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POD-6.01

Outcome of 2287 bladder cancer patients treated with radical cystectomy: the Canadian Bladder Cancer Network experience

Yafi F[1], Aprikian A[1], Chin J[2], Fradet Y[3], Izawa J[2], Estey E[4], Fairey A[4], Rendon R[5], Cagiannos I[6], Lacombe L[3], Lattouf J[7], Bell D[5], Drachenberg D[8], Kassouf W[1]
[1]McGill University Health Centre, Montréal, QC; [2]University of Western Ontario, London, ON; [3]Laval University, Québec, QC; [4]University of Alberta, Edmonton, AB; [5]Dalhousie University, Halifax, NS; [6]University of Ottawa, Ottawa, ON; [7]University of Montréal, Montréal, QC; [8]University of Manitoba, Winnipeg, MB

Introduction and Objective: Radical cystectomy remains the gold standard in the management of muscle-invasive transitional cell bladder carcinoma. We present our data from a large, multi-institutional, contemporary Canadian series of patients who underwent radical cystectomy in a single-payer health care system.

Materials and Methods: We collected and pooled a database of 2287 patients who have underwent radical cystectomy between 1993 and 2008 in 8 different centres across Canada. Collected variables included age, race, gender, presence of hydronephrosis, clinical stage and nodal status, concomitant carcinoma in situ, histology, ECOG performance, Charleson comorbidity score, smoking, pelvic lymph node dissection, pathological stage and nodal status, grade, surgical margins, postoperative chemotherapy/radiation, recurrence and salvage therapy. Survival data were analyzed using Kaplan–Meier method and Cox regression analysis.

Results: Mean age of patients was 67 years with a mean follow-up time of 35 months. The 5-year overall, recurrence-free and bladder cancer specific survival was 57%, 49% and 67%, respectively. Pathological stage distribution was < pT2N0: 498 (23%), pT2N0: 365 (17%), pT3N0: 463 (21%), pT4N0: 170 (8%), and pT1–4N+: 507 (23%). Only 3% of patients were given neoadjuvant chemotherapy and 17.3% received adjuvant chemotherapy. On multivariate analysis, pathological stage, surgical margin status, adjuvant chemotherapy and smoking were associated with bladder cancer-specific and overall survival.

Conclusion: These results confirm the validity of radical cystectomy as effective treatment for invasive urothelial carcinoma of the bladder and the prognostication using traditional clinical and pathological variables. Smoking is an independent prognostic factor for disease-specific survival. Neoadjuvant chemotherapy continues to be underutilized in Canada.

POD-6.02

Early cystectomy prior to muscle invasion improves cancer survival in patients with urothelial carcinoma

Breau R[1], Leibovich B[1], Karnes R[1], Farmer S[1], Cagiannos I[2], Morash C[2], Blute M[1], Frank I[1]
[1]Department of Urology, Mayo Clinic, Rochester, MN, USA; [2]Division of Urology, University of Ottawa, Ottawa, ON

Introduction and Objective: Despite aggressive surveillance and timely cystectomy, many patients who initially present with non–muscle invasive urothelial carcinoma (UC) eventually experience metastatic progression and cancer related mortality. The purpose of this study was to evaluate the impact of early cystectomy on cancer outcome in patients with organ-confined UC.

Materials and Methods: At the Mayo Clinic 814 patients with stage pT2 or higher UC were treated with radical cystectomy. Of these, 282 had non–muscle invasive disease (Group 1), 217 presented with non–muscle invasive disease but progressed to muscle invasion on surveillance (Group 2), and 315 were pT2 on presentation (Group 3). Metastasis-free, cancer-specific, and overall survival rates were compared between the groups.

Results: For groups 1 to 3, 5-year metastasis-free survival rates were 84%, 58%, and 61% ($p < 0.001$); 5-year cancer-specific survival rates were 86%, 55% and 54% ($p < 0.001$); and 5-year overall survival rates were 71%, 45% and 40% ($p < 0.001$). Of the 499 patients who initially presented with non–muscle invasive disease, after adjusting for intravesical therapy and number of recurrences, progression to muscle invasion on surveillance was associated with worse metastases-free survival (HR 2.8, 2.0–4.0), disease specific survival (HR 1.9, 1.5–2.3) and overall survival (HR 1.9, 1.5–2.3).

Conclusion: Many patients who present with non–muscle invasive urothelial carcinoma eventually develop systemic disease. Unfortunately, even with close surveillance and prompt cystectomy, those who progress to muscle invasion experience a high risk of cancer death. These findings highlight the importance of aggressive early surgical therapy for high-risk patients.

