urgency or dysuria. Gross hematuria is generally well documented by family members, as this usually results in prompt referral for evaluation. The COG Guidelines recommend that survivors treated with alkylating agents undergo annual urinalysis to screen for microscopic hematuria. This test is readily available and can screen for occult bladder malignancy and renal disease. The finding of >5 RBC/HPF on at least two occasions should prompt a urine culture, spot urine calcium/creatinine ratio and ultrasound of the kidney and bladder [Table I]. Patients with culture-negative microscopic hematuria and macroscopic hematuria and/or abnormal calcium/creatinine ratio should be referred to a nephrologist or urologist.

In patients with a positive history, the physical examination should begin with palpation of the abdomen to detect a distended bladder. Examination of the genitalia includes direct visualization of the urethral orifice. Rectal examination is also done to exclude a pelvic mass and to assess anal sphincter tone. A limited neurologic examination can assess innervation of the genital and perineal area. It may be useful to observe the patient's urinary stream during voiding. If there is any suggestion of decreased force of the urine stream (stranguria), a urinary flow rate and ultrasound measurement of residual urine is performed. The urinary flow rate is calculated by measuring volume voided divided by the number of seconds required to empty the bladder, and can be compared to established normal values.

Patients with bladder dysfunction should be referred to an urologist. A renal and bladder ultrasound can assess bladder thickness, capacity, and adequacy of emptying, as well as identify hydronephrosis and renal abnormalities. Voiding cystourethrography may be indicated in patients with a history of infection and or hematuria. This study can visualize the urethra in males with stranguria and exclude vesicoureteral reflux, which is more common in patients with a decreased functional bladder capacity. More formal urodynamic evaluation of bladder function is undertaken in patients with incontinence. Cystometry can measure the bladder capacity and determine bladder compliance. If the urinalysis shows hematuria, with or without elevated protein, cystoscopy may be indicated.

Treatment of Bladder Late Effects

Hemorrhagic Cystitis

When HC occurs as a late effect of treatment, the degree of hematuria determines the intervention. Most cases of that occur following therapy are mild and can be managed with increased hydration. For persistent or recurrent bleeding, alternative therapeutic considerations include prostaglandins,⁴⁹ hyperbaric oxygen to promote wound healing,⁵⁰ conjugated estrogens that may decrease capillary fragility,⁵¹ or pentosan polysulfate to serve as an anti-fibrinolytic and anti-coagulant.⁵² Recently, use of anti-Factor VII a has had

success in survivors following radiation-induced hemorrhagic cystitis for pelvic malignancies.⁵³⁻⁵⁴ If the bleeding fails to improve with these measures or results in urinary retention, cystoscopy and clot extraction with instillation of astringents such as alum or silver nitrate is the next step. If these measures fail or there is life threatening hemorrhage, formalin may be instilled. It can be effective in stopping life threatening hemorrhage but poses a risk of bladder fibrosis and contracture.⁵⁵ Other measures that can be utilized for severe hemorrhage include embolization of the vesical arteries, or urinary diversion.⁵⁶ If symptoms of a urinary tract infection are present (i.e., fever, flank or back pain, urinary urgency, hesitancy, and/or frequency), a urinalysis, urine culture, complete blood count, and determination of BUN and creatinine may be indicated.

Non-Surgical Treatment of Bladder Dysfunction

The bladder capacity may be physically reduced due to partial cystectomy. Capacity may be functionally reduced due to fibrosis or nerve damage. The consequences of a reduced bladder capacity vary. In some survivors, the only symptom may be urinary frequency and/or urgency. Other patients will present with urge incontinence; either the result of a significant reduction in bladder capacity or inability to inhibit the detrusor contraction.

Although most patients seek treatment for the symptoms of a reduced capacity, reduced bladder compliance may have a greater impact on the kidneys. The ability of the bladder to store urine at low intravesical pressures is essential to prevent upper urinary tract damage.³ A bladder storing urine at elevated pressures may impede ureteral peristalsis and result in hydronephrosis and renal damage over time. These changes can occur silently if the patient does not manifest voiding complaints.

Decreased bladder compliance is usually initially managed with antimuscarinic medication (e.g. oxybutinin, tolterodine) to ensure frequent complete emptying of the bladder. A therapeutic effect should be observed within a few weeks of starting these medications. The patient should be observed to have decreased urinary frequency or decreased incontinent episodes after initiation of therapy. However, repeat urodynamic evaluation to assess improvement in bladder compliance is needed.

