Debates on Bladder Cancer

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Highlight presentations on bladder carcinoma at the 25th Congress of the European Association of Urology (EAU)

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Abstract

In the time from 16-20 April 2010, the 25th Annual EAU congress has been held in Barcelona, Spain. In this article, we present highlights of the conference in the field of bladder cancer.

Key words: bladder cancer, 25th Anniversary EAU Congress Barcelona 2010, urothelial cancer

The 25th EAU congress has been held in Barcelona, Spain. We would like to provide significant research results on bladder cancer as presented at this congress.

Non-muscle invasive urothelial cancer of the bladder (UCB)

In the "Epidemiology and pathology of urothelial cancer" session, D. Garcia-Rojo et al. presented the results of a Spanish multicenter study that investigated the effect of increased urination frequency on bladder cancer risk. In their study, 884 newly diagnosed UCB cases were compared to 996 controls between 1998 and 2001. Voiding of the bladder for 2 times or more per night vs. no voiding reduced the risk of UCB about 40-50% (men: p=0.0003; women: p=0.07). Additional water intake of at least 1.4 l per day led to a reduction of 80% vs. no voiding and less than 0.4 l water consumption per day (p<0.0001). Furthermore, nocturia seemed to reduce the risk associated with cigarette smoking. The authors ascribed the protective effect of nocturia on bladder cancer risk to the reduced contact time of the urothelium with carcinogens in urine [1].

Seretta et al. studied the clinical value of positive NMP22 testing when accompanied by negative cytology and cystoscopy is doubtful. The authors presented data on 95 patients with positive NMP22 testing but negative cytology and cystoscopy that have been maintained in follow-up for pTa-T1 G1-3 disease with a median follow-up of 51 months

(range: 2-174) since 1996. Thirty-seven (39%) patients had recurrent disease. There was no significant difference in NMP22 levels between recurring and recurrence-free patients (p=0.26). Therefore, the authors concluded that high levels of NMP22 during the follow-up of patients with previous non-muscle invasive urothelial cancer of the bladder do not represent an increased risk of recurrence if

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Conference report

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associated with negative cytology and cystoscopy [2].

In 2004, the WHO introduced a new grading classification system. As this system is not sufficiently validated against the old WHO classification system from 1973, both are advocated by the EAU guidelines. In a study from two expert centers, 327 specimens from patients with primary non-muscle invasive urothelial cancer of the bladder underwent central review for both classifications. Furthermore, the presence of FGFR3 mutation, a marker for genetically unstable non-muscle invasive bladder cancer (NMI-BC), and aberrant expression of MIB-1, p53 and p27 as marker for genetically unstable NMI-BC were evaluated. In their study, the authors concluded that the 2004 WHO classification leads to higher grading than the 1973 WHO classification and so, they recommended to use both grading systems jointly [3].
Another study from this group evaluated the impact of sub-stage, clinico-pathological parameters and 4 molecular markers (FGFR3 mutation and MIB-1, p53, p27 expression) on the clinical outcome of primary pT1 bladder cancer treated with intravesical Bacille Calmette-Guérin (BCG). Multiplicity was the strongest predictor of recurrence, whereas the additional value of molecular markers was modest [4].
Furthermore, this group reviewed pathological slides of 134 newly diagnosed pT1 bladder tumors from two university hospitals that were initially treated with BCG. All cases were substaged into pT1m (micro-invasive), pT1e (extensive-invasive) and pT1a, pT1b or pT1c disease according to invasion of the muscularis mucosae. In multivariate analyses, sub-staging using pT1m and pT1e was significant for progression (p=0.001) and disease specific survival (p=0.021), whereas sub-stage according to pT1a/b/c did not show any significances [5].

Pfister et. al presented preliminary results from a multicenter study on the usefulness of hexaminolevulinate (Hexvix®) fluorescence-guided cytoscopy for high-risk superficial bladder tumors after BCG induction treatment (n=38). Using Hexvix® fluorescence cystoscopy, 11 out of 14 residual tumors were detected, whereas urinary cytology was only positive in 7 cases. Residual tumors were found in 7 patients that showed unsuspicious bladder mucosae under white light [6].
Another group investigated the impact of two different BCG doses (standard [81 mg] or one-third dose [27 mg]) for treatment of carcinoma in situ (CIS) of the bladder associated or not associated to non-muscle invasive transitional carcinoma in a cohort of 138 patients with a follow-up of at least 5 years. There were no significant differences either in the rate of recurrence or in the time to recurrence between both doses [7].
Oosterlinck et al. presented the results of the EORTC GU Group randomized phase II study 30993 that investigated the sequential chemo-immunotherapy with mitomycin C (MMC) and BCG versus BCG alone in patients with carcinoma in situ (CIS) of the urinary bladder. In this study, 96 patients received either weekly MMC (6 instillations) followed by weekly BCG (6 instillations) or weekly BCG alone (6 instillations, 3 weeks rest, 3 instillations) between 2001 and 2005. Sequential chemo-immunotherapy with MMC and BCG showed acceptable toxicity and yielded similar complete response rates to BCG alone, but no synergistic effect were seen [8].
A further randomized prospective trial of 352 patients with non-muscle invasive bladder cancer evaluated the single immediate preoperative intravesical instillation of electromotive MMC for primary non-muscle invasive bladder cancer. It was shown that one immediate pre transurethral resection (TUR) intravesical EMDA/MMC instillation decreases the risk of recurrence and enhances the disease-free interval in patients with multiple, intermediate and high risk, NMI-BC, compared with one immediate post-TUR intravesical PD/MMC instillation and TUR alone [9].

