

## **A PROGRESSIVE TRAINING PROGRAM IN ROBOTIC-ASSISTED LAPAROSCOPIC PROSTATECTOMY: COMPARATIVE OUTCOMES WITHIN A VETERANS' AFFAIRS POPULATION**

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(Presentation to be made by Dr.Cohen)

**Introduction:** As robotic laparoscopic surgery becomes a defined skill set, questions remain as how to implement and share this technology with novice robotic surgeons. In this study, we sought to determine if surgeons participating in a progressive training program in robotic-assisted laparoscopic prostatectomy had similar perioperative outcomes.

**Methods:** 90 robotic-assisted laparoscopic prostatectomies were successfully performed, under the auspices of a progressive training program. A single experienced robotic surgeon provided extended mentorship during the first 30 cases for a novice robotic surgeon. The initially novice surgeon went on to amass her own case series during the following 30 cases. In the last 30 cases, she was then the senior mentor for urology residents, operating as the primary surgeons. Independent t-test, Chi<sup>2</sup>, ANOVA, and Kruskal-Walls tests compared the demographics and operative outcomes in these patient populations.

**Results:** The patient populations (n=30) were similar in age (p=0.867), clinical T-stage (p=0.247), and D'Amico Risk Group (p=0.076). There was a statistically significant difference in the median pre-operative prostate specific antigens (PSAs) of these populations (p<0.001), with the last 30 patients having the highest median (IQR) preoperative PSA, 8 (5-12.8). The last 30 patients also had the largest prostates, 47.8 grams (35.8-62.9 grams, p=0.044). Estimated blood loss (p=0.568), rate of blood transfusion (p=0.129), length of hospital stay (p=0.075), pathologic T-stage (p=0.357), and rate of positive margins (p=0.812), were comparable in all groups.

**Conclusion:** Using this model of progressive training, perioperative outcomes of surgeons, trained under the tutelage of a relatively new robotic mentor, are similar to the outcomes of surgeons trained directly by an experienced robotic mentor.

**Source of Funding:** None

## **2<sup>ND</sup> PLACE WINNER – JOSEPH F. McCARTHY / OLYMPUS PHYSICIAN ESSAY CONTEST**

### **NATURAL ORIFICE TRANSLUMINAL ENDOSCOPIC RADICAL PROSTATECTOMY (NOTES RP): INITIAL PERI-OPERATIVE AND PATHOLOGICAL RESULTS**

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(Presentation to be made by Dr. Humphreys)

**Introduction:** Natural orifice transluminal endoscopic surgery (NOTES) represents the evolution of minimally invasive surgery. The conceptual feasibility has been shown in careful laboratory and animal studies, but there is a scarcity of information regarding clinical applications. The purpose of this report is to describe the first clinical experience, pathologic and peri-operative outcomes of NOTES radical prostatectomy (NOTES RP).

**Materials and Methods:** After IRB approval two patients consented to undergo a NOTES RP for localized prostate cancer. The prostate was radically resected using a 26 Fr resectoscope, 550  $\mu$ m laser fiber, and holmium laser. The prostate was delivered into the bladder and was removed at the conclusion of the procedure through a suprapubic cystotomy for histopathologic analysis. The vesicourethral anastomosis was completed using a cannula scope, urethral-vesico suturing device and titanium knot applier (LSI Solutions Inc, Victor NY). Cystograms were taken immediately post-operatively and at time of catheter removal.

**Results:** Both patients tolerated the procedure without operative complication. All intra-operative cystograms showed water tight anastomoses. The pathology revealed Gleason 3+3, pT2aNxMx, and Gleason 3+4, pT2cNxMx, in each patient with negative margins. No blood transfusions were required. Patient 2 experienced some left sided suprapubic pain post-operatively.

**Conclusion:** NOTES RP appears to be a safe and feasible option for the management of carefully selected organ confined prostate cancer. Peri-operative and pathological outcomes show promise with this new technique, but the high standards of oncologic and functional outcomes demand close and longer follow up before adoption into the surgical armamentarium can be recommended.

