

## IDENTIFICATION OF A BIOMARKER PANEL THAT PREDICTS BLADDER CANCER OUTCOME INDEPENDENT OF ROUTINE PROGNOSTIC FACTORS AND SMOKING HISTORY

Anirban P. Mitra, M.D., Ph.D., Jose E. Castelao, M.D., Ph.D.\*, Debra Hawes, M.D.\*, Denice D. Tsao-Wei, M.S.\*, Xuejuan Jiang, Ph.D.\*, Shan-Rong Shi, M.D.\*, Lillian L. Young, B.S.\*, Ram H. Datar, Ph.D.\*, Eila C. Skinner, M.D., John P. Stein, M.D., Susan Groshen, Ph.D.\*, Mimi C. Yu, Ph.D.\*, Ronald K. Ross, M.D.\*, Donald G. Skinner, M.D., Victoria K. Cortessis, Ph.D.\*, Richard J. Cote, M.D., FRCPath, FCAP\*- Los Angeles, CA, Miami, FL.  
(Presentation to be made by Dr. Mitra)

**Objectives:** Bladder cancer is known to be a disease of alterations in several cellular pathways. Routine molecular profiling investigations do not account for cigarette smoking, the most well established risk factor for bladder cancer in the western world, and its influence on outcome. This study employed a multi-pathway profiling approach at the protein level to examine molecular alterations across all bladder cancer stages in a population-based cohort. The prognostic potential of the panel was assessed after stratifying for clinicopathologic factors and smoking history.

**Patients and Methods:** 212 patients from the Los Angeles County Cancer Surveillance Program, a part of the NCI/SEER cancer registry, were included. To analyze the biologic and molecular impact of smoking history, a novel "smoking intensity" variable was introduced that combined a patient's smoking status, duration of smoking and number of cigarettes smoked per day into a composite covariate. Primary bladder tumors were immunohistochemically profiled for alterations in Bax, caspase-3, Apaf-1, Bcl-2, p53, p21, cyclooxygenase-2, vascular endothelial growth factor, and E-cadherin. Univariate analyses and multivariable modeling were used to examine associations with outcome.

**Results:** Median follow-up for the entire cohort was 13.2 years. The cohort comprised of 78 (37%) noninvasive, 101 (48%) organ-confined, and 33 (15%) advanced bladder tumor patients. 67 (32%), 93 (44%) and 52 (24%) patients were categorized as low, intermediate and high smoking intensity candidates, respectively. Increasing pathologic stage and smoking intensity were independently associated with poor survival ( $p < 0.001$ ). p53, E-cadherin, p21 and Apaf-1 expressions were significantly associated with pathologic stage. E-cadherin and p53 were univariately prognostic for outcome ( $p = 0.014$  and  $p = 0.032$ , respectively), and remained predictive after stratifying by smoking intensity. Individually, Apaf-1 was prognostic by univariate analysis ( $p = 0.005$ ), and after stratification by stage ( $p = 0.029$ ), smoking intensity ( $p = 0.03$ ), and both stage and smoking intensity combined ( $p = 0.025$ ). Multivariable modeling confirmed this significance in association. When analyzed in combination, alterations in all nine biomarkers were significantly prognostic for survival by univariate and multivariate stratification.

**Conclusions:** The study confirms detrimental effects of smoking on bladder cancer prognosis. Apaf-1, E-cadherin and p53 can individually predict survival in bladder cancer. Increasing number of biomarker alterations was significantly associated with worsening survival independent of stage and smoking history, although some markers contained in the panel were not necessarily prognostic individually.

**Source of Funding:** NIH

## **VALUE OF URETHRAL FROZEN SECTION AT RADICAL CYSTECTOMY AND IMPACT ON INTRAOPERATIVE DECISION MAKING**

Glen Yang, Jared M. Whitson, Ardalan E. Ahmad, Anobel Y. Odisho, Peter R. Carroll, and Badrinath R. Konety; San Francisco, California  
(Presentation to be made by Dr. Glen Yang)

**PURPOSE:** It remains unclear which patients should remain candidates for urethral preservation during radical cystectomy and what factors should influence this decision. The aim of this study was to assess the accuracy of intraoperative urethral frozen sections (FS) during radical cystectomy and to evaluate factors associated with a positive urethral frozen section and urethral recurrence.

**METHODS:** Consecutive patients undergoing radical cystectomy at UCSF who had urethral FS were identified. Data on preoperative clinical and pathologic factors, intraoperative decision making, urethral margins, and urethral recurrence were recorded.

**RESULTS:** 243 patients with mean age of 65 years and median follow-up of 20 months were included. A positive urethral FS was present in 23 patients (9.3%). Urethral recurrence occurred in 7 patients (2.9%). Tumor number, size, location, grade, histology, and the presence of CIS were not associated with positive urethral FS or with urethral recurrence. Positive urethral FS was associated with positive final urethral margin ( $p < 0.001$ ), prostatic urethral tumor involvement at cystectomy ( $p = 0.05$ ), and urethral recurrence ( $p = 0.03$ ). The positive and negative predictive values of urethral FS for predicting urethral recurrence were 30% and 97%, respectively. Urethral frozen section altered intraoperative decision making in 6 (2.4%) cases.

