

## Invasive bladder cancer - overview

{niftybox width=180px,float=right,textalign=left}European Urology Ass.: Management Guidelines on muscle-invasive and metastatic bladder cancer, and more. {/niftybox}

In the United States more than 60,000 new cases of bladder cancer were diagnosed in 2005. Approximately 25% of all new patients have muscle-invasive bladder cancer at the time of diagnosis. Of the remaining 75% who initially present with superficial disease, 10%-15% will progress to invasive disease.

### Cystectomy

Radical cystectomy with pelvic lymph node dissection [removal] is the standard treatment for patients with invasive bladder cancer. However, many alternative techniques to spare the bladder are being actively investigated.

An article which reviewed the latest literature comparing cystectomy with bladder-sparing techniques would seem to be implying that surgery remains the gold standard for giving the best chance at long term survival. Most comparative studies have indicated that local recurrence and survival outcomes using bladder sparing protocols [transurethral resection, chemotherapy and radiation] for muscle-invasive disease are inferior to those from radical cystectomy to control muscle-invasive bladder cancer.<sup>1</sup>

Continuous improvement in surgical techniques and post-operative care greatly reduced morbidity and late effects of surgery, including sexual dysfunction. Consequently, neobladder and continent diversions are being increasingly accepted by patients. The article concludes that bladder preservation, with all of its associated risks, currently is not a better alternative to cystectomy for the majority of patients.

The author uses the following points to further underline this rationale:

- (1) Muscle-invasive disease is associated with a high incidence of CIS, multifocal field disease, and a high recurrence rate that can be invasive and lethal
- (2) The role of radiation therapy in bladder preservation needs further evaluation and remains experimental at this time
- (3) Improvements are needed for chemotherapy to provide better results and reduce toxicity
- (4) The incidence of upper tract tumors in patients who have not had a cystectomy is high
- (5) The strict criteria for patient selection and the need of a specialized team of urologists and uropathologists make it difficult to recommend bladder preservation in a community setting
- (6) Based on experience at our center<sup>1</sup>, the long-term results of bladder preservation support the need for early cystectomy

(7) Salvage cystectomy compromises the option for neobladder formation.

### Chemotherapy

A major advancement in the treatment of invasive bladder cancer occurred with the advent of effective chemotherapy with the M-VAC protocol, consisting of methotrexate, vinblastine, doxorubicin, and cisplatin. Recent trials have led many uro/oncologists to switch to other, newer chemo protocols (namely, cisplatin/Platinol and gemcitabine/Gemzar known also as "GP, or gemcitabine/carboplatin-GC; see chemotherapy). However, the role of systemic chemotherapy, as either an adjuvant or a neoadjuvant treatment, continues to evolve, and its impact on survival remains investigational. Continued improvements in chemotherapy may permit a more aggressive approach in some patients, even those with micrometastases, and thus allow combined radical surgery and effective adjuvant chemotherapy.

### Radical TUR

Transurethral Resection Transurethral resection (TUR) is used primarily in muscle-invasive bladder cancer to establish the diagnosis and local extent of the disease. The use of TUR for definitive treatment of muscle-invasive bladder cancer would depend on tumor volume, multifocality, and associated carcinoma in situ (CIS). Understaging of the depth of tumor involvement occurs in up to 40% of cases. Nevertheless, several series have shown that TUR provides disease control, particularly in patients with lower clinical disease stages. The ideal candidate for radical TUR has a primary, solitary, or papillary tumor that is 3 cm or less in size, and the patient must be amenable to follow-up.

### Partial Cystectomy

Partial cystectomy is not a commonly used technique by the urologist and remains an incompletely evaluated surgical option in the treatment of bladder cancer. Partial cystectomy permits complete pathologic staging of the tumor and pelvic lymph nodes while preserving bladder and sexual functions. No randomized trials have been conducted to compare this.

### Radiation

The results of radiation therapy as a primary treatment for muscle-invasive bladder cancer are similar to TUR alone. Radiation therapy has been reserved primarily for patients who are unfit for cystectomy based on age, comorbid conditions, and extent of disease.

### Combined Modality

For tumors 5 cm in size, a combination modality [TUR+chemo/radiotherapy] could be used for bladder preservation in this group of patients with higher rates of nodal metastasis and disease control. The use of markers such as p53, p21, or Rb could assist in distinguishing between patients who will respond well to bladder preservation and those who will be better served with radical surgery. For high-stage tumors (T3b to T4), combined modality offers only 20% control. In this situation, even radical cystectomy has failed to achieve high cure rates, principally due to extravesical and nodal disease. The role of adjuvant chemotherapy for this patient population continues to be investigational.

With new chemotherapeutic agents that offer similar response rates to M-VAC but with less toxicity, it is hoped that the future will see treatment able to be offered to a broader selection of patients and possibly decrease the morbidity of bladder preservation. Presence of an experienced urologist and cytologist is key to performing bladder preservation protocols successfully. The decisions made in a bladder preservation protocol regarding candidates and follow-up are affected by the expertise of the pathologist, urologist, and oncologist. This can be done only in major centers, and at the present time, bladder preservation cannot be performed routinely in the community.

In the future, new markers may allow us to more appropriately select patients for bladder preservation.

New targeted, FDA approved anti-angiogenic agents are being actively investigated for advanced disease, among these: Sunitinib malate ([www.sutent.com](http://www.sutent.com)) and Sorafenib/Nexavar. 2

1. Bladder-Sparing Treatment of Invasive Bladder Cancer Inoel Rivera, MD, and Zev Wajzman, MD From the Division of Urology at the University of Florida College of Medicine, Gainesville, Fla. July/August 2000, Vol. 7, No.4 Cancer Control 341 <http://www.moffitt.usf.edu/pubs/ccj/>

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2. Sunitinib malate and sorafenib may be beneficial at the treatment of advanced bladder cancer due to their anti-angiogenic effects Mesrur Selcuk Silay Corresponding Author Information email address, Cengiz Miroglu March 2007; Medical Hypothesis Volume 69, Issue 4 Pages 892-895