**Source of Funding:** None

## **THE IMPACT OF ROBOTICS ON RADICAL PROSTATECTOMY TRAINING IN UROLOGY RESIDENCY: A SURVEY OF AUA RESIDENT MEMBERS WORLDWIDE**

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(Presentation to be made by Dr. McDonough)

**Purpose:** The impact of robotic surgery on urology resident education is unknown. We set out to determine the current status of open (RRP), laparoscopic (LP), and robotic (RARP) radical prostatectomy training in urology residency. In consideration of the well defined learning curve necessary to become proficient at RARP, we hypothesized that urology residents would be of the opinion that the addition of RARP to their training program would have a negative impact on their radical prostatectomy (RP) training. To this end, we queried resident opinion to assess their perceptions regarding the impact of robotic surgery on their RP training.

**Materials and Methods:** This IRB approved project consisted of a 21 question survey that was intended to assess the state of RP and robotic surgical training in urology residency programs. The survey was sent worldwide via electronic mail to all resident members of the AUA and it was kept open for responses for a three week period in April of 2011.

**Results:** A total of 2,437 surveys were sent and responses were received by 356 residents for an overall response rate of 15%. Of respondents, 80% were US residents and 20% were international residents. Respondents were evenly distributed from each year of urology residency. RARP is the most common approach to prostatectomy reported within U.S. residency programs whereas RRP remains more common abroad. LP was rarely reported throughout residency. Of respondents, 74% reported no defined robotic training curriculum required prior to performing as console surgeon. A dual console was available to 23% of respondents, 46% reported access to a robot for training purposes, and 24% reported access to a virtual reality robotic simulator. Only 9% of respondents reported having protected time for robotic training built into their residency. Using the ACGME criteria for "Surgeon," 54% of US residents are exposed to fewer than 25 RRP's, whereas 61% of US residents report exposure to greater than 25 RARP's during their training. When participating as "Surgeon," 42% of US residents agreed that their level of participation was greater during RRP than RARP, 27% were neutral, and 31% disagreed with this statement. Of respondents, 29% agreed that their program's transition from RRP to RARP has had a negative impact on their education with regard to prostatectomy, 25% were neutral, and 46% disagreed with this statement.

**Conclusions:** RARP is the most common approach to RP within U.S. training institutions, yet a minority of residents report having a defined robotic training curriculum, access to a robot for training, or protected time for robotic training. A significant proportion of residents believe that the emergence of robotic surgery has decreased their participation in RP as learners and has negatively impacted their surgical education. These results suggest a need to improve resident training and participation in RARP.

## **DOES THE USE AND TIMING OF ANDROGEN DEPRIVATION THERAPY FOR BIOCHEMICAL RECURRENCE AFTER RADICAL PROSTATECTOMY AFFECT PROSTATE CANCER SPECIFIC MORTALITY?**

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(Presentation to be made by Dr. Punnen)

**Background:** Randomized trials show a benefit of early androgen deprivation therapy (ADT) in men with node positive prostate cancer. Although ADT is used frequently in the setting of biochemical recurrence (BCR) after radical prostatectomy (RP), data to support this practice is limited. Furthermore, uncertainty surrounds the appropriate timing of such ADT. Thus, given these issues as well as the emerging evidence regarding long-term adverse affects of ADT, we sought to determine the impact of ADT on prostate cancer specific mortality (PCSM) in men with BCR after surgery.

**Methods and Materials:** Among men in the CaPSURE database, patients with a BCR (PSA>0.2ng/ml) post surgery for localized prostate cancer were selected. Men receiving secondary treatments other then salvage ADT were excluded. Proportional hazards regressions were used to assess whether there was an association between ADT use and PCSM. In addition, the association between timing of ADT after BCR on PCSM amongst those who were placed on ADT was examined. An exploratory analysis of various time to ADT (6 and 12 months) and PSA (2 ng/ml) cut-points were performed.