**CONCLUSIONS:** Urethral recurrence rates after radical cystectomy are low. Given its minimal morbidity for patients, intraoperative urethral FS during cystectomy is a useful tool. However, because of low positive predictive value, the decision to forego orthotopic bladder replacement or perform prophylactic urethrectomy must be combined with other risk factors for urethral recurrence as well as patient preferences.

## FACTORS AFFECTING LYMPH NODE YIELD DURING RADICAL CYSTECTOMY

Raveen Syan, B.S.\*, Anirban P. Mitra, M.D., Ph.D., Eila C. Skinner, M.D., Gus Miranda\*, Siamak Daneshmand, M.D.: Los Angeles  
(Presentation to be made by Raveen Syan)

**Purpose:** Lower lymph node density has been associated with favorable prognosis in patients with bladder cancer. Proposed mechanisms are removal of micrometastases and improved risk stratification. While the number of lymph nodes may vary between patients, the influence of patient and tumor characteristics on lymph node yield (LNY) during radical cystectomy have not been well explored. In this study, we seek to evaluate how these variables influence LNY, thereby influencing lymph node density and hence prognosis.

**Materials and Methods:** A retrospective database review of 2,464 patients who underwent radical cystectomy and lymph node dissection at the USC Norris Cancer Center and affiliated institutions between 1973-2008 was conducted. LNYs were split into 4 numerical brackets of  $\leq 20$ , 21-40, 41-60, and  $\geq 60$ . Associations between LNYs and clinicopathologic and demographic covariates were analyzed.

**Results:** The median age of patients was 68 years. Fewer patients  $\leq 65$  years had LNY  $\leq 20$  (21%) compared to patients  $>65$  years (31%,  $p < 0.001$ ). Greater proportion of obese patients had LNY  $>60$  (39%) as compared to overweight (34%) and underweight/normal patients (27%,  $p = 0.018$ ). A greater proportion of patients with ASA score 3-4 had LNY  $\leq 20$  (21%) versus patients with ASA scores 1-2 (11%,  $p < 0.001$ ). LNY  $>60$  was significantly associated with node-positive disease (54%) compared to patients with node-negative OC or EV disease (18-21%,  $p < 0.001$ ). The presence of multiple tumors was also associated with LNY  $>60$  versus single or no tumor count (18% versus 14% and 9%, respectively;  $p = 0.022$ ). 79% of patients who underwent cystectomy with the intent to cure had LNY  $>20$ , compared to 49% of those without intent to cure ( $p < 0.001$ ). Those who received neoadjuvant radiotherapy ( $n = 180$ , 7%) tended to have lower LNY, with 63% having LNY  $\leq 20$  and 3% having LNY  $>60$ , versus 23% and 21%, respectively, in those who did not receive neoadjuvant radiation ( $p < 0.001$ ). 44% of patients with positive surgical margins had LNY  $\leq 20$  compared to 26% of patients with negative surgical margins ( $p < 0.001$ ). Calculated LNYs were higher since the institution of node packeting at USC ( $p < 0.001$ ).

**Conclusions:** Several individual patient characteristics including age, BMI, ASA score, stage, multifocality and positive surgical margins influence LNY. The influence of the interplay between these factors on node dissection is a subject of further investigation.

**Source of Funding:** None

## A DECISION TREE APPROACH TO IDENTIFYING PATIENTS WITH CLINICAL T2 BLADDER CANCER WHO MAY BENEFIT FROM NEOADJUVANT CHEMOTHERAPY

Anirban P. Mitra, M.D., Ph.D., Eila C. Skinner, M.D., Gus Miranda\*, Siamak Daneshmand, M.D.: Los Angeles, CA  
(Presentation to be made by Dr. Mitra)

**Purpose:** Neoadjuvant cisplatin-based combination chemotherapy is an established standard for advanced bladder cancer in several centers. Level one evidence supports its beneficial role in combination with surgery, especially for extravesical disease or with nodal metastases. However, the magnitude of this benefit is fairly small. This can result in significant overtreatment, especially in patients with organ-confined, node-negative disease who generally have higher recurrence-free rates. This study aimed to define pre-cystectomy factors in patients with clinically organ-confined muscle-invasive bladder cancer that could predict poor prognosis, thereby identifying those who might benefit the most from neoadjuvant chemotherapy.