Surgical Treatment of Bladder Dysfunction

Surgery may be necessary for management of bladder complications of cancer treatment. Abnormalities of bladder storage due to either reduced capacity or poor bladder compliance with elevated pressures require bladder enlargement or augmentation. Augmentation is most often performed by incorporating a bowel segment into the native bladder in order to increase its capacity and lower storage pressures. The intestinal segment is sutured to the native bladder after it is reconfigured to create a spherical structure.

Complete removal of the bladder, cystectomy, mandates reconstruction of a new urinary reservoir. In some patients, a passive conduit can be constructed to drain the urine to an abdominal stoma that drains continuously to a bag. Ileal conduit diversion or the similar colonic conduits utilize an intestinal segment to create an incontinent abdominal stoma. While one end of the segment is brought to the skin, the other is closed off and the ureters are then implanted into the bowel segment. This type of diversion is used less commonly today, but may be a temporary measure until a continent reconstruction can be performed at the completion of therapy or when the patient is older. Continent reconstructions using intestinal segments to replace the bladder are most commonly performed today. The two major subtypes are orthotopic neobladders and continent diversions. The orthotopic neobladder is anastomosed to the native urethra, with preservation of the sphincteric mechanisms [Figure 1]. In a continent diversion, a cutaneous channel is brought out the

anterior abdominal wall and is used as a route for catheterization [Figure 2].⁵⁷ Central to all of these techniques is the principle of clean intermittent catheterization which allows for safe and efficient emptying of reconstructed bladders that cannot be emptied volitionally.

Counseling the Patient with Bladder Complications

Survivors who have received potentially bladder-toxic therapy should be counseled about the symptoms and signs of urinary tract complications and the risk of renal impairment posed by inadequate treatment of bladder dysfunction. The COG Health Link “Bladder Health After Childhood Cancer” is a useful patient education tool that provides a lay summary of long-term bladder complications and guidelines for seeking medical intervention (available at www.survivorshipguidelines.org).

Patients with HC should contact their physician whenever the HC fails to resolve promptly, or if symptoms of a urinary tract infection or unexplained complication are present. Survivors with neurologic impairment of the bladder need frequent evaluation of bladder function by the urologist. Urodynamic studies of the bladder can monitor bladder pressures to ensure that filling pressures remain low. Frequent emptying of the bladder is necessary to avoid high sustained bladder pressures that can lead to hydronephrosis or vesicoureteral reflux. This will also decrease risk for urinary tract infections. Patients who have undergone bladder reconstructive procedures with intestinal segments also require careful monitoring and annual evaluation by the urologist. Bladder reconstruction with intestinal segments does increase the risk of urinary infections, urinary calculi, electrolyte disturbances and bladder perforation. The latter can present as acute peritonitis and may be fatal if not recognized promptly.⁵⁸ Although rare, a more ominous late complication of such surgery is secondary tumor formation with an estimated risk of 1-3%.⁵⁹ The development of malignancy after enterocystoplasty has been reported with a latency period of 5-10 years. These patients may benefit from yearly endoscopy of the bladder to detect any premalignant changes.

Conclusions

The COG LTFU guidelines offer a comprehensive summary of the risk factors associated with long-term bladder complications after treatment for childhood cancer, based on evidence in the medical literature and expert panel review. Further studies will be required to confirm the validity of the screening recommendations and to better define more precisely the risk factors associated with certain late effects.

Survivors who have been exposed to therapies that are potentially toxic to the bladder deserve careful ongoing follow-up in order to detect bladder complications so that intervention can be accomplished in a timely fashion. Urologists, internists, pediatricians, nurses, and psychologists, as well as other medical specialists, may be necessary to provide appropriate interventions for the patient at risk for bladder complications following treatment of cancer in childhood.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Ileal Neobladder