**Results:** Among the 375 men meeting study criteria, 102 received ADT. Mean follow up time of the cohort was 65 months, during which 35 prostate cancer deaths occurred. KM estimated 3 and 5-year survivals were 99% and 94%, respectively. There was no association between the use of ADT and PCSM (HR 0.44, 95% CI 0.1-1.93, P=0.3). Furthermore, in a subset of patients who received ADT, there was no association between the timing of ADT and PCSM (HR 1.0, 95% CI 0.99-1.01, P=0.46). Stratification at 12 months did not change the findings, however, using a cut point of 6 months, early versus late treatment showed a trend towards an 80% reduction in the risk of PCSM (HR 0.2, 95% CI 0.04-1.13, P=0.07). When using a PSA cutoff of 2 ng/ml, early versus late treatment resulted in a significant 90% reduction in the risk of PCSM (HR 0.1, 95% CI 0.02-0.48, P=0.004).

**Conclusion:** This study failed to detect an association between ADT use and improved PCSM in men with BCR after radical prostatectomy. Men who receive ADT within 6 months of BCR or before a PSA of 2ng/ml may represent a high-risk subset who benefit from early ADT.

**Source of Funding:** Abbott

## **POSITIVE MARGINS AT THE SEMINAL VESICLES IN PROSTATECTOMY PATIENTS: LONG-TERM OUTCOME AND RATIONALE FOR ADJUVANT THERAPY**

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(Presentation to be made by Dr. Wilson)

**Purpose:** Recently published randomized clinical trials identify patients with localized prostate cancer who may be considered for adjuvant radiotherapy following radical prostatectomy. Indications include extraprostatic extension (T3a), positive margins (R0), and seminal vesicle (SV) invasion (T3b). Among these indications, seminal vesicle invasion is considered the most adverse pathologic feature because of its association with the development of systemic disease. While implementation and interpretation of the outcomes of these trials remains controversial, there is reported improvement in overall survival, metastasis free survival and biochemical relapse free survival with adjuvant radiotherapy. Nevertheless, local treatment in the form of adjuvant radiation therapy to the prostate and seminal vesicle bed is associated with improved outcome of patients with seminal vesicle invasion. The purpose of this study is to examine pathologic characteristics of seminal vesicle invasion which may provide a basis for this finding.

**Materials and Methods:** A total of 416 consecutive radical retropubic prostatectomy specimens from three urologic surgeons were submitted for total embedding and whole mounting between 1991 and 1993. Clinical data was collected in a prospectively maintained database. Specimens were examined for the presence of extra-seminal vesicle extension or positive margins at the site of the seminal vesicle specimen. These pathologic features were examined with respect to any progression, local/systemic progression, or prostate cancer death. The number of patients identified with seminal vesicle invasion was 51 and those available for analysis in this study was 36.

**Results:** Mean age of the group was 66 years (range: 44 – 76). Ten-year overall survival was 68% and the prostate cancer survival rate was 89%. Ten patients (28%) were found to have cancer at the margin of the seminal vesicle specimen and twenty patients (56%) were found to have extra-seminal vesicle cancer. The 5 and 10 year progression free survival was 23% and 12% for patients with extra-SV extension, compared to 53% and 23% for those patients without this feature ( $p=0.04$ ). Ten year prostate cancer survival rates were 100% for patients without extra-SV extension and 81% for patients with this finding ( $p=0.19$ ). Patients with cancer at the seminal vesicle specimen margin had a 67% 10 year prostate cancer death rate versus 96% for patients who did not ( $p=0.23$ ).

**Conclusions:** Although margin status of the seminal vesicles and extra-SV extension are not routinely reported in prostatoseminal vesiculectomy specimens, in this study their presence is associated with poorer outcome. Thus, local radiation therapy may serve to limit recurrence when seminal vesicle invasion is present which is consistent with observations from clinical trials. This observation is consistent with the rationale for adjuvant radiotherapy in the setting of positive prostate margins following radical prostatectomy.