**Patients and Methods:** A retrospective database review of patients who underwent cystectomy for bladder cancer at USC between 1971-2008 was conducted. Inclusion criteria were patients diagnosed with cT2N0M0 transitional cell carcinoma (TCC) of the bladder who did not receive neoadjuvant chemotherapy and subsequently underwent cystectomy with a curative intent. Patients with nodal and/or distant metastasis at the time of diagnosis were excluded. Several patient demographic and pre-cystectomy clinicopathologic parameters were examined for their association with pathological upstaging and outcome. Pathological upstaging was defined as tumor upstaging (T stage) and/or detection of nodal and/or distant metastasis at cystectomy. An exhaustive chi-squared automatic interaction detector-based decision tree technique was employed to assess the hierarchical interaction of the significant variables, thereby identifying patients who were at the highest risk for pathological upstaging.

**Results:** The cohort consisted of 948 patients with cT2N0M0 bladder TCC. Pathological upstaging was significantly associated with higher probability of recurrence and lower overall survival (both,  $p < 0.001$ ). Age ( $p = 0.01$ ), cT2 substage (cT2a/b determined by TURBT,  $p < 0.001$ ), lymphovascular invasion on TURBT specimen ( $p = 0.01$ ), tumor growth pattern (papillary and/or flat,  $p < 0.001$ ), multifocality ( $p = 0.004$ ), and presence and laterality (uni/bilateral) of hydronephrosis (both,  $p < 0.001$ ) were associated with pathological upstaging. These factors were included in a multivariate decision tree model to determine their relative importance in upstaging and predicting outcome. Presence of hydronephrosis was the first-tier discriminator among all patients; 70% of patients with hydronephrosis experienced upstaging. In patients without hydronephrosis, tumor growth pattern was a second-tier discriminator, with 64% of patients with papillary tumors not experiencing upstaging. In patients with non-papillary tumors, cT2 substage was a third-tier discriminator, with 70% of cT2b patients being upstaged. For patients with combined papillary and non-papillary features, age was a third-tier discriminator; 68% of patients  $\leq 65$  yrs were not upstaged. The decision tree resulted in 6 terminal branches, and it was able to significantly predict time to recurrence and overall survival (both,  $p < 0.001$ ).

**Conclusions:** This study identified pre-cystectomy variables that are significantly associated with pathological upstaging in cT2N0M0 bladder cancers. The decision tree approach enables identification of the most crucial variables that determine prognosis, and can aid the physician to identify patients in a stepwise fashion who may be candidates for combined modality treatment.

**Source of Funding:** None

## EFFECT OF NEOADJUVANT CHEMOTHERAPY ON COMPLICATION RATE FOLLOWING ROBOT ASSISTED RADICAL CYSTECTOMY

Chinedu Mmeje, M.D., Rafael Nunez-Nateras, M.D., Erik Castle, M.D., Scott Cheney, M.D.: Phoenix, AZ

(Presentation to me made by Dr. Mmeje)

**Purpose:** To determine whether neoadjuvant chemotherapy increases incidence of complications during robot assisted radical cystectomy (RARC)

**Methods:** Ninety patients underwent RARC for urothelial cell carcinoma of the bladder at our institution from March 2007 until October 2010. We retrospectively analyzed perioperative outcomes and morbidity between those who received neoadjuvant chemotherapy plus RARC versus those who were treated with RARC alone. All complications within the 30 day perioperative period were analyzed. Complications were classified using the Clavien complication classification system grading score<sup>1</sup>. Complication requiring intervention (Clavien grade III or higher) were considered significant.

**Results:** A total of 29 patients received neoadjuvant chemotherapy prior to RARC, and 61 patients had RARC alone. Of all the pre-operative characteristics (age, sex, BMI, ASA), only age was found to be significantly different between the two groups with the neoadjuvant group having an average age of 66.6 years versus 72.3 years for the RARC alone cohort ( $p = 0.0032$ ). The neoadjuvant chemotherapy group had slightly longer operative time (343.4 v. 326.8 min), estimated blood loss (EBL) (287.9 v. 258.3 ml), and hospital stay (6.3 v 5.9 days) compared to the RARC alone group, though none were found to be statistically significant. The robot console time (184.2 v. 180.9 min) was similar between the two groups. Seven (24%) patients in the neoadjuvant group had neobladders performed compared to 6 (9.8%) in the RARC alone group, this difference is likely the cause of the longer operative time in the neoadjuvant group. The neoadjuvant group had better outcomes in terms of lymph node yield (18.6 v. 17.6) and positive margin rate (0% v. 4.4%). When examining overall morbidity (any Clavien grade) patients that received neoadjuvant chemotherapy had a significantly higher rate of morbidity (62.1% v. 34.4%,  $p = 0.01$ ) compared to the RARC alone group (odds ratio = 3.12 CI: 1.24 – 7.80). Majority of the complications in the neoadjuvant group were the need for post-operative blood transfusions, which is classified as a Clavien grade II complication. When analyzing for significant complications, those requiring intervention, the rates were similar: 13.8% for the neoadjuvant chemotherapy group versus 11.5% for the RARC alone group (odds ratio = 1.23, CI: 0.33 – 4.60). The only independent predictors of significant complications were EBL and BMI. After multivariate analysis only BMI remained a predictor of significant complications. Patients who had a significant complication had a mean BMI of 33.7 (31.1 – 36.3) versus 27.0 (26.0 – 27.9) for patients without any significant complications.