Tilki et al. reviewed a series of 243 patients with clinical CIS only disease before surgery from a large international cohort including

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3207 patients who underwent radical cystectomy. One fourth of patients treated with radical cystectomy for clinical CIS only were upstaged to muscle-invasive disease and 5.8% had metastasis to regional lymph nodes after pathological evaluation of the surgical specimen [10].
Chade et al. reported data from a retrospective analysis from a single institution of 155 consecutive patients that were diagnosed with isolated primary high-grade CIS from 1990 to 2008 and treated with BCG within 6 months of diagnosis. Patients with primary CIS showed a high rate of disease progression. Response to BCG therapy within 6 months was significantly associated with progression to ≥cT1 (p=0.029) and to ≥cT2 (p=0.015) [11]. Another randomized trial analyzed the role of one-year maintenance after a 6-week cycle of early intravesical chemotherapy with epirubicin in 482 patients with intermediate risk NMI-BC. After 18 months, there was no significant prophylactive action for 1-year maintenance, but disadvantages by prolonged intravesical chemotherapy [12].

Muscle invasive urothelial cancer of the bladder (UCB)

Krause et al. evaluated single center experience on 473 patients treated with transurethral resection of the bladder (TURBT) and radiochemotherapy (RCT)/radiation (RT) for bladder cancer. In this study, only those patients achieved same good long-term success as patients undergoing standard radical cystectomy (RC) that provided a maximum stage of pT1, no lymphatic vessel invasion (pL0), a microscopically complete TURBT (R0), no evidence of local and distant metastasis (cN0/cM0), and a complete RCT with complete response in the control-TURBT [13].
A Japanese group presented data on outcome of patients that received a bladder-sparing protocol with TURBT and full-dose chemoradiotherapy (LCRT) against muscle-invasive bladder cancer. In these patients, partial cystectomy after LCRT reduced recurrence of muscle invasive cancer and showed longer metastasis-free and cancer-specific survival when compared to patients that declined surgery [14].

Shariat et al. showed in a multicenter study of patients who underwent radical cystectomy that lymphovascular invasion (LVI) is strongly associated with clinical outcome in patient with negative lymph node status. Therefore, the assessment of LVI might be helpful for risk stratification and might help select patients who could benefit from adjuvant treatment after surgery [15].
Another study of this group analyzed a large international cohort of patients with pT4 bladder cancer to describe the cancer-specific outcomes of these patients. The outcome in these patients was highly variable. Female patients had a worse outcome than men. Metastatic tumor dissemination and local disease burdens were associated with poor outcome [16].
A retrospective comparison of 363 patients undergoing radical cystectomy showed that surgery in elderly patients is feasible, whereas delayed cystectomy might lead to worsed histopathology in these patients [17]. A prospective, randomized study in 108 consecutive patients undergoing cystectomy and ileal urinary diversion showed that early post-operative enteral nutrition seems to be effective and associated with a lower incidence of complications compared to postoperative parenteral nutrition [18]. A longterm comparism study of ileal conduit (n=131) or ileal orthotopic neobladder (n=94) in a series of patients that underwent radical cystectomy did not show any significant differences in the probability of renal function decline and new onset chronic kidney disease for both urinary diversions [19].
Brausi et al. compared two cohorts of patients at a single institution that underwent radical cystectomy for bladder cancer. In this study, 303 patients underwent standard RC between 2000 and 2005. In 2006 and 2007, 90 patients

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underwent minimal invasive anatomical extraperitoneal radical cystectomy at this institution. The authors showed that the minimal invasive approach was simple and safe and associated with a reduction in blood loss, lower complication rate and lower local recurrence rate compared to standard RC [20].

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Conflict of interest

The authors declare that there are no conflicts of interest.

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