**Source of Funding:** None

# 1<sup>st</sup> PLACE WINNER – MILEY B. WESSON / OLYMPUS RESIDENT ESSAY CONTEST

## QUANTITATIVE GLEASON GRADING IMPROVES PROSTATE CANCER RISK STRATIFICATION

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(Presentation to be made by Dr. Reese)

**Purpose:** We propose a modification of the Gleason grading system, based on the weighted average of the Gleason patterns present in the pathology specimen. We hypothesized that this quantitative Gleason score, when applied to prostate biopsy and radical prostatectomy (RP) specimens, can improve prostate cancer risk stratification.

**Material and Methods:** We developed the quantitative Gleason score, a modification of the current scoring system based on the weighted average of Gleason patterns present in the pathology specimen. We applied this modified grading system to patients in our institutional urologic oncology database with Gleason 7 tumors on prostate biopsy or final pathology after radical prostatectomy. Using ROC curve, Kaplan-Meier, multivariable logistic regression, and decision curve analyses, we assessed the ability of the quantitative Gleason score to predict pathological Gleason grade from biopsy and the risk of recurrence after RP.

**Results:** 225 men were included in the analysis of biopsy specimens and 618 men in the assessment of RP specimens. Quantitative Gleason score of prostate biopsies was higher in those men with Gleason 4+3 disease on final pathology compared to those with 3+4 tumors (6.89 vs. 6.35,  $p < 0.01$ ). Compared to traditional Gleason grade, the quantitative Gleason score resulted in improved concordance between biopsy and pathological Gleason score on decision curve and ROC analyses (AUC 0.79 vs. 0.71). On regression and decision curve analyses, quantitative Gleason grading of RP specimens improved the prediction of biochemical recurrence after radical prostatectomy.

**Conclusions:** Quantitative Gleason grading, a simple modification of our current Gleason grading system, improves the correlation between biopsy and pathological Gleason score, and improves the prediction of biochemical recurrence after radical prostatectomy.

**Source of Funding:** None

# THE STANFORD PROSTATE CANCER RISK CALCULATOR

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(Presentation to be made by Dr. Ngo)

**Purpose:** The Prostate Cancer Risk Calculator (PCRC) was derived from the placebo arm of the Prostate Cancer Prevention Trial (PCPT) and is used widely by clinicians and patients to assess the pre-biopsy risk of prostate cancer and high grade prostate cancer. We recently showed that the PCRC underestimates the risk of high grade prostate cancer approximately by a factor of two. In contrast to the cohort used to derive the PCRC, the subjects in our cohort were contemporary, referred for a suspicion of prostate cancer due to an abnormal DRE or elevated PSA, were more ethnically diverse, and underwent an extended prostate biopsy scheme. Therefore, our cohort more closely resembles patients who would most likely use the PCRC. One of the limitations of our earlier study was its small size relative to the cohort used to derive the PCRC (636 vs. 5519). To address this limitation, we analyzed data from an updated Stanford Prostate Needle Biopsy Database (SPNBD) and developed a new risk calculator.

**Materials and Methods:** The SPNBD is an institutional review board approved, prospectively maintained registry of all prostate needle biopsies performed at our institution. We reviewed this database and selected all patients referred for a suspicion of prostate cancer who underwent an extended prostate biopsy scheme (at least 12 cores). Clinical variables examined were patient age (years), race (White, Black, Asian, Hispanic, Other), PSA (ng/mL), abnormal DRE (yes/no), family history of prostate cancer (yes/no), and prior negative biopsy (yes/no). High grade prostate cancer (yes/no) was defined as having a Gleason score of 7 or higher. We constructed a new model to predict the presence of cancer and high grade cancer in our referral population. Internal validation of the models was performed using the 10-fold cross validation method.