POD-6.03

Hexaminolevulinate fluorescence cystoscopy improves detection and resection of papillary bladder cancer lesions and reduces early recurrences

Fradet Y[1], Mynderse L[2], Stenzl A[3], Denzinger S[4], Soloway M[5], Karl A[6], Kriegmair M[7], Witjes F[8], Morales A[9], Grossman H[10]
[1]Department of Urology, University of Laval, Québec, QC; [2]Mayo Clinic, Rochester, MN, USA; [3]University of Tübingen, Tübingen, Germany; [4]University of Regensburg, Regensburg, Germany; [5]University of Miami, Miami, FL, USA; [6]Ludwig-Maximilians-University, Munich, Germany; [7]Urology Clinic, Munich-Planegg, Germany; [8]UMC St Radboud, Nijmegen, The Netherlands; [9]Queen's University, Kingston, ON; [10]University of Texas, Houston, TX, USA

Introduction and Objective: Fluorescence-guided diagnosis using hexaminolevulinate (HAL) can identify tumours not visible under white light cystoscopy. The purpose of this study was to compare fluorescence-guided and white light cystoscopy in the detection of non–muscle invasive papillary bladder tumours, and to compare early recurrence rates following HAL or white light resection of identified tumours.

Materials and Methods: A prospective, controlled, randomized, phase III multicentre study of patients with high likelihood of recurrence within 9 months of initial tumour resection (TURB). Patients with multiple papillary tumours, or patients having at least one recurrence within 12 months of their last tumour diagnosis were randomized to white light or HAL fluorescence cystoscopy. All patients were first inspected under white light and all visible lesions were recorded. Patients randomized to HAL underwent a second inspection and mapping under blue light. All suspicious areas were then biopsied, and tumour resection of identified papillary lesions was carried out in both groups. Tumor was confirmed by histology. Completeness of resection was checked in blue light for all HAL patients. Follow-up at 3, 6 and 9 months was with white light; recurrence was verified by histology. At each follow up, patients with confirmed recurrent tumour were discontinued.

Results: Seven hundred sixty-six patients (ITT) were randomized in 28 US and European centres. Of the patients randomized to HAL, 278 were diagnosed as Ta/T1. Within-patient comparison showed that in 16.9% of these patients at least one additional Ta/T1 tumour was detected with HAL compared with white light ($p = 0.0005$). Also in the HAL arm, 41 patients had CIS, and 13 of them (32%) were diagnosed only with HAL, an improvement in CIS detection rate of 46%. False positive rates were 12% for HAL and 11% for white light. Comparing the 402 patients with Ta or T1 lesions (202 white light, 200 HAL) who completed the study, a significant reduction in tumour recurrence was seen in the HAL arm: 72 (36%) compared with 92 (46%) in the white light group ($p = 0.029$).

Conclusion: In patients with papillary bladder cancer, HAL fluorescence cystoscopy improves detection and resection of non–muscle invasive papillary bladder tumours, leading to a reduction in recurrence rates at 9 months. This is the first demonstration that improved detection with HAL fluorescence cystoscopy can reduce tumour recurrence rates.

POD-6.04

Impact of substage on the clinical outcome of pT1 bladder cancer

Van Rhijn B[1], Van der Kwast T[2], Kakiashvili D[1], Fleshner N[1], Van der Aa M[3], Vajpeyi R[1], Alkhateeb S[1], Bangma C[3], Jewett M[1], Zlotta A[1]
[1]Division of Urology, University Health Network, Toronto, ON; [2]Department of Surgical Pathology, University Health Network, Toronto, ON; [3]Department of Urology, Erasmus MC, Rotterdam, The Netherlands

Introduction and Objective: Management of pT1 bladder cancer is controversial. We evaluated the impact of substage on the clinical outcome of a large series of primary pT1 bladder cancer patients treated with BCG.

Material and Methods: The slides of 134 primary (first diagnosis) bladder tumours from 2 university hospitals (Rotterdam, the Netherlands $n = 60$ and Toronto, Canada $n = 74$) were reviewed and the pT1 diagnosis was confirmed. Substaging was done in 2 separate rounds, using pT1microinvasive (pT1m) and pT1extensive-invasive (pT1e)[1] and according to invasion of the muscularis mucosae (pT1a/pT1b/pT1c)[2]. If the muscularis mucosae was not present at the invasion front, the case was assigned to pT1a or pT1c based on the extent of invasion into the lamina propria. All 134 patients were initially managed conservatively (BCG). Grade review was done according the WHO 1973 and 2004 classifications systems. Multivariate analyses for progression and disease specific survival were performed with substage, size, hospital, CIS, gender, age, grade-1973 and grade-2004 as variables.

Results: Mean follow-up was 6.8 (median 6.4, range 0.3–21.6) years, 25/134 patients were female. Mean age was 68.5 years. CIS was found in 48 (36%) cases. Forty-two patients remained recurrence-free (31%). Progression to pT2 or metastasis was observed in 40 (30%) patients and 19 patients (14%) died of their disease. The muscularis mucosae was not present at the invasion front in 50 (37%) of tumours. The slides were substaged as follows: 40 pT1m and 94 pT1e; 81 pT1a, 18 pT1b and 35 pT1c. Grade review resulted in 56 G2 and 78 G3 lesions (WHO 1973 system) and 26 low-grade and 108 high-grade lesions according to the WHO 2004 system. In multivariate analyses, substaging using pT1m and pT1e was significant for progression ($p = 0.001$) and disease specific survival ($p = 0.021$), whereas substage according to pT1a/b/c was not significant in any multivariate analysis. Female gender ($p = 0.006$) and CIS ($p = 0.035$) were also significant predictors for progression in multivariate analysis.