**Conclusion:** Patients who receive neoadjuvant chemotherapy prior to RARC had slightly more blood loss, and a higher perioperative transfusion rate. Their higher transfusion rate is likely due to preexistent anemia secondary to chemotherapy. However, neoadjuvant chemotherapy prior to RARC does not increase the incidence of significant complications. The only predictor of complications requiring intervention was BMI. This information can be used for risk stratification and patient counseling.

## **DIAGNOSTIC AND SURGICAL DELAY IN BLADDER CANCER AND ITS IMPACT ON PATIENT OUTCOME**

Selma Masic, BS\*, Anirban P. Mitra, MD, PhD, Eila C. Skinner, MD, Jie Cai, MS\*, Gus Miranda\*, Siamak Daneshmand, MD: Los Angeles, CA  
(Presentation to be made by Selma Masic)

**Objectives:** Previous studies have demonstrated that a delay in radical cystectomy beyond 12 weeks after diagnosis and female gender are associated with worse disease-specific and overall survival. The primary aim of this study was to examine the impact of delayed diagnosis and surgery on outcome in patients with bladder cancer who were subsequently managed by cystectomy, and whether worse outcome seen in female patients is due to diagnostic delay.

**Patients and Methods:** A retrospective database review of patients who underwent cystectomy for bladder cancer with a curative intent at the USC Norris Cancer Center and affiliated institutions between 1973-2008 was conducted. Selected subjects were patients who were initially referred for urologic evaluation and definitively diagnosed by cystoscopy and TURBT. Durations between symptom onset to diagnosis, diagnosis to cystectomy, and symptom onset to cystectomy were determined. Univariate and multivariate Cox regression analyses were conducted using the above durations, age, gender, and pathologic stage as covariates in the proportional hazards model.

**Results:** The cohort comprised of 1,553 men and 411 women (total n=1,964). There was no significant difference in the symptom-to-diagnosis interval between the sexes, with median delay of 49 days in men, and 59 days in women ( $p=0.165$ , Wilcoxon test). Similarly, there was no significant difference in the diagnosis-to-cystectomy interval between the sexes, with median delay of 71 days in men, and 74 days in women ( $p=0.71$ , Wilcoxon test). By univariate analysis, a diagnosis-to-cystectomy delay interval  $\geq 11$  weeks was associated with an increased risk of disease recurrence (RR=1.31,  $p<0.001$ ), and mortality (RR=1.18,  $p=0.005$ ) when compared to a delay  $\leq 10$  weeks. Multivariate Cox regression analysis confirmed that cystectomy delay following diagnosis  $\geq 11$  weeks was associated with an increased risk of recurrence (RR=1.43,  $p<0.001$ ) and mortality (RR=1.15,  $p=0.016$ ), even after controlling for age, gender, and pathologic stage. There was no significant association between recurrence and survival with an increasing symptom-to-diagnosis interval.

**Conclusions:** Appropriate and timely management of invasive bladder cancer is critical from the initial onset of symptoms. A prolonged diagnosis-to-cystectomy delay confers an increased risk of disease recurrence and death. Theoretically, a prolonged diagnostic delay may contribute to a delay in surgical management and the risk of pathologic upstaging at the time of cystectomy, however, delay in diagnosis does not explain the difference in outcome seen in women. Further work is being performed to ascertain this relationship.

**Source of Funding:** None

## **SURVIVAL FOLLOWING UROTHELIAL RECURRENCE IN PATIENTS POST-RADICAL CYSTECTOMY FOR TRANSITIONAL CELL CARCINOMA OF THE BLADDER**

Brianna N. Harris, M.A.\*, Anirban P. Mitra, M.D., Ph.D., Eila C. Skinner, M.D., Gus Miranda\*, Siamak Daneshmand, M.D.: Los Angeles, CA  
(Presentation to be made by Brianna Harris)

**Objective:** Radical cystectomy offers excellent local control for high grade muscle-invasive bladder cancer. While the overall survival is excellent for organ-confined disease, the prognosis following recurrence is very poor. Presentation and subsequent treatment of urothelial recurrence are highly variable. The goal of this study was to report mode of presentation and subsequent treatment of urothelial recurrence following radical cystectomy, with an emphasis on the predictive value of urethrectomy or nephroureterectomy on clinical outcomes and survival.

