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POD-05.01
External Validation of a Biomarkers Based Algorithm to Predict Pathological Stage Prior to Radical Cystectomy

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Introduction: The role of neoadjuvant chemotherapy prior to radical cystectomy in patients with muscle invasive bladder cancer remains debated. The need of tools to identify patients who would benefit from chemotherapy is pertinent. We have previously published a preoperative algorithm to predict extravesical disease. This algorithm included oncofetal tumor markers (CEA CA-125 and CA 19 9) as well as clinical parameters. Our aim was to validate the accuracy of this algorithm in an independent, external cohort.
Patients and Methods: We used the Toronto, University Health Network, Genitourinary Bio-bank to measure preoperative serum levels of CEA, CA 125 and CA 19-9 in 76 consecutive patients with clinically organ confined bladder cancer (cT2 or less) who underwent radical cystoprostatectomy. Clinical stage, presence of hydronephrosis, presence of carcinoma in situ, and initial tumor size >3 cm were retrieved from our prospective bladder information system (Blis) database and incorporated into our marker-based algorithm. A numeric score was generated for each patient and a previously published cut-off was used to predict the presence extravesical disease. The accuracy of the model was quantified with the area under the curve (AUC) and the positive and negative predictive values were calculated.
Results: On pathologic evaluation, 38 patients (50%) were found to have organ-confined tumors and 38 patients (50%) had extravesical disease. The AUC of the algorithm was 0.79 (95% CI, 0.69-0.89). The positive and negative predictive values were 79% (95% CI, 71%-87%) and 74% (95% CI, 66%-82%), respectively.
Conclusions: We have externally validated a precystectomy model to predict pathological stage based on clinical parameters and oncofetal serum markers. The algorithm may possibly aid in selecting patients who would benefit from neoadjuvant chemotherapy prior to cystectomy.

POD-05.02
Prognostic Factors and Outcome in Patients with High-Grade T1 Bladder Cancer: McGill University Experience

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Introduction and Objectives: T1HG urothelial carcinoma of the bladder represents up to 25% of all non-muscle invasive bladder cancer (NMIBC). The rate of progression is variable but can be as high as 50-70%. Our purpose was to assess outcome in these patients and determine prognostic factors that can help in counseling patients towards early aggressive intervention.
Methods: Records of 2570 patients with bladder cancer treated at a single academic institution from 1995-2005 were retrospectively reviewed. Only patients diagnosed with T1HG disease were included in the analysis. Collected variables included various clinic-pathologic parameters, and dates of recurrence, progression, radical cystectomy, death. Recurrence-free (RFS) and worsening-free survival (WFS) were analyzed using Kaplan-Meier plots. Multivariate Cox proportional regression analysis methods were employed to verify the prognostic significance of various variables.
Results: A total of 278 (10.8%) patients were identified to have T1HG disease on transurethral resection (TURBT). Of these, 66% of patients recurred, and 36.3% developed stage progression after a median follow-up of 3 years (range 0.1-15.4 years). Overall, 30% of patients underwent radical cystectomy, and 9% were dead of disease. The 5-year RFS and WFS rates were 26.6% and 49.4%. On multivariate analysis, nontrigonal tumor location, repeat TUR, history of previous NMIBC, and adjuvant BCG therapy were significantly associated with prolonged RFS, whereas papillary tumor architecture, history of previous NMIBC and adjuvant BCG therapy were significantly associated with prolonged WFS.
Conclusions: Patients with T1HG bladder cancer are at a significant risk of progression and death from disease. Primary tumors, sessile architecture, and trigonal location are factors associated with worse outcome and may be used to counsel patients for early cystectomy.

