

Abstracts for CUAJ Bladder Cancer Supplement Volume 3, Issue 6, Supplement 4

BC1

Screening for bladder cancer: the best opportunity to reduce mortality

Yves Fradet, MD, FRCSC

Hôtel-Dieu de Québec (CHUQ), University of Laval, Québec, QC

Bladder cancer kills more women than cervical cancer and is also a significant cause of mortality in men. Little progress has been made in improving survival in patients with advanced bladder cancer. Two pilot studies using microhematuria screening have shown that screening for bladder cancer results in close to 80% downstaging, with high-grade cancers being detected before they have invaded the bladder wall. Results of long-term follow-up even suggest a striking reduction in bladder cancer mortality. The main obstacles to screening for bladder cancer may be overcome if a higher-risk population is identified by designing a risk scale for exposure to cigarette smoke and occupational carcinogens, and through genetic testing for susceptibility to cancer and home hematuria screening, which in itself identifies a population with approximately 3% to 4% risk of bladder cancer. The feasibility and cost effectiveness of screening for bladder cancer can be significantly improved by incorporating a secondary screening strategy using a more sensitive and specific bladder cancer marker that is currently available, and by limiting urological evaluations to patients who show positive results on one or more of these tests. Bladder cancer is the most costly cancer to treat in the United States and pharmacoeconomic studies suggest that screening for bladder cancer could not only save lives but also reduce costs per year-life saved.

BC2

Chemoprevention in bladder cancer: What's new?

Jean-Baptiste Lattouf, MD, FRCSC

Urologic Oncology Section and Minimally Invasive Section, University of Montréal Health Centre (CHUM), Montréal, QC

Bladder cancer (BC) is one of the most expensive cancers to treat in North America due to its recurrent nature necessitating investigative follow-up and intravesical treatments, and due to comorbidities related to major surgery in cases of invasive cancer. In Canada, BC represents the sixth-most common tumour type and ranks eighth with respect to cancer mortality. Of the 3 main histological variants of BC, transitional cell carcinoma is the most prevalent in North America and thus constitutes the object of this review.

BC3

The optimal management of T1 high-grade bladder cancer

Kenneth G. Nepple, MD; Michael A. O'Donnell, MD

University of Iowa Department of Urology, Iowa City, IA

Stage T1Hg bladder cancer should be considered an aggressive and potentially lethal disease. The importance of initial re-resection to identify unrecognized muscle-invasive disease is significant. Most patients with high-risk disease are candidates for initial bladder salvage with intravesical Bacillus Calmette-Guerin vaccine for immunotherapy, a procedure with a high survival rate; however, failure of the procedure may result in a guarded prognosis. Even after apparent success, patients should be informed of the risks of the disease progressing to muscle-invasive or metastatic disease and the need for vigilant monitoring. Despite optimal management, a significant number of patients relapse or progress to invasive disease requiring cystectomy. This review provides insight into the optimal management of T1Hg bladder cancer.

BC4

Histologic variants of urothelial bladder cancer and nonurothelial histology in bladder cancer

Venu Chalasani, MD; Joseph Chin, MD, FRCSC; Jonathan I. Izawa, MD, FRCSC

Departments of Surgery and Oncology, Divisions of Urology and Surgical Oncology, London Health Sciences Centre-Victoria Hospital, London, ON

Bladder cancer can be classified histologically as urothelial or non-urothelial. Urothelial cancer has a propensity for divergent differentiation, which has increasingly been recognized in recent years due to heightened awareness and improved immunohistochemistry techniques. Furthermore, the recent World Health Organization classification of urothelial cancers improved clarity on this issue, with its listing of 13 histologic variants of urothelial cancer. The divergent differentiation patterns include, amongst others, squamous, glandular, micropapillary, nested, lymphepithelioma-like, plasmacytoid and sarcomatoid variants of urothelial cancer. Attempts to quantify the amount of divergent differentiation present, such as using the nonconventional differentiation number (NDN), have been made recently, which will improve the ability to compare publications from different centres. Genetic-based studies have indicated that the histologic variants of urothelial cancer arise from a common clonal precursor. Mostly, the current evidence suggests that urothelial cancer with divergent differentiation has a worse prognosis when compared with pure urothelial cancer. This article will review the current literature on variant histologies of urothelial cancer, as well as new developments in pure squamous cell carcinoma, small cell carcinoma and adenocarcinoma of the bladder.

BC5

The management of BCG failure in non-muscle-invasive bladder cancer: an update

Alexandre R. Zlotta, MD, FRCSC;* Neil E. Fleshner, MD, FRCSC;** Michael A. Jewett, MD, FRCSC****

**Department of Surgery, Division of Urology, University of Toronto; †Department of Surgery (Urology), Mount Sinai Hospital; ‡Department of Surgical Oncology, University Health Network, Toronto, ON*

Up to 40% of patients with non-muscle-invasive bladder cancer will fail intravesical BCG therapy. There is, unfortunately, no current gold standard for salvage intravesical therapy after appropriate BCG treatment. Indeed, outcomes are at best suboptimal. The vast majority of low-grade NMIBC are prone to recur but very rarely progress. Failure after intravesical BCG in these patients is usually superficial and low-grade. At the other end of the spectrum, failure to respond to BCG in high-risk T1 bladder cancer and/or CIS (Tis) is more problematic, since those tumours often have the potential to progress to muscle invasion. In these cases, radical cystectomy remains the mainstay after BCG failure. With appropriate selection, certain patients who "fail" BCG (but with favourable risk factors) can be managed with intravesical regimens, including repeated BCG, BCG plus cytokines, intravesical chemotherapy, thermochemotherapy or new immunotherapeutic modalities. In this review, reasons explaining BCG failure, how to define BCG failure, optimal risk stratification and prediction of response and management of BCG failures are discussed.