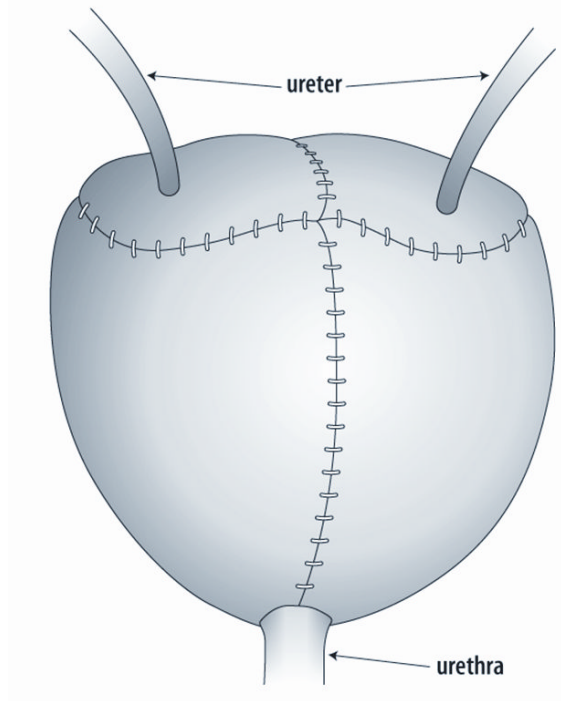


Figure 1. Ileal neobladder. This figure shows a bladder constructed of ileum to replace the native bladder removed at time of cystectomy. The small intestine is opened and reconfigured into a spherical shape. The bowel segment is sewn to the native urethra above the pelvic floor. The ureters are reimplanted into the new reservoir. The patient may be able to void spontaneously but some patients require intermittent catheterization to empty the neobladder.

Continent Urinary Diversion

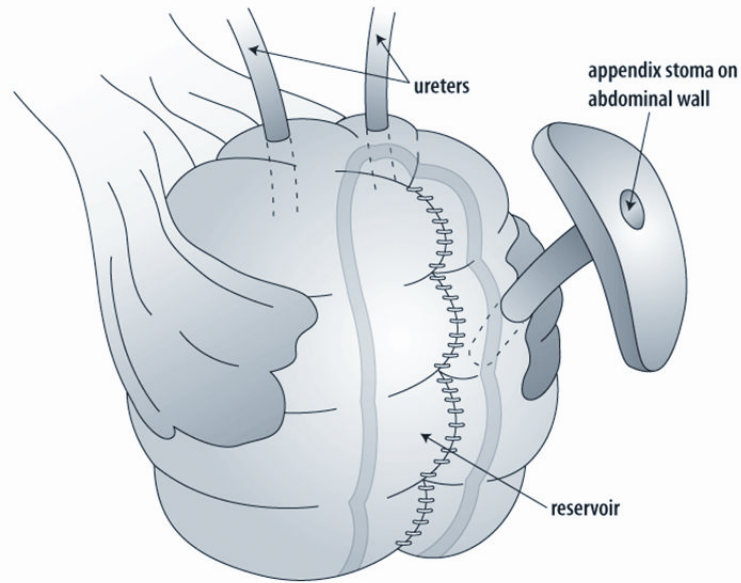


Figure 2.

Continent urinary reservoir. This figure shows a continent diversion made to replace the bladder following cystectomy. These reservoirs can be constructed from either the colon alone or a combination of colon and ileum. A catheterizable channel is constructed from either the native appendix or a small piece of ileum tapered into a narrow channel. This is implanted into the reservoir and then brought to the skin. The reservoir is emptied intermittently by catheterization. The ureters are reimplemented into the new reservoir.

Table 1

COG LTFU Screening Guidelines for Bladder Late Effects

Therapeutic Exposure	Potential Late Effect	Risk Factors	Highest Risk Factors	Recommendations	Guideline Score	Health Counseling/ Further Considerations
Section 11: Cyclophosphamide Ifosfamide	Hemorrhagic cystitis Bladder fibrosis Dysfunctional voiding Vesicoureteral reflux Hydronephrosis	Higher cumulative doses (decreased incidence with use of Mesna) Combined with pelvic radiation Alcohol use Smoking	Cyclophosphamide dose \geq 3 gm/m ² Pelvic radiation dose \geq 30 Gy	Annual history, including hematuria, urinary urgency/frequency, urinary incontinence/retention, dysuria, nocturia, abnormal urinary stream Annual urinalysis	1	Counseling: Counsel to promptly report dysuria or gross hematuria. Further Considerations: Urine culture, spot urine calcium/creatinine ratio, and ultrasound of kidney and bladder for patients with microscopic hematuria (defined as \geq 5 RBC/HFP on at least 2 occasions). Nephrology or urology referral for patients with culture-negative microscopic hematuria AND abnormal ultrasound and/or abnormal calcium/creatinine ratio. Urology referral for patients with culture negative microscopic hematuria
Section 12: Cyclophosphamide	Bladder malignancy	Combined with pelvic radiation Alcohol use Smoking		Annual history, including hematuria, urinary urgency/frequency, urinary incontinence/retention, dysuria, nocturia, abnormal urinary stream Annual urinalysis	2A	Same as Section 11
Section 80: Radiotherapy \geq 30 Gy to whole abdomen, pelvis, sacral spine	Hemorrhagic cystitis	Higher radiation dose (\geq 30 Gy to entire bladder; \geq 60 Gy to portion of bladder)	Combined with cyclophosphamide and/or ifosfamide	Annual history, including hematuria, urinary urgency/frequency, urinary incontinence/retention, dysuria, nocturia, abnormal urinary stream	2A	Same as Section 11