**Results:** From 1998-2010, 1944 patients were referred for a suspicion of prostate cancer and underwent an extended prostate needle biopsy scheme at our institution. With respect to overall cancer detection, our new model performed similarly to the PCRC. We confirmed our prior observation that the PCRC underestimates the risk of high grade cancer by a factor of two. With respect to overall prostate cancer detection, age, race, PSA, abnormal DRE, family history of prostate cancer, and previous biopsy were independent predictors for cancer. In the original PCRC model, age and race were not independent predictors. The AUC for this model and its cross-validation model was 0.699 and 0.692, respectively. With respect to high grade prostate cancer detection, age, race, PSA, abnormal DRE, and previous biopsy were independent predictors, similar to the original PCRC model. The AUC for this model and its cross-validation model were 0.754 and 0.748, respectively.

**Conclusions:** The PCRC was derived from patients who participated in a chemoprevention trial and were pre-selected to be at low risk for developing prostate cancer. It underestimates the risk of high grade prostate cancer in contemporary, ethnically diverse, referral cohorts. The Stanford Prostate Cancer Risk Calculator may be more generalizable, although external validation is needed.

**Sources of Funding:** None

## **OUTCOMES OF PATIENTS WITH LYMPH NODE POSITIVE PROSTATE CANCER TREATED WITH SURGERY ONLY IN THE PSA ERA**

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(Presentation to be made by Dr. Dorin)

**Purpose:** Patients undergoing radical prostatectomy for clinically localized prostate cancer are occasionally found to have lymph node (LN) metastases on pathological exam. We examined the clinical outcomes of a consecutive cohort of LN positive (LN+) patients who underwent open radical retropubic prostatectomy (RRP) with bilateral pelvic lymph node dissection (PLND) in the PSA era.

**Materials and Methods:** We reviewed an IRB approved, prospectively maintained prostate cancer database and identified patients with clinically organ confined (cT1/cT2) prostate adenocarcinoma who underwent open RRP and PLND between July 1988 and June 2008, and who were found to have metastatic LNs on pathologic exam. Patients were excluded if they had undergone preoperative radiation or androgen deprivation, or if their preoperative D'Amico risk group was indefinable. Kaplan Meier curves were constructed to estimate overall survival (OS), clinical recurrence free survival (CRFS), and biochemical recurrence free survival (BCRFS). Clinical recurrence was defined as biopsy proven palpable local disease, or distant metastases seen on imaging. Biochemical recurrence was defined as a rise in a postoperatively undetectable PSA to above the undetectable ultrasensitive level (currently <0.03 ng/ml) and verified by two consecutive increases.

**Results:** Median follow-up for the entire cohort was 7.2 years (range 1-21 years), and a median of 16 LNs were removed per patient. There were 150 patients with LN+ disease (80 with 1 positive LN (+LN), 40 patients with 2 +LNs, and 30 patients with  $\geq 3$  +LNs), and of these there were 49 patients (33 with 1 +LN, 13 with 2 +LNs, and 3 with  $\geq 3$  +LNs) who did not undergo any adjuvant therapy. The median follow up for this subgroup was 10.4 years, and 51% of these patients were over age 65. In this surgery only cohort, 29% of patients were high risk, 54% were intermediate risk, and 78% had pT3a or pT3b primary tumors. The 5 and 10 year BCRFS rates for patients treated with surgery only were 82% and 59%, respectively, 5 and 10 year CRFS rates were 88% and 80%, respectively, and the 10 year OS for this cohort was 81%. Of the 24 patients treated with surgery only who experienced no recurrences, 96% had <3 +LNs, 79% were intermediate or high risk, 33% had pT3a primary tumors, and 46% had pT3b primary tumors.

**Conclusions:** There is a low incidence of unexpected LN metastases in patients with clinically localized prostate cancer undergoing RRP. Open RRP with a thorough PLND was curative in a subset of patients with intermediate risk disease, pT3a/ pT3b primary tumors, and low volume lymph node metastases.

**Source of funding:** none