

LOCALLY ADVANCED PROSTATE CANCER: A POPULATION-BASED STUDY OF TREATMENT PATTERNS

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(Presentation to be made by Dr. William T. Lowrance)

PURPOSE: There are numerous modalities and variable recommendations for the treatment of locally advanced prostate cancer (LAPC). We aimed to identify treatment patterns and predictors of receiving multimodality therapy in men with LAPC.

MATERIALS and METHODS: From Surveillance, Epidemiology and End Results (SEER) cancer registry records linked with Medicare claims, we identified men 66 years and older with clinical stage T3 or T4 nonmetastatic prostate cancer diagnosed between 1998-2005. We classified treatments (radical prostatectomy [RP], radiation therapy [RT], and androgen deprivation therapy [ADT]) received within 6 and 24 months of diagnosis. We assessed trends over time and used multivariable logistic regression to identify predictors of multimodality treatment.

RESULTS: Within the first 6 months of diagnosis, 1,060 of 3,095 patients (34%) were treated with a combination of RT and ADT, 1,486 (48%) received monotherapy (RT alone, ADT alone, or RP alone), and 461 (15%) received no active treatment. The proportion of men who received RP increased, exceeding 10% in 2005. Use of combined RT and ADT and use of ADT alone fluctuated throughout the study period. Six percent of men received RT alone in 2005. Multimodality therapy was less common in patients who were older, African American, unmarried, lived in the South, had comorbidities, or stage T4 disease.

CONCLUSIONS: Treatment of LAPC varies widely, and treatment patterns shifted during the study period. The increased use of multimodality therapy since 2003 is encouraging, but further work is needed to increase combination therapy and define the role of RP.

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PREOPERATIVE FISH OIL SUPPLEMENTATION DOES NOT ALTER OPERATIVE BLOOD LOSS OR TRANSFUSION REQUIREMENTS IN PATIENTS UNDERGOING RADICAL PROSTATECTOMY

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(Presentation to be made by Dr. Stepanian)

Purpose: The cardio-protective effect of fish oil supplementation may be due, in part, to the ability of omega-3 fatty acids to limit thrombosis, possibly by reduction in thromboxane A2 and inhibition of platelet aggregation. We sought to determine if high dose fish oil supplementation leads to increased blood loss in men undergoing prostatectomy who participated in a randomized trial.

Materials and Methods: In a prospective, randomized study evaluating a low-fat fish oil intervention, 48 patients were randomized to either a western (40% kcal fat) diet (WD) or a low-fat (15% kcal fat) diet supplemented with 5 grams of fish oil (FO) daily for 4-6 weeks prior to open radical retropubic prostatectomy (RRP), or minimally invasive radical prostatectomy (MIP) (laparoscopic or robotic prostatectomy). The primary aim of the trial was to evaluate the effects of the diet and fish oil on prostate cancer related biomarkers. Here, we report the effect of FO supplementation on mean estimated blood loss (EBL), the mean preoperative and postoperative hematocrit (Hct), and transfusion requirements.

Results: Twenty-two, and 26 patients completed the trial in the WD and FO groups respectively. In the WD group, 15 and 7 patients underwent RRP and MIP respectively, and in the FO group, 13 patients underwent RRP and 13 underwent MIP. Patients in the WD and FO groups had similar EBL regardless of whether they underwent RRP (WD 727mL, FO 1058, $p=0.15$), or MIP (WD 207mL, FO 223, $p=0.93$). Mean preoperative Hct was similar in each group (WD 40.9%, FO 42.0, $p=0.36$). Regardless of surgical approach, Hct levels did not differ significantly between groups in the immediate postoperative period (RRP: WD 32.1%, FO 30.6, $p=0.20$; MIP: WD 33.3%, FO 35.6, $p=0.25$), or on postoperative day one (RRP: WD 30.1%, FO 29.4, $p=0.60$; MIP: WD 33.2%, FO 34.7, $p=0.43$). Among patients undergoing RRP, five patients in the WD group (26.7%) and four patients in the FO group (38.5%) required blood transfusions ($p=0.69$). Six and ten total blood transfusions were administered for RRP patients in the WD and FO groups respectively, and mean number of transfused units per patient were similar between the groups (WD 0.40, FO 0.77, $p=0.34$).

