

## Bladder Preservation Strategies

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#### **KEYWORDS**

Bladder cancer 
Cystectomy 
Chemotherapy 
Radiotherapy 
Organ preservation

### **KEY POINTS**

- Organ preservation by concurrent chemoradiotherapy following an aggressive transurethral resection (TUR) of muscle-invasive bladder cancer (MIBC) is an established treatment of selected patients with bladder cancer as an alternative to cystectomy with or without chemotherapy.
- Established patient and disease factors must be considered when deciding to offer patients with bladder cancer organ-preserving chemoradiotherapy, and attention must also be paid to the treatment regimen and the radiation technique.
- Ongoing biomarker studies of the TUR of bladder tumor (TURBT) specimen suggest that subsets of patients may respond favorably to an organ-preservation approach using radiation or chemoradiotherapy regimens, but prospective studies are needed to validate these observations.
- Concurrent chemoradiotherapy following a complete TURBT for organ preservation is now being studied prospectively for patients with non-MIBC who are refractory to intravesical therapy.

#### INTRODUCTION

Bladder cancer has a significant incidence and mortality, with approximately 75,000 new cases and 15,000 deaths in the United States in 2013.<sup>1</sup> Management of muscle-invasive bladder cancer (MIBC) has evolved significantly over the past few decades. Cystectomy remains the standard treatment, but organ-preservation approaches combining concurrent chemotherapy and radiation following an aggressive transure-thral resection of bladder tumor (TURBT) have emerged as appropriate alternatives in selected patients.<sup>2–11</sup> Although preoperative radiotherapy followed by cystectomy was found to initially improve local control, this approach was later abandoned.<sup>12,13</sup>

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Postoperative nonconformal radiotherapy was associated with significant toxicity when earlier radiotherapy techniques were used, but postoperative radiation using intensity-modulated radiotherapy (IMRT) is now again under study.<sup>14–17</sup> Although the addition of radiotherapy with surgery (in either the preoperative or postoperative study) is not currently standard, the addition of neoadjuvant (and probably adjuvant) chemotherapy with surgery has been demonstrated to improve survival. The combination of surgery and chemotherapy is now the optimal standard in patients suitable for cisplatin-based multidrug therapy from the standpoint of cancer control outcomes, with a 5-year overall survival of approximately 70% for muscle-invasive disease.<sup>18–21</sup>

The morbidity of surgery must be weighed into consideration, particularly because of the extensiveness of the surgery and associated recovery.<sup>6–11</sup> In this context, a trimodality therapeutic organ-preservation approach (TURBT plus concurrent chemotherapy and radiation) was developed in order to attempt to achieve a high cancer control rate while preserving good bladder function and a good quality of life. Organ-preservation approaches are now commonly used in other areas of cancer treatment whereby extensive surgeries were once standard: lumpectomy plus radiotherapy in place of modified radical mastectomy for breast cancer, chemoradiotherapy in place of abdominoperineal resection for anal cancer, chemoradiotherapy and limb-sparing surgery in place of amputation for sarcomas, and chemoradiotherapy in place of extensive surgery for head and neck cancers. In all of these disease sites, an organ-preservation technique (with the more extensive surgery reserved for salvage therapy), achieved similar rates of local control and overall survival as up-front extensive surgery.

It is with this same general goal that bladder preservation strategies were developed. Although radiotherapy alone in general has poorer cancer control outcomes in comparison with cystectomy, the addition of chemotherapy to radiotherapy produced results commensurate with cystectomy series.<sup>2,22–33</sup> Recently, cooperative group trials (Radiation Therapy Oncology Group [RTOG] 0233 and BC2001) report 5-year cystectomy-free survival rates of more than 60% for selected patients with muscle-invasive disease without any demonstrated compromise to the overall survival in comparison with up-front cystectomy series.<sup>30,31</sup>

#### PATIENT EVALUATION OVERVIEW

Risk factors for bladder cancer are smoking, chronic physical irritation (such as bladder stones, schistosoma haematobium, or indwelling catheter), and chronic chemical irritation (such as phenacetin, cyclophosphamide, and occupational factors in the dye, rubber, and paint industries).<sup>34</sup> Urothelial carcinoma (formerly called transitional cell carcinoma) is the most common histologic variant (representing more than 90% of bladder cancer cases in North America), and further discussion in the current article is restricted to urothelial carcinoma. Diagnostic workup initially begins with a thorough physical examination with particular attention to a bimanual examination to determine the extent of pelvic involvement. A cystoscopic/TURBT examination is critical, with biopsies taken from all visualized areas of abnormalities and often random normal areas (including prostatic urethra biopsies, as indicated). The size, number, and morphology of each lesion should be documented as well as a tumor map. It may be important to evaluate by imaging the upper urinary tract for synchronous lesions, although these are rare. The laboratory workup consists of a urinalysis, cytology, and basic chemistry/blood counts. The radiological workup consists of computed tomography (CT) or MRI of the pelvis and abdomen and a chest radiograph or CT; a bone scan is typically obtained for muscle-invasive lesions, particularly if the

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