# Multidisciplinary Management of Patients with Localized Bladder Cancer

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#### **KEYWORDS**

- Muscle-invasive bladder cancer
   Radical cystectomy
- Pelvic lymph node dissection Chemotherapy Chemoradiation

#### **KEY POINTS**

- Surgeon-controlled variables including negative surgical margins and extended lymph node dissection are essential to achieve optimal outcomes for patients treated by radical cystectomy.
- Neoadjuvant chemotherapy with methotrexate, vinblastine, doxorubicin, and cisplatin
  significantly improves the survival of patients undergoing radical cystectomy and represents the optimal treatment approach for patients with muscle-invasive bladder cancer.
  The use of carboplatin-based regimens is not recommended.
- In addition to insufficient evidence for use of adjuvant chemotherapy, its use and tolerability may be compromised after major surgery because of surgical complications.
- In select patients, bladder-preservation protocols may result in acceptable survival and low toxicity rates, although it has not been widely embraced in the genitourinary oncology community.

### INTRODUCTION

Optimal management of invasive bladder cancer involves a multidisciplinary therapeutic approach for improved disease-free and overall survival. Approximately 30% of patients present with muscle-invasive bladder cancer at diagnosis. A total of 50% to 70% of those with high-grade, non-muscle-invasive disease recur and up to 50% progress to muscle-invasive disease. If left untreated, 85% of patients with muscle-invasive bladder cancer die of disease within 2 years of diagnosis. Because of high morbidity and mortality of muscle-invasive bladder cancer, single therapeutic modality may not provide optimal cancer control.

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Radical cystectomy plays a pivotal role in the care of patients with invasive bladder cancer and has been the mainstay of treatment for decades. Overall survival for patients with muscle-invasive bladder cancer treated by radical cystectomy ranges from 50% to 60%. Per stage, survival for pT0-2 N0, pT3-4 N0, and pTany N1-3 is 70% to 80%, 45% to 55%, and 25% to 35%, respectively. Despite significant advances in the understanding and management of bladder cancer, outcomes have largely remained unchanged in the last 30 years. Bladder-preservation strategies involving a visibly complete transurethral bladder tumor resection followed by radiation therapy and chemotherapy may achieve similar survival rates in select patients. This article reviews different treatment options and discusses possible management strategies to improve outcomes.

## SURGICAL ISSUES Quality of Radical Cystectomy

Radical cystectomy is a critical component in the treatment of invasive bladder cancer. Suboptimal surgery dramatically decreases overall survival. Modifiable surgical factors that can significantly improve survival include surgical margin status and number of lymph nodes removed. Analysis of the SWOG 8710 trial showed that positive margins and removal of fewer than 10 nodes were associated with significantly poorer outcomes. The adjusted hazard ratio for death of patients with positive versus negative surgical margin was 2.7 (95% confidence interval, 1.4–2.8). When compared with negative-margin group, local recurrence was 11.2 times greater in the positive-margin group. In a recent paper by Mitra and colleagues, a review of 447 patients showed that positive surgical margin status was significantly associated with worse postrecurrence overall survival.

Number of lymph nodes removed and overall survival have a linear correlation with continuous rise in survival with increasing number of lymph nodes removed. Herr and colleagues showed that disease-specific survival was greater for patients with more than 14 nodes removed as compared with removal of 9 to 14 nodes and 1 to 8 nodes. The quality of surgery may be improved by striving for negative surgical margins and removing adequate number of lymph nodes at the time of surgery.

Another factor that may influence outcomes is surgeon training. In the analysis of the SWOG 8710 study, 106 surgeons were included from 1987 to 1998, of which 38% were fellowship-trained urologic oncologists. <sup>14</sup> No pelvic lymph node dissection (PLND) was done in 9% of the cases and in 50%, less than 10 nodes were removed. Positive surgical margin rate was 10% overall, but 4% for urologic oncologist and 16% for others. Local recurrence rate for urologic oncologist was 6% versus 23% for others. The type of surgeon (fellowship-trained vs others) was a significant predictor of number of nodes removed, local recurrence, and survival. The surgical volume among urologic oncologists does not play a significant role in terms of surgical outcomes. <sup>14</sup> Sixteen surgeons from four centers of excellence with varying experience were compared. Seven surgeons had done fewer than 50 radical cystectomies, whereas four had done more than 100 procedures over a 3-year period. No significant difference was found among urologic oncologists with regards to number of lymph nodes removed and surgical margin status.

To summarize, positive margins are associated with increased local recurrence and worse survival. Surgery by a fellowship-trained urologic oncologist versus others is associated with greater number of nodes removed, lower local recurrence, and higher survival.

## Standard Versus Extended PLND

Clinical staging for lymph nodes relies on imaging including computed tomography or magnetic resonance imaging; however, studies have shown that 19% to 28% of those

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