Conclusions: In this prospective, randomized study, 5 grams of fish oil supplementation daily for four to six weeks prior to open or minimally invasive radical prostatectomy did not result in greater blood loss or transfusion requirements compared to a western diet group. This data suggests that fish oil supplementation does not need to be discontinued prior to radical prostatectomy.

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ANATOMICAL EXTENDED PELVIC LYMPH NODE DISSECTION AT ROBOT-ASSISTED LAPAROSCOPIC RADICAL PROSTATECTOMY

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(Presentation to be made by Dr. Yuh)

Introduction: For improved oncologic staging and potentially therapeutic reasons, an extended pelvic lymph node dissection may be beneficial to patients with localized prostate cancer. The 3-dimensional magnification of the surgical robot (da Vinci) allows for clear visualization of the pelvic anatomy and known potential drainage sites for prostate cancer.

Methods: 83 consecutive patients with localized moderate or high risk biopsy proven adenocarcinoma of the prostate underwent robot-assisted laparoscopic radical prostatectomy and concomitant extended pelvic lymph node dissection at a single institution. Lymph node dissection was performed bilaterally in all patients from the common iliac bifurcation to the Node of Cloquet. A pelvic drain was placed in every patient.

Results: For each patient separate bilateral lymph node packets were sent from the common iliac, external iliac, internal iliac, obturator, and Node of Cloquet groups. Mean lymph node yield was 19(range 9-39). No intraoperative complications occurred and no patients developed a postoperative symptomatic lymphocele. Total time of lymph node dissection was 45 minutes. 9 (10.8%) patients were found to have metastatic prostate cancer in the lymph nodes. Positive margin rate was 18.1% and 21 (25.3%) were pT3 or above.

Conclusions: Extended sampling of pelvic lymph nodes in the context of prostate cancer leads to increased detection of positive lymph nodes. Methodical anatomic dissection does not appear to increase surgical complication rates.

MANAGEMENT OF COMPLICATIONS FOLLOWING PROSTATE CANCER THERAPY

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(Presentation to be made by Dr. Uwais Zaid)

Purpose: Prostate cancer is the most common malignancy and second leading cause of cancer death in American men. We sought to characterize complications of prostate cancer therapy in patients referred to our institution for surgical intervention.

Materials and Methods: Data was abstracted from a prospectively collected single surgeon database. Variables included age, prostate cancer therapy, complication(s) arising from this therapy, management of these complications, and outcome. Outcome was defined by the attending surgeon's assessment of patient progress at follow up clinic visits.

Results: From 2006-2010, 870 patients underwent genitourinary reconstructive surgery; 134 of these cases were to treat complications arising from prostate cancer therapy (Figure 1). Of the complications we managed, 49 (36.6%) patients had previously undergone radical prostatectomy (RP) monotherapy, 32 (23.9%) underwent RP with adjuvant external beam radiation therapy (XRT) or brachytherapy (BT), 11 (8.2%) underwent XRT monotherapy, 11 (8.2%) were treated with BT monotherapy, and 22 (16.4%) underwent both BT and XRT. Additional treatment modalities include salvage RP in 7 (5.2%), high intensity focused ultrasound and cryotherapy both in 1 (0.7%) of patients. With regards to complications arising from treatment of prostate cancer, there were 59 cases of urinary incontinence (UI). 52 (88.1%) occurred in the RP monotherapy group, 24 (40.7%) occurred in the RP with XRT or BT group, 6 (10.2%) occurred in the radiation therapy groups, and 1 (1.7%) in the salvage RP group. There were 24 cases of fistulas (rectovesical or rectourethral). 10 (41.2%) occurred in the RP monotherapy group, 1 (4.2%) in the RP with XRT or BT, 8 (33%) in the radiation groups, and 6 (16.7%) in the salvage RP group. 52 cases of urethral stenosis were reported. 7 (13.4%) occurred in the RP monotherapy group, 10 (19.2%) in the RP with XRT or BT group, 33 (63.5%) in the radiation group, and 1 (1.9%) in the salvage RP cohort. There were 25 cases of bladder neck contracture. 12 (48.0%) occurred in the RP monotherapy group, 10 (40.0%) occurred in the RP with XRT or BT group, 1 (4.0%) occurred in the radiation group, and 2 (8.0%) in the salvage RP group. Common interventions undertaken included urethral sling, artificial urinary sphincter placement, urethral reconstruction, UroLume urethral stent placement, direct vision internal urethrotomy (DVIU), and repair of fistula. The majority of patients reported a clinical improvement (81%).