**Methods:** A retrospective database review of 1,964 patients who underwent a radical cystectomy for bladder transitional cell carcinoma with a curative intent at USC between 1973-2008 was performed. Inclusion criteria were patients who experienced recurrence in the upper tract or urethra, with a minimum 2-year post-recurrence follow-up if alive. Exclusion criteria were presence of urethral or upper tract primaries, or distant metastasis at diagnosis, and patients undergoing salvage surgical procedure after failure of definitive radiotherapy. Associations of clinicopathologic factors with post-recurrence outcomes and survival were analyzed.

**Results:** A total of 80 patients (74 male and 6 female) were identified who experienced upper tract or urethral recurrence following radical cystectomy. Following radical cystectomy, 43 patients demonstrated an abnormal filling defect on IVP or positive urine cytology or urethral washings on routine follow-up, while another 31 patients presented with a specific complaint of urethral discharge or gross hematuria. One patient complained of meatal itching with a subsequent diagnosis of Bowen's disease of the penis. There were 25 (1.3% of 1,964) upper tract recurrences diagnosed at a median of 28.2±9.4 months of whom 24 underwent nephroureterectomy. Following surgical intervention, median post-recurrence survival was 70.9±19.8 months. There were 55 (2.8% of 1,964) urethral recurrences diagnosed at a median time of 25.3±1.6 months, of whom 49 underwent total urethrectomy. Following surgical intervention, median post-recurrence survival was 40.5±13.8 months. Of the 80 total patients, those who recurred ≤2 years after surgery (n=32) had a median post-recurrence survival of 19.6±2 months, while those who recurred >2 years after surgery (n=48) had a median post-recurrence survival of 70.9±15.5 months (p=0.003) following surgical intervention. There was no statistically significant difference between urethral or ureteral recurrence, or between patients who did or did not receive adjuvant chemotherapy with respect to post urothelial recurrence survival.

**Conclusion:** Patients who recur in the urethra or upper tract following radical cystectomy for bladder cancer who subsequently undergo total urethrectomy or nephroureterectomy can have prolonged survival. Those recurring 2 or more years following cystectomy have a significantly longer post-recurrence survival rate than those undergoing surgical intervention prior to that.

**Source of Funding:** None

## **URETHROPLASTY FOR PELVIC FRACTURE URETHRAL DISTRACTION DEFECTS: FACTORS INFLUENCING SURGICAL OUTCOME AND ERECTILE DYSFUNCTION**

Adam Kinnaird, MD, Jeff Zorn, MD, Keith Rourke, MD: Edmonton, Alberta  
(Presentation to be made by Dr. Rourke)

**Purpose:** Pelvic fracture with urethral distraction injury (PFUDD) is a challenging urologic entity. Typical complications of this injury include urethral fibrosis (stricture), erectile dysfunction and incontinence. Controversy exists as to the best initial management and factors determining optimal outcome. The purpose of this study is to identify factors that influence erectile dysfunction (ED) and successful surgical repair.

**Methods:** A retrospective database review of 536 urethral reconstructions was performed. All procedures were performed by a single surgeon (KR) from August 2003 to February 2011. Data was abstracted from patient charts and electronic medical records. Factors examined were cause of pelvic fracture, aligning catheter placement, patient age, co-morbidities, previous intervention, length of defect, infrapubectomy, and time from injury to repair. Primary outcomes measures were urethral patency and the occurrence of erectile dysfunction. Chi-square analysis was performed on categorical variables ( $p \leq 0.05$ ).

**Results:** 49 patients were identified that underwent urethroplasty after PFUDD during the study period. Mean age was 40.4 years with an average follow-up of 3.3 years. Motor vehicle collision (38/49, 77%) was the most common etiology. Urethroplasty alone successfully established urethral patency in 85% of patients. Seven patients (14%) developed recurrent stenosis. Almost all of these recurrences (6/7, 86%) were salvaged by a single endoscopic procedure. One patient required repeat open urethroplasty. 69% of patients presented pre-operatively with erectile dysfunction. Surgery increased the overall incidence of erectile dysfunction by 5%. Placement of an aligning catheter at the time of injury did not decrease stricture recurrence (11% vs. 13%  $p=0.43$ ) but increased the rate of ED (84% vs. 56%  $p=0.03$ ). A failed attempt at aligning catheter placement substantially increased the risk of ED (91% vs. 56%  $p=0.04$ ) but did not increase rate of stricture recurrence (27% vs. 13%  $p=0.17$ ).

**Conclusions:** PFUDD injuries are amenable to repair by a single open urethroplasty in 85% of cases. The majority of recurrences (86%) can be treated with a single minimally invasive technique. Overall urethral patency after these injuries approaches 98%. Placement of aligning catheter at time of injury increases the rate of erectile dysfunction without improving operative outcome. There is evidence that a failed attempt at urethral realignment (likely reflecting severity of injury) highly predicts the occurrence of erectile dysfunction.