BC6

Role of lymphadenectomy for invasive bladder cancer

Faysal A. Yafi, MD; Wassim Kassouf, MD, FRCSC

Division of Urology, McGill University Health Centre, Montréal, QC

Radical cystectomy with pelvic lymphadenectomy remains the standard of care in the treatment of muscle-invasive and refractory non-invasive bladder cancer. Evidence supports the role of lymphadenectomy as both a therapeutic and prognostic variable in patients with invasive bladder cancer. Over the past decade, variations in the extent of lymphadenectomy have been advocated by several studies. We review the literature regarding the role and extent of lymphadenectomy, as well as their impact on patient outcomes.

BC7

Management of the urethra in urothelial bladder cancer

Androniki Kanaroglou, MD;* Bobby Shayegan, MD FRCSC[†]

**Division of Urology; [†]Urologic Oncology, Department of Surgery, McMaster University, Hamilton, ON*

The standard of care in management of invasive urothelial cancer of the bladder is radical cystectomy and pelvic lymphadenectomy. Although uncommon, recurrence of disease in the retained urethra following cystectomy carries a poor prognosis. The need for assessment of risk of recurrence is greater now than ever, with wider adoption of orthotopic bladder substitution. This review will address the contemporary management of the urethra following cystectomy for urothelial cancer.

BC8

Point/Counterpoint: The case for prostate capsule-sparing radical cystectomy in selected patients

Laurence Klotz, MD, MSc, FRCSC;* Jehonathan Pinthus, MD, PhD[†]

**Department of Surgery, Division of Urology, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON [†]Division of Urology, McMaster University, Hamilton, ON*

BC9

Point/Counterpoint: The debate continues on prostate-sparing cystectomy

Ahmed Kotb, MD; Armen G. Aprikian, MD, FRCSC

McGill University Health Centre, McGill University, Montréal, QC

BC10

Perioperative chemotherapy for muscle-invasive bladder cancer

Peter Black, MD, FRCSC; Alan So, MD FRCSC

Department of Urologic Sciences, UBC, Vancouver, BC

Considerable debate exists concerning the combined use of systemic chemotherapy and radical surgery for muscle-invasive bladder cancer. While there is evidence for a survival benefit after neoadjuvant chemotherapy, the benefit is modest and the potential toxicity and delay of time to surgery prior to cystectomy appear to be deterring many surgeons from its administration. The evidence for adjuvant chemotherapy, on the other hand, is less compelling and substantial. Furthermore, the role of adjuvant compared to salvage chemotherapy requires further investigation. Similarly, research continues on identifying molecular and clinical markers to best stratify patients for optimal perioperative therapy. In this article, the evidence for radical cystectomy and chemotherapy, given either in a neoadjuvant or adjuvant setting, will be reviewed.

BC11

Management of metastatic urothelial cancer: the role of surgery as an adjunct to chemotherapy

Robert S. Svatek, MD;* Arlene Siefker-Radtke, MD;[†] Colin P. Dinney, MD*

**The University of Texas MD Anderson Cancer Center, Department of Urologic Oncology; [†]The University of Texas MD Anderson Cancer Center, Department of Genitourinary Medical Oncology, Houston, TX*

Metastatic or unresectable disease is identified in approximately 20% of patients presenting with invasive urothelial cancer. In addition, up to 50% of patients will develop metastases following radical cystectomy for clinically localized disease. Multiagent cisplatin-based chemotherapy is considered standard first-line treatment for these patients. Although urothelial cancer is considered a chemosensitive tumour, metastatic disease is associated with poor prognosis and short-term survival. Here, we review the role of a multidisciplinary approach to treating patients with metastatic urothelial cancer.

BC12

Personalized medicine in advanced urothelial cancer: when to treat, how to treat and who to treat

Behfar Ehdai, MD;* Steven C. Smith, MD, PhD;[†] Dan Theodorescu, MD, PhD**

**Department of Urology; [†]Department of Molecular Physiology; **Paul Mellon Urologic Cancer Institute, University of Virginia, Charlottesville, VA*

The past decade has contributed to an improved understanding of the molecular mechanism of bladder cancer by defining distinct pathways in tumorigenesis and progression. Advances in technologies, such as high-throughput transcript profiling, microarrays and proteomics, offer a systematic approach to identifying targets for bladder cancer diagnostics and drug discovery. This review presents a select overview of advances in the development of biomarkers and targets for patient prognosis and therapy selection. It describes what is believed to be a representative cohort of recent studies that have the potential to significantly impact the management of muscle-invasive and metastatic urothelial carcinoma of the bladder. In addition, approaches are suggested that further the development of "personalized selection" of different combination therapies for bladder cancer patients. Finally, space constraints do not permit this review to be comprehensive; as such, apologies are offered to authors whose works were not cited.

BC13

Surveillance strategies after definitive therapy of invasive bladder cancer

Ilias Cagiannos, MD, FRCSC; Christopher Morash, MD, FRCSC

Department of Urology, University of Ottawa, Ottawa, ON

Following definitive therapy for muscle-invasive bladder cancer, patients remain at risk for local and distant recurrence. Additionally, recurrences can result from formation of new tumours elsewhere in the urinary tract. We review patterns of recurrence and the prognosis associated with recurrence. Optimal surveillance strategies are discussed.