

# Follow-up Management of Cystectomy Patients



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## KEYWORDS

• Cystectomy • Functional outcomes • Follow-up • Recurrence • Muscle-invasive bladder cancer

## KEY POINTS

- After cystectomy, follow-up with laboratory assessment and imaging is critical in diagnosing recurrence and preventing functional complications.
- Recurrence after cystectomy occurs in 35% of patients.
- Distant metastases are the most common sites of recurrence; however, local, upper tract, and urethral recurrence can also occur.
- Functional complications after urinary diversion can include bowel dysfunction, vitamin B12 deficiency, acidosis, electrolyte abnormalities, osteopenia, nephrolithiasis, urinary tract infections, renal functional decline, and urinary obstruction.
- These complications can be reversed when diagnosed early.

## INTRODUCTION

Bladder cancer is the 6th most commonly diagnosed cancer in the United States. An estimated 79,000 new cases of bladder cancer will be diagnosed in 2017, with a median age at diagnosis of 73 years.<sup>1</sup> Of these patients, 25% to 30% will have muscle-invasive bladder cancer (MIBC) at diagnosis. In addition, 15% to 20% of patients with non-MIBC (NMIBC) will progress to muscle invasion. Of all the patients with MIBC, only 39% will undergo cystectomy.<sup>2</sup> Anywhere from 8000 to 10,000 cystectomies are performed every year in the United States. Although cystectomy is the gold standard for the treatment of MIBC, a significant number of patients will have recurrence and functional complications after cystectomy and, therefore, long-term follow-up is mandatory.

## RECURRENCE

Recurrence after cystectomy and bladder cancer-specific mortality can occur in up to 35% and

28% of the patients, respectively. Higher stage pathologic stage T3 or T4 grade, lymphovascular invasion, and presence of lymph node (LN) metastases have been shown to be poor prognosticators for recurrence.<sup>3</sup>

### *Distant Metastasis*

Of all the patients with recurrence, more than 50% are with distant metastases. Risk factors for distant metastases are higher stage, Lymphovascular invasion (LVI), positive margins, smaller extent of LN dissection, and lack of neoadjuvant chemotherapy. Of the distant metastases, 80% to 90% will occur in the first 3 years. The most common sites of metastases are bone (11%–13%), liver (10.7%), and lungs (9.9%–11%). Prognosis after the development of distant metastases is poor, with a median survival of 13.8 to 14.8 months.<sup>4</sup> Primary treatment of distant metastases consists of chemotherapy or immunotherapy. However, there may be a role for metastasectomy in carefully selected patients.<sup>5,6</sup>

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### ***Pelvic (Local) Recurrence***

Contemporary literature has shown local recurrence in 5% to 15% of the cases. Higher stage, LN-positive disease, positive margins, lesser extent of LN dissection, and lack of neoadjuvant chemotherapy are some of the risk factors for local recurrence. Most of these cases are diagnosed in the first 2 years after surgery. Local recurrence results in a poor prognosis with associated systemic recurrence in 36% to 64% of the patients, and survival is generally less than a year.<sup>4</sup> Sites of local resection are the original surgical site, including the prerectal space and incompletely resected pelvic LNs. Treatment most commonly consists of chemotherapy, radiotherapy, surgical resection in select cases, or any combination of these.

### ***Upper Tract Recurrence***

Upper tract recurrence is generally diagnosed later (median time >3 years) and has an incidence of 2% to 6%. Some of the risk factors are presence of tumor in the distal ureter, multifocal or recurrent urothelial carcinoma (UC), NMIBC, and presence of carcinoma in situ (CIS). Patients who had none of these risk factors had an upper tract recurrence rate of only 0.8% at 15 years, whereas those with greater than 3 of these risk factors had a 13.5% risk of recurrence in the same time frame.<sup>7</sup> Greater than 50% of these recurrences are diagnosed after the onset of symptoms, and about 70% are diagnosed at an advanced stage. Urine cytology results in primary detection of 7% of these recurrences, whereas upper urinary tract imaging primarily diagnoses 29.6%.<sup>8</sup> Symptoms of upper tract recurrence include flank pain and hematuria. Unfortunately, the prognosis is poor with 18% to 33% of the patients having metastases at diagnosis.<sup>4</sup> Unlike other types of recurrence, the risk of upper tract recurrence is lifelong.

### ***Urethral Recurrence***

The incidence of urethral recurrence has been reported to be approximately 1.5% to 6% in male patients and 0.83% to 4.3% in female patients who underwent urethral-sparing cystectomy.<sup>9</sup> Most of these cases are diagnosed in the first 3 years. The incidence of urethral recurrence is lower in patients undergoing orthotopic bladder replacements, likely secondary to patient selection. Symptoms of urethral recurrence include hematuria, change in urinary stream in patients with orthotopic neobladders, urethral bleeding, and induration of periurethral tissue in those with a cutaneous diversion. Some of the risk factors for urethral recurrence are presence of prostatic

urethral involvement by the UC (especially stromal involvement), multifocal UC, NMIBC, and presence of CIS.<sup>4</sup> Patients diagnosed with urethral recurrence by surveillance have a significant survival advantage when compared with those who are diagnosed symptomatically.<sup>10</sup> Hence, follow-up of the male urethra is indicated in patients who are at an increased risk of urethral recurrence. Treatment of urethral recurrence consists of transurethral resection, Bacillus Calmette-Guerin (BCG) in cases of CIS, and urethrectomy in patients with invasive disease localized to the urethra.<sup>11</sup>

### **SURVEILLANCE FOR RECURRENCE OR METASTASES**

The NCCN guidelines recommend the following surveillance for patients who underwent cystectomy for NMIBC: 1) CT Urogram (CTU) or MR Urogram (MRU) at 3 and 12 months and then annually for 5 years. Beyond 5 years they recommend renal imaging annually and, 2) Urine cytology with urethral washings every 6–12 months for the first 2 years for high risk pts (Positive urethral margin, multifocal CIS, prostatic urethral involvement). For MIBC, they recommend CTU/MRU, CXR every 3–6 months for 2 years and then annually for 3–5 years. Beyond 5 years they recommend renal imaging annually and, 2) Urine cytology with urethral washings every 6–12 months for the first 2 years for high risk percentages.<sup>12</sup> It should be noted that the follow-up for urethral recurrence in men using urethral washings for cytology is controversial. A retrospective study of 85 male subjects with urethral recurrence showed an improved cancer-specific rate in men diagnosed before the onset of symptoms ( $P < .0001$ ).<sup>10</sup> However, another retrospective study of 24 subjects who had undergone urethrectomy did not find a statistical difference in overall survival in these groups when controlling for original bladder tumor stage ( $P = .769$ ).<sup>13</sup> With the limited data present and the lack of consensus, cytology of urethral washings and urethroscopy should be performed in symptomatic patients, and cytology of urethral washings in asymptomatic patients should be performed at the discretion of the clinician, bearing in mind the aforementioned risk factors.

Even with the high incidence of recurrence and progression after cystectomy, there is debate regarding the role of surveillance imaging in improving survival in patients who have recurrence. An observational study of 1270 subjects in Germany who underwent cystectomy showed that, of the 444 recurrences noted, 154 were detected in asymptomatic subjects with imaging

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