**Source of Funding:** None

## **SECONDARY URETHROPLASTY FOR FAILED PRIOR URETHRAL RECONSTRUCTION: OUTCOMES OF A 33 YEAR EXPERIENCE**

Sarah D. Blaschko, MD, Seth K. Bechis, MD, Jeremy B. Myers, MD, Benjamin N. Breyer, MD, and Jack W. McAninch, MD. San Francisco, CA.

(Presentation to be made by Dr. Sarah D. Blaschko)

**Purpose:** Male urethral stricture disease accounts for over 5000 hospitalizations in the US annually. Estimated US healthcare costs exceeded \$200 million in 2000. Although much research has been completed on treatment of urethral strictures, fewer studies have addressed treatment of strictures in men with recurrent stricture disease after failed prior urethroplasty. We sought to elucidate outcome results in secondary urethroplasties.

**Materials and Methods:** From 1978 to 2010, 117 patients were treated with secondary or tertiary urethroplasty for failed urethral reconstruction. Prior urethroplasty type, time until urethroplasty failure, location of stricture, and successful secondary urethroplasty intervention were evaluated.

**Results:** The patients' median age was 45 with a mean of 45.7. The age range was 20 to 77. Median followup was 15 months with an average of 44 months. Followup ranged from one month to 291 months. In 117 patients with multiple prior procedures and comorbidities, 102 patients (87%) were successfully treated without requiring repeat urethroplasty. Urethroplasty failure occurred between 7 and 144 months.

**Conclusions:** Secondary urethroplasties may successfully be completed in many patients. However, long-term follow up is recommended and may reveal patients who require additional intervention several years after secondary urethroplasty.

**Source of Funding:** None

# **ONCE A STRICTURE ALWAYS A STRICTURE; A PARADIGM MAY NOT ALWAYS BE TRUE: DURABLE RESULTS AND RESTITUTION OF NORMAL URETHRA IN SOME PERSONS FOLLOWING LASER VAPORIZATION.**

Inder Perakash, M.D., FACS: Palo Alto VA Health Care system and Stanford University, CA  
(Presentation to be made by Dr. Perakash)

**Introduction and Objective:** A recent national survey of board certified urologists (1) indicates that 93% of the urethral strictures are treated with repeat dilatations and 85.6% with optical internal urethrotomy with 58 to 84 % failures after one urethrotomy. Literature supports a reconstructive ladder with few urologists (4.2%) who performed buccal mucosal grafts after repeat failures of endoscopic procedures. Long term follow up results are presented following circumferential vaporization of both anterior and posterior urethral strictures. Follow up study was approved by the Institutional review board at Stanford.

**Methods:** Sixty three males and one female patient, 26–72 years old (51 spinal cord injured and 13 others)) were managed with circumferential vaporization of their 1 to 5 cm long urethral strictures. An initial urethrotomy was made at the 12 o'clock position by retrograde vaporization of the scarred tissue through the length of the stricture so that a cystoscope could be passed to determine the extent of stricture, and also to define the external urethral sphincter. Low level energy (10 to 15 W) was used and only fibrous tissue was vaporized without damaging islands of normal tissues. Initially Nd: YAG and later Ho: YAG lasers were used in a contact mode. Urethral catheter was removed after 24 hours....

**Results:** The mean operation time was 32 minutes (range 15 to 57 minutes). No significant bleeding was encountered. Two earlier patients developed extravasations in the scrotum that were extensively vaporized posteriorly. Subsequently 6 o'clock vaporization was restricted to minimal. Patients have been followed from 2 to 9 years. (Mean 7.1 years). Repeat vaporization was required in 17% patients with 10% needing during the first year. Repeat vaporization was easy and the patients left the hospital within first 24 hour. Follow up in random selected patients on Cystoscopy and or ultrasound showed virtually normal urethra in 9 patients with no evidence of stricture. Others 83% maintained adequate stream and did not require periodic dilatations.

**Conclusions:** For strictures of the urethra, the durable results following the technique employed appear gratifying when compared to the other reported series. Restitution of the normal urethra in some patients was an unexpected finding and needs further evaluation. Lower level laser energy has a potential for the regeneration of tissues. It may be considered a minimally invasive procedure instead of repeated dilatations with resultant repeated bacteraemia, or stents which are difficult to remove, or even open urethroplasty.

## References

1.Bullock LT, Brandes BS, Anterior urethral strictures: A national practice... J.Urol.2007; 177(2):685-90.

# **SURGICAL RECONSTRUCTION OF RECTOURETHRAL AND URETHROPELVIC FISTULAS**

Bryan B. Voelzke, MD: Seattle, WA  
(Presentation to be made by Dr. Voelzke)

**Purpose:** Surgical repair of rectourethral and urethropelvic fistulas emanating from the posterior urethra are challenging. The etiology is commonly iatrogenic following cancer-related pelvic therapy. We present a case series of nine men who have undergone definitive surgical repair at our tertiary medical center over the past three years.