POD-05.03
Mycobacterial Cell Wall DNA Complex for Patients with High Risk Non-Muscle Invasive Bladder Cancer Refractory to BCG: Efficacy and Safety

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Introduction and Objective: Radical cystectomy is the standard of care in patients whose tumors are refractory to Bacillus Calmette-Guérin (BCG). The response to second-line therapies in patients who are not eligible for or willing to undergo surgery is poor.
An open-label, single-treatment arm study was performed to evaluate the efficacy and safety of MCC in patients with non-muscle invasive bladder cancer (NMIBC) who were refractory to BCG therapy and at high risk of progression.
Methods: Patients with high grade urothelial carcinoma (papillary NMIBC and/or carcinoma *in situ* [CIS]) who failed to respond to one or more courses of BCG were enrolled. The regimen of treatment administration consisted of 6 weekly intravesical instillations of 8 mg MCC for Induction followed by 3 weekly instillations at Month 3, 6, 12, 18 and 24. Clinical efficacy assessments included cystoscopy, urine cytology and biopsy. Safety variables included adverse events (AEs) and serious AEs (SAEs) and clinical laboratory assessments. The primary efficacy endpoint was the disease - free survival (DFS) rate at one year based on the intent-to-treat population and was determined using Kaplan-Meier estimates. Patients were considered disease-free when absence of recurrent bladder cancer was confirmed on biopsy by a central pathologist.
Results: A total of 129 patients were enrolled from 25 centers in the US and Canada. The median age was 71 years (range of 41–90). All 129 patients were white and 95 (73.6%) were male. At study entry, 91 (70.5%) patients had CIS, either primary or concomitant with papillary tumors, and 38 (29.5%) had only papillary tumors. All papillary tumors were resected prior to start of treatment.

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Preliminary analysis showed the overall one-year DFS rate was 25.0% with a median DFS interval of 177 days. Sub-analysis showed that patients with CIS tumors (primary or concomitant with papillary tumors) at study entry had a one-year DFS rate of 21.0%, while patients with only papillary tumors had a one-year DFS rate of 35.1%. Intravesical administration of MCC was very well tolerated — most AEs were mild to moderate in severity and few lead to discontinuation of treatment. Two SAEs (hematuria, urinary tract infection) were reported as being possibly related to the investigational treatment.

Conclusion: The preliminary results indicate that MCC has activity in patients with BCG-refractory NMIBC and may provide an alternative to cystectomy in this patient population.

POD-05.04

Surgeon Volume-Outcome Relationships in the Treatment of Renal Masses

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Introduction and Objective: Volume-outcome relationships have been noted in a number of major surgical procedures. Outcomes of these complex procedures tend to be better for high volume hospitals and providers. The aim of our study was to determine the relationship between provider volume, and partial nephrectomy (PN) use and morbidity in the treatment of renal masses.

Methods: Using data from a national discharge abstract database, we performed a population-based, retrospective, observational study. Data were available on 24,579 patients treated surgically for a renal mass from April 1998 to March 2008. Surgeon volume quartiles were created using the total number of nephrectomies during the 10-year observation period. In-hospital complications and comorbidity were identified using specific ICD-9 and 10 diagnosis and procedure codes. The Charlson-Deyo Index was used to adjust for comorbidity. PN use, complication rates, and 30-day mortality were compared between surgeon volume quartiles using the Chi-square test. The effect of surgeon volume on our outcome variables was determined using multivariable logistic regressions, adjusted for covariates (including hospital volume).

Results: Overall, PN use, in-hospital complications and mortality occurred in 4,292 (17.5%), 8,406 (34.2%) and 295 (1.2%) patients, respectively. PN use occurred in 10.9% of low volume, compared with 24.7% of very high volume surgeons ($p<.0001$). A modest decrease in complications was observed with increasing surgeon volume (37.6% among low vs 34.5% among very high volume, $p<.0001$). The effect of in-hospital mortality was more dramatic, with rates of 1.71%, 1.20%, 0.97% and 0.92% observed among low, intermediate, high and very high volume surgeons, respectively ($p<.0001$). After adjusting for covariates, compared with low volume surgeons, patients treated by very high volume surgeons had 1.54 the odds of being treated with PN (95% CI 1.37-1.72, $p<.0001$), 0.84 the odds of experiencing an in-hospital complication (95% CI 0.77-0.92, $p<.0001$), and 0.69 the odds of dying in-hospital (95% CI 0.47-1.01, $p=0.16$).

Conclusions: Our large, population-based study suggests that surgeon volume-outcome relationships exist in kidney surgery for renal masses. Higher volume surgeons use PN more often, experience lower complication rates, and may have lower in-hospital mortality rates than lower volume surgeons.