Conclusion: Substage (pT1m and pT1e) was possible in all the cases and very predictive of pT1 bladder cancer behaviour. Future studies may lead to the incorporation of substage in the TNM classification system for urinary bladder cancer.

POD-6.05

Intravesical gemcitabine for the treatment of superficial bladder cancer not responded to bacillus Calmette-Guerin

El-Koushy M
Urology Department, Faculty of Medicine, Suez Canal University, Ismailia, Egypt

Introduction and Objective: Intravesical bacillus Calmette-Guerin (BCG) is the mainstay of superficial bladder cancer (SBC) treatment in reducing tumour recurrences and disease progression. About one-third of patients do not respond to BCG. Gemcitabine is a chemotherapeutic drug being tested intravesically for BCG-resistant bladder cancer as well as in BCG-intolerant patients. The aim of this study is to determine the efficacy of gemcitabine administered as intravesical agent in patients with BCG-refractory SBC.

Materials and Methods: Twenty-three patients were included who have Ta-T1 (G2-G3) or CIS bladder transitional cell carcinoma refractory (have previously received at least 2 courses of failed intravesical BCG) or intolerant to intravesical BCG therapy. Two weeks after complete tumour resection, patients received intravesical gemcitabine twice weekly at a dose of 2000 mg/100 mL normal saline for 6 consecutive weeks. Gemcitabine was instilled and remained in the bladder for 2 hours. Two months after the last dose, patients underwent cystoscopy, urinary cytology and 6 random bladder biopsies if there was no recurrence detected. Thereafter, patients were evaluated by the same measures every 3 months, as long as there was no recurrence. Patients revealed complete response after the first follow-up cystoscopy (in terms of negative cytology and random biopsies) received a maintenance similar dose once weekly for another 6 consecutive weeks.

Results: Twenty-one patients completed the study (15 male and 6 female) with a mean age of 48.1 (standard deviation 15.6) years. The median duration of follow-up was 15 (2–19) months. Complete response was achieved in 61.9% of patients (13/21). Superficial recurrences were detected in 6 patients (28.6%) and progression by stage in 2 patients (9.5%). Throughout follow-up, 8 patients had tumour recurrences and 2 of them had progression to a higher stage. The median recurrence-free survival time was 7.4 (4.3 to 19) months. The drug was tolerable and side effects were mild in most patients apart from 2 patients; one of them had controlled haematuria and the other had leucopenia.

Conclusion: Gemcitabine appears to be a promising option in management of high-risk patients with BCG-refractory superficial bladder carcinoma especially those who refuse or unfit for cystectomy. Long-term efficacy has to be properly investigated.

POD-6.06

Patients with microscopic and gross hematuria: practice patterns among general practitioners in the province of Québec

Yafi F, Tanguay S, Aprikian A, Kassouf W
McGill University Health Centre, Division of Urology, Montréal, QC

Introduction and Objective: Hematuria is one of the most common findings on urinalysis in patients encountered by general practitioners (GPs). It can also be the first presentation of a serious urological problem in many instances. As such, we sought to shed the light on the current practices adopted at the primary care level in its work-up and screening.

Materials and Methods: We conducted a survey which was mailed in both French and English to over 8000 registered GPs in the province of Quebec. The questions covered each physician's personal approach to men and postmenopausal women with painless gross hematuria or with asymptomatic microscopic hematuria as well as screening techniques, general knowledge with regards to urine collection and sampling, and referral patterns.

Results: Of the surveys mailed, 520 (6.5% response rate) were returned. Mean years from graduation was 24.8 (median 25, range 3–58) years. In an older male with painless gross hematuria, only 62% of GPs recommended further evaluation by a urologist with 9% opting to reassure the patient and see him in follow-up. On the other hand, in a postmenopausal woman with 2 consecutive events of significant microscopic hematuria, only 49.4% recommended referral to urology despite the fact that 94% of GPs stated that microscopic hematuria is associated with bladder cancer. Interestingly, 47% of GPs perform a routine screening urinalysis with the annual physical examination on all male and female patients and 26% do not order it in asymptomatic patients regardless of risk factors. Finally, when asked what represented significant microscopic hematuria on 2 consecutive urine samples, only 43.4% responded 3 red blood cells or more per high-power field whereas the majority of GPs (50%) stated greater than 10/hpf.

Conclusion: There seems to be reluctance among primary care physicians to refer patients with gross or significant microscopic hematuria to a urologist for further investigation. A higher level of suspicion should be encouraged in order to possibly detect serious conditions and offer earlier intervention when possible.