**Materials and Methods:** A retrospective review was performed of all surgically treated rectourethral and urethropelvic fistulas from August 2008 to present. All fistulas were repaired via a transperineal or abdominal-perineal approach with selective use of a gracilis interposition muscle flap or ventral onlay buccal mucosa graft (BMG). Two additional patients, who have undergone successful repair of their fistulas, were not included in this series as the follow up is < 1 month since all catheters were removed.

**Results:** Successful closure of the urethral defect was achieved in 9/9 patients. The median age was 61 years. Median follow up was 14.2 months. Fistula etiology was secondary to pelvic-related cancer treatments in 9/9 patients (prostate cancer: 5, rectal cancer: 2, bladder cancer: 1, congenital disorder: 1). 5/9 patients had prior radiation/ablative therapy, and 1/9 had a concomitant urethral stricture. 2/9 patients had a failed attempt at fistula repair prior to referral. A gracilis interposition flap was utilized in all patients except for one non-radiated patient. Two patients treated with radiation underwent urethral closure with a BMG. An abdominal-perineal incision was required in 2/9 patients for rectal mobilization.

One patient with a history of prostate HIFU had a persistent leak following surgical repair, which closed with conservative management after nine months. A gracilis flap was placed during the initial surgery. Postoperatively, 2/9 patients required a permanent colostomy due to their medical history. Fecal undiversion has occurred in 3/7 patients remaining patients.

**Conclusions:** Transperineal, sphincter-preserving, repair of rectourethral fistulas is a reliable method to treat radiation and non-radiation induced rectourethral fistulas. A gracilis flap is essential to assist with wound healing for radiation-related fistulas. When appropriate, surgical reconstruction of the lower urinary tract and rectum is recommended to avoid permanent urinary and/or fecal diversion.

**Source of Funding:** None

## INCREASED NUMBER OF NODES REMOVED AT RETROPERITONEAL LYMPH NODE DISSECTION IMPROVES OVERALL- AND CANCER-SPECIFIC SURVIVAL IN PATIENTS WITH TESTICULAR CANCER

Dan J. Lewinshtein, M.D., Sandra J. Koo, M.D. Christopher R. Porter,  
M.D.: Department of Urology, Virginia Mason Medical Center, URO,  
Seattle, WA

(Presentation to be made by Dr. Lewinshtein)

**Background:** The benefit of a thorough retroperitoneal lymph node dissection (RPLND) for testicular cancer has been well established and essentially eliminates retroperitoneal recurrence of disease. RPLND is known to be a complex, advanced procedure and the number of nodes removed may vary amongst institutions. Thus, we explored whether number of nodes removed at RPLND may predict overall- and cancer-specific survival in patients who have undergone RPLND.

**Methods:** We retrospectively searched the Surveillance Epidemiology and End Results (SEER) database for all patients who had undergone RPLND for primary testicular cancer between 1973 and 2006. We performed logistic regression to assess the ability of number of nodes removed at RPLND to predict overall and cancer specific survival. We adjusted for stage, age, and tumor histology. In addition, we used Kaplan-Meier life table analysis to evaluate actuarial survival probability as a function of removed nodes at the time of RPLND. Finally, we performed these analyses in a subgroup of patients with nonseminomatous germ cell tumor (NSGCT).

**Results:** The cohort consisted of 1494 patients. The median age and median number of nodes removed at RPLND were 30 years (0-87) and 14 (+/- 13.9 SD). Of all patients, 46.2%, 45.4%, and 8% were stage I, II and III, respectively. There were 1262 (84.5%) NSGCT and 178 (11.9%) seminoma diagnoses. On multivariate analysis, stage (<0.001), age (HR 0.057; p<0.001), and number of nodes removed (p<0.024) were all significant predictors of overall mortality. On Kaplan-Meier analysis, mean time to overall mortality (16.939 vs. 18.583 years, p<0.001) and cancer specific mortality (17.69 vs. 18.7 years, p<0.001) were significantly shorter for patients that had 5 or fewer nodes removed compared to those than had 6 or more removed.

**Conclusions:** The number of nodes removed at RPLND significantly predicted the overall- and cancer-specific survival in patients with NSGCT. Moreover, patients with fewer nodes removed at time of RPLND had significantly shorter mean actuarial overall survival and cancer specific survival. This analysis emphasizes the critical importance of a thorough RPLND on survival in patients with testicular cancer.

## **ROBOTIC-ASSISTED LAPAROSCOPIC RETROPERITONEAL LYMPH NODE DISSECTION FOR TESTICULAR CANCER: EARLY EXPERIENCE AND INITIAL RESULTS**

Michael Santomauro, M.D., Jason M. Durbin, D.O., Brian K. Auge, M.D.,  
James O. L'Esperance M.D.: San Diego, CA  
(Presentation to be made by Dr. Santomauro)

**Purpose:** Laparoscopic and robotic assisted retroperitoneal lymph node dissection (r-RPLND) is typically performed in the flank position. Thus, it is traditionally performed unilaterally, with limited contralateral exposure. Versatility of robotic surgery allows for excellent access to the entire infrarenal retroperitoneum. We report on our initial series, present our technique, and compare robotic patients to our most recent open RPLND (o-RPLND) patients.