POD-05.05

Oncological Outcomes of Partial Nephrectomy for Tumors Greater than 4-cm: A 10-Year Systematic Review

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Background: Partial nephrectomy (PN) is the standard of care for tumors smaller than 4 cm. Moreover, many medical associations (AUA, EAU, NCCN) have recommended nephron-sparing surgery for some tumors larger than 4 cm amendable to PN. These recommendations are based on reports from several relatively small case series. We herein present a systematic review of literature for oncological outcomes of partial nephrectomy procedures performed for tumors larger than 4 cm, published over the past decade.

Materials and Methods: A medline search was carried out using keywords "partial nephrectomy" and "nephron sparing" for records dating back to 1999. The search was limited to non-case report papers, published in English. Inclusion criteria included PN performed for tumors larger than 4 cm, with oncological outcomes described. After removing duplicate results, 1463 titles and abstracts were further analyzed while filtering out technical and perioperative studies. 108 papers were finally scrutinized, and a total of 25 manuscripts were found to fulfill the inclusion criteria. These references were subsequently analyzed for patient population, statistical methods, tumor size, 5-year recurrence rates as well as overall and cancer-specific survival rates (OS, CSS). Sample contamination with smaller and/or benign masses was taken into consideration.

Results: A total of 3118 patients with renal tumors larger than 4 cm had undergone PN between the years 1999, and 2010. This sample included 1756 with tumors between 4-7 cm, 1169 patients with tumors larger than 7 cm, and 193 patients with tumors greater than 4 cm (exact size unknown). Analysis revealed 5-yr OS rates of 91%, 92% and 91.4% for tumors 4-7 cm, >7 cm, and all tumors >4 respectively. The respective 5-yr CSS rates were 94%, 92%, and 93%.

Conclusion: This systematic review reveals excellent 5-yr overall and cancer-specific survival for patients with tumors 4 to 7 cm treated with PN. These outcomes compare favorably to those reported in historical radical nephrectomy (RN) series for similarly sized tumors. For carefully selected tumors larger than 7 cm, similar outcomes have been reported. These excellent oncological outcomes, coupled with the advantages of renal function preservation support the use of PN for tumors from 4 to 7 cm, and even larger.

POD-05.06

Non-Risk Adapted Surveillance in Clinical Stage I Non-Seminomatous Germ Cell Tumors (NSGCT): The Princess Margaret Hospital's Experience

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Introduction and Objective: Since 1981 Princess Margaret Hospital has used initial active surveillance (AS) with delayed treatment at relapse as the preferred management for all patients with clinical stage I non-seminomatous germ cell tumors (NSGCT), regardless of baseline risk of relapse. We report our overall AS experience and compare outcomes over different periods using this non-risk adapted approach.

Methods: 371 patients with stage I NSGCT were managed by AS from 1981 to 2005. Patients were followed at regular intervals and treatment only given for relapse. Recurrence rates, time to relapse, risk factors for recurrence, disease specific and overall survival were determined. For analysis by time period, patients were divided in two cohorts based on diagnosis date, [Initial=1981-1992 (n=157) and Recent=1993-2005 (n=214)].

Results: With a median follow-up of 6.3 years, 104 (28%) patients relapsed; 53/157 (33.8%) in the initial group and 51/214 (23.8%) in the recent. Median time to relapse was 7 months. Lymphovascular invasion ($p<0.0001$) and pure embryonal carcinoma ($p= 0.02$) were independent predictors of recurrence; 125 (33.7%) patients were designated as 'high-risk' based on the presence of one or both factors. In the initial cohort, 66/157 (42.0%) patients were high risk and 36/66 (54.5%) relapsed versus 17/91 (18.7%) low-risk ($p<0.0001$). In the recent cohort, 59/214 (27.6%) patients were high-risk and 29/59 (49.2%) recurred, versus 22/155(14.2%) low-risk ($p<0.0001$). Three patients (0.8%) died from testis cancer. The estimated 5-year disease specific survival was 99.3% in the initial group and 98.9% in the recent one.

Conclusion: Non-risk adapted surveillance is an effective, simple strategy for the management of all stage I NSGCT.