Bladder cancer

ORGAN-SPARING MULTIDISCIPLINARY TREATMENT FOR MUSCLE-INVASIVE BLADDER CANCER

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TRIAL SUMMARY: Trimodality bladder preservation therapy.
Chen RC and Shipley WU. Update on multidisciplinary treatment of bladder cancer. Presented at the ASTRO annual meeting, September 2014. Educational Session 201.

Potentially curative treatments for patients with muscle-invasive bladder cancer (MIBC) are underused, especially in the elderly. Trimodality bladder preservation therapy, which includes a maximally safe transurethral resection of the bladder tumour, followed by concurrent chemoradiation, fulfills this unmet need. In multiple prospective clinical trials and large institutional series, trimodality therapy (TMT) has demonstrated excellent 5-year overall survival rates of 48% to 65%, comparable to those reported in cystectomy studies. Approximately 75% to 80% of long-term survivors maintain their native bladders, which tend to function well and allow patients to maintain excellent quality of life. Salvage cystectomy for patients who develop a local invasive recurrence can be performed with acceptable operative complication rates, and results in excellent long-term disease control and survival outcomes. For patients with MIBC who are noncystectomy candidates, or select patients who are motivated to keep their native bladders, trimodality bladder preservation therapy is recognized by the International Consultation on Urological Diseases—European Association of Urology and the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology for Bladder Cancer as an effective alternative to radical cystectomy and should be considered.

COMMENTARY: Radical cystectomy with pelvic lymph node dissection is currently viewed as the standard of care for MIBC, with 5-year overall survival rates in contemporary cystectomy series in the range of 55% to 60%. However, although sophisticated techniques for urinary diversion have been developed, even the construction of an orthotopic neobladder with continent urinary diversion cannot substitute for the patient’s original bladder. Removal of the entire organ may lead to significant morbidity and affect patients’ comfort and quality of life. In recent decades, organ-preserving multimodality therapies have been established in many malignancies, including breast, anal and head and neck cancers, and soft tissue sarcoma, among others. Similar outcomes for patients with MIBC can be achieved in a multidisciplinary setting where surgeons, medical and radiation oncologists, and other specialists jointly assess whether limited forms of organ-sparing surgery, supplemented by local radiotherapy and systemic therapy, can allow radical and partially mutilating extirpation to be avoided without compromising the survival of the patient.1

An update on multidisciplinary treatment of bladder cancer was presented at the ASTRO annual meeting by Ronald C. Chen from the University of North Carolina at Chapel Hill and William U. Shipley from Massachusetts General Hospital and Harvard Medical School. The incidence of bladder cancer in the US consists of 74,690 cases annually. Bladder cancer is diagnosed more frequently in men (56,390 cases) than in women (18,300 cases). Twenty-five percent of bladder cancers involve muscle-invasive disease. Many etiologic factors can contribute to the development of this disease, though smoking is a major contributor.1

Clinical staging is necessary to establish the depth and local extent of bladder invasion, as well as to rule out distant metastases. Transurethral resection of bladder tumour (TURBT) down to and including muscularis propria (biopsy alone is not sufficient), prostatic biopsies, computerized tomography (CT) scan or magnetic resonance imaging (MRI) of pelvis and abdomen for hydronephrosis and nodes, bone scan, and chest CT scan are the recommended staging investigations. Understaging is common for patients with bladder cancer.2 19% of patients from the urology series with cN0 disease were upstaged to pN+.

The treatment goals for MIBC are optimal survival and prevention of pelvic failure and distant metastases, with functional urinary reservoir and high quality of life (QOL). These goals can be achieved by cystectomy and reconstructive approaches or by bladder conservation approaches. Radical cystectomy, which used to be a gold standard approach for MIBC, is an extensive, mutilating surgery that consists of removing the entire bladder, lymphadenectomy, prostate and seminal vesicles in men, and uterus, cervix, ovaries and anterior vagina in women. Multidisciplinary management for organ preservation for cancer treatment has been practiced in many malignancies including breast, anal, larynx, prostate, gastrointestinal, sarcomas and bladder cancer.

TMT that includes maximal transurethral resection of the bladder tumour (TURBT) followed by radiotherapy combined with various chemotherapy protocols has been investigated in series at single institutions and in prospective clinical trials by cooperative groups, such as the Radiation Therapy Oncology Group (RTOG), over several decades.
With this approach, radical cystectomy is reserved as a salvage option for patients with incomplete responses to (induction) chemoradiotherapy or with invasive local recurrence. Preoperative morbidity and mortality from cystectomy can be as high as 10%, particularly in older patients. In contrast, TMT is well tolerated in all groups of patients, including older patients. The rate of late induced grade 3 genitourinary toxicities related to reduced bladder capacity is 2%, and gastrointestinal toxicities (surgery for bowel obstruction) occur in 1.5% of cases. Modern bladder radiation concurrent with chemotherapy results in good to excellent long-term bladder function. More than 70% of survivors are able to preserve their bladders. The literature indicates that the acceptance of chemoradiation used in modern bladder-sparing therapy should not be limited by concerns of high rates of late pelvic toxicity.

Comparing cure rates of modern bladder-preserving approaches to cystectomy series is difficult as most of the cystectomy studies reported pathologic staging, while chemoradiotherapy trials report clinical staging. However, in appropriately selected patients, bladder preservation therapy offers excellent disease control and survival outcomes, similar to cystectomy in all groups of patients. A multidisciplinary approach is extremely important for successful treatment outcomes for patients with MIBC. Maximal TURBT with ongoing lifelong bladder surveillance and salvage cystectomy in patients who do not respond to TMT needs to be incorporated into the treatment plan.

The data from Massachusetts General Hospital presented this year at ASTRO indicate that salvage cystectomy, whether immediate due to inadequate tumour response or delayed due to invasive recurrence, is effective, produces long-term disease-free survival, and can be successfully conducted by experienced surgeons.

In conclusion, modern trimodality bladder-sparing therapy for selected patients offers a proven alternative to cystectomy. In interested and motivated patients, and with urologic involvement, the cure rates from a TMT approach can now be discussed as comparable to cystectomy, rather than pursued only as a default treatment for patients unfit for radical surgery.

References