**Methods:** A retrospective review of four patients who underwent a planned r-RPLND for testicular cancer was conducted. Preoperative and pathologic comparisons were made to four patients who underwent o-RPLND. Steep trendelenburg position, 3 robotic arms, 2 assistant ports, and 1 camera port were used in r-RPLND.

**Results:** All 8 patients had non-seminomatous germ cell tumors. Four patients (2 in each group) underwent bilateral dissection: 3 post-chemo RPLND's and 1 r-RPLND for high risk features in the primary tumor. The remaining RPLND's were unilateral template dissections.

r-RPLND vs. o-RPLND results: 326 vs. 227 minutes ( $p < .05$ ) OR time; 4.5 vs. 6 days ( $p = .05$ ) hospital stay; 34 vs. 231 mg morphine equivalents ( $p < .05$ ). Pathological staging revealed an average of 28.3 vs. 20.5 lymph nodes obtained. There were no complications in the r-RPLND group. There was a fascial dehiscence and a chylous ascites, in the same patient, in the o-RPLND group. With early follow-up, there have been no recurrences in either group.

**Conclusion:** Robotic-assisted RPLND is feasible for experienced robotic surgeons and potentially minimizes an otherwise morbid procedure, while maintaining oncologic principles and outcomes. The supine position affords excellent exposure to both sides of the retroperitoneum and allows for safe and meticulous dissection. Further study looking at long-term results is warranted.

## **NERVE-SPARING RETROPERITONEAL LYMPH NODE DISSECTION IN METASTATIC TESTICULAR CANCER**

Emmanuel J. Mitsinikos, B.S., Nick Tadros, M.D., Siamak Daneshmand,  
M.D.: Los Angeles, CA

(Presentation to be made by Emmanuel Mitsinikos)

**Objective:** As most cases of testicular cancer occur in patients 20-35 years of age, preservation of fertility is of significant concern. Nerve-sparing RPLND (NS-RPLND) procedures have been introduced to reduce the incidence of retrograde ejaculation in patients undergoing RPLND, but factors such as prior chemotherapy and large retroperitoneal masses can make the procedure more challenging with an increased risk of nerve damage and subsequent retrograde ejaculation. In this study we report rate of preservation of ejaculatory function in a group of patients with metastatic testicular cancer undergoing NS-RPLND.

**Methods:** Since 2004, 100 patients have undergone RPLND (90 post-chemotherapy (PC), 10 primary) by a single surgeon (SD). Of these, 43 patients with metastatic testicular cancer underwent either primary (4) or PC (39) NS-RPLND. Post-ganglionic sympathetic nerves were spared at least unilaterally in all cases. Data regarding surgery including dissection template and laterality of nerve sparing were obtained from the patient's operative report, and size and microscopic evaluation of the retroperitoneal mass were obtained from the pathology reports. Information regarding the patient's ejaculatory status was acquired either from 3 month follow-up clinic notes or via telephone contact. Four patients underwent primary NS-RPLND with a retroperitoneal mass (3 stage IIA, 1 Stage IIB), 37 underwent PC NS-RPLND (35 BEP<sub>x</sub>3-4; 1 EP<sub>x</sub>3; 1 VAC<sub>x</sub>3) and 2 underwent salvage chemotherapy prior to their NS-RPLND (BEP + TIP/VIP).

**Results:** Follow-up data was available for 37 patients for a response rate of 86%. Mean follow-up was 10 months (1-58 months). Median size of the retroperitoneal mass was 4.4cm in largest dimension. Thirty-three of the 37 patients (89.1%) who underwent NS-RPLND retained normal ejaculatory function, including both patients who underwent salvage chemotherapy. There was no statistically significant difference in rates of antegrade ejaculation with preservation of right nerve fibers only (14/15), left nerves only (3/4), or bilateral nerves (16/18), (chi-square, p=0.58) Three patients had retroperitoneal recurrence, and two other patients had extra-abdominal recurrence, at a mean of 12 months post-operatively (6-19 months). The patients with retroperitoneal recurrence were high risk (2 with metastatic seminoma and viable germ cell tumor found at PC-RPLND, and 1 with IIB who underwent primary RPLND secondary to dialysis dependent end-stage renal disease). The two extra-abdominal recurrences were in patients with a non germ cell tumor (rhabdomyosarcoma) and a large (12cm) teratoma who developed lung metastases.

**Conclusion:** NS-RPLND in the metastatic and post-chemotherapy setting is a technically demanding procedure however can preserve ejaculatory function in the majority of patients, thus improving quality of life. Preservation of at least one post-ganglionic sympathetic nerve fiber on either side appears to prevent retrograde ejaculation in most cases.