Therapeutic Exposure	Potential Late Effect	Risk Factors	Highest Risk Factors	Recommendations	Guideline Score	Health Counseling/ Further Considerations
Section 81: Radiotherapy ≥ 30 Gy to whole abdomen, pelvis, sacral spine	Bladder fibrosis Dysfunctional voiding Vesicoureteral reflux Hydronephrosis	Higher radiation dose (≥ 45 Gy) Radiation to entire bladder Combined with: - Cyclophosphamide - Ifosfamide - Vincristine		Annual history, including hematuria, urinary urgency/frequency, urinary incontinence/retention, dysuria, nocturia, abnormal urinary stream Annual urinalysis	1	Urologic consultation for patients with incontinence or dysfunctional voiding
Section 82: Radiotherapy to whole abdomen, pelvis, sacral spine	Bladder malignancy	Combined with cyclophosphamide or ifosfamide Alcohol use Smoking		Annual history, including hematuria, urinary urgency/frequency, urinary incontinence/retention, dysuria, nocturia, abnormal urinary stream Annual urinalysis	2A	Same as Section 11
Section 109: Cystectomy	Cystectomy-related complication: Chronic urinary tract infection Renal dysfunction Vesicoureteral reflux Hydronephrosis Reservoir calculi Spontaneous neobladder perforation Vitamin B12/folate/ carotene deficiency			Annual urology evaluation	1 except reservoir calculi = 2A and Vitamin B12/ folate/ carotene deficiency = 2B	None
Section 119: Neurosurgery – spinal cord	Neurogenic bladder Urinary incontinence	Tumor adjacent to or compressing spinal cord or cauda equina Radiation dose ≥ 45 Gy to lumbar and/or sacral spine and/or cauda equina	Injury above the level of the sacrum Radiation ≥50 Gy to lumbar and/or sacral spine and/or cauda equina	Annual history, including hematuria, urinary urgency/frequency, urinary incontinence/retention, dysuria, nocturia, abnormal urinary stream	1	Counseling: Counsel regarding adequate fluid intake, regular voiding, seeking medical attention for symptoms of voiding dysfunction or urinary tract infection, compliance with recommended bladder catheterization regimen. Further Considerations: Urologic consultation for patients with

Therapeutic Exposure	Potential Late Effect	Risk Factors	Highest Risk Factors	Recommendations	Guideline Score	Health Counseling/ Further Considerations
Section 126: Pelvic surgery	Urinary incontinence Urinary tract obstruction	Tumor adjacent to or compressing spinal cord or cauda equina Retropertitoneal node dissection Extensive pelvic dissection Radiation to the bladder, pelvis, and/or lumbar-sacral spine and/or lumbar/sacral spine		Annual history, including hematuria, urinary urgency/frequency, urinary incontinence/tetention, dysuria, nocturia, abnormal urinary stream	1	dysfunctional voiding or recurrent urinary tract infections Same as section 119

Guideline scores for the COG Long Term Follow-up Guidelines

1. There is uniform consensus of the panel that: (1) there is high-level evidence linking the late effect with the therapeutic exposure and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members
- 2A. There is uniform consensus of the panel that: (1) there is lower-level evidence linking the late effect with the therapeutic exposure and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members
- 2B. There is non-uniform consensus of the panel that: (1) there is lower-level evidence linking the late effect with the therapeutic exposure and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members
3. There is major disagreement that the recommendation is appropriate

Table II

Dysfunctional Voiding Scoring System

Over the last month	Almost never	Less than half the time	About half the time	Almost every time	Not available
1. I have had wet clothes or wet underwear during the day	0	1	2	3	NA
2. When I wet myself, my underwear is soaked.	0	1	2	3	NA
3. I miss having a bowel movement every day.	0	1	2	3	NA
4. I have to push for my bowel movements to come out.	0	1	2	3	NA
5. I only go to the bathroom one or two times each day.	0	1	2	3	NA
6. I can hold onto my pee by crossing my legs, squatting or doing the "pee dance".	0	1	2	3	NA
7. When I have to pee, I cannot wait.	0	1	2	3	NA
8. I have to push to pee.	0	1	2	3	NA
9. When I pee it hurts.	0	1	2	3	NA
10. <i>Parents to answer.</i> Has your child experienced something stressful e.g. new baby, new school, School problems, Abuse (sexual/physical), Home problems (divorce/death)	No (0)		Yes (3)		
TOTAL					

Abnormal values: >9 (males), >6 (females)

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