Conclusions: We operatively managed patients treated with both non-surgical and surgical modalities for their prostate cancer. Complications included urinary incontinence, fistula formation, urethral strictures, and bladder neck contractures. These were managed with a variety of operative interventions, including urethral sling, artificial urinary sphincter, urethral reconstruction, and repair of fistula.

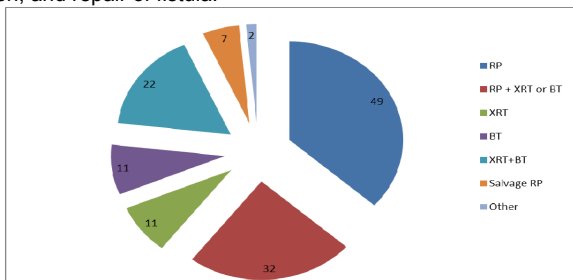


Figure 1: Number of patients referred to our practice for surgical management of complications stratified by initial prostate cancer treatment modality(RP: radical prostatectomy, XRT: external beam radiation therapy, BT: brachytherapy, Other: High intensity focused ultrasound and cryotherapy)

USE OF T3 MRI FOR SURGICAL PLANNING OF PROSTATE CANCER PRIOR TO ROBOT-ASSISTED RADICAL PROSTATECTOMY

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(Presentation by Dr. Yuh)

Introduction: Pretreatment staging of prostate cancer can be important for assessing local extension and distant spread of disease as it impacts survival. When a surgical approach is considered this may beget a patient specific excision based on anatomical imaging or help determine the need for combination therapy.

Methods: Between January and October 2010, 21 patients with biopsy proven adenocarcinoma of the prostate underwent Tesla-3(T3) magnetic resonance imaging (MRI) prior to robot-assisted laparoscopic radical prostatectomy.

High-resolution images of the prostate gland and pelvis were obtained in multiple phases. No endorectal coil was used. All patients were also evaluated with bone scan and/or computed tomography of the abdomen and pelvis. Ipsilateral wide resection of the neurovascular bundle with intraoperative frozen sections was undertaken if strong evidence of extracapsular extension or seminal vesicle invasion was noted from MRI. We correlated the accuracy of predicting pathologic stage, seminal vesicle invasion, and lymph node metastases from MRI.

Results: Mean age of patients was 62 (range 49-73). 15 of 21 patients (71%) had an abnormal digital rectal exam. Mean PSA was 10.5 (range 4-20) ng/ml. Despite enhanced vision and magnification, intraoperative findings were difficult to correlate to MRI abnormalities. The accuracy of T3 MRI was 71%, 86%, 91% for predicting extracapsular extension, seminal vesicle invasion and lymph node disease respectively.

Conclusion: MRI is reasonably accurate at predicting adverse stage characteristics in prostate cancer. Improved resolution of imaging modalities, in particular T3 MRI, will continue to improve diagnostic power in the future. This is important not only for assessing appropriateness of treatment, but for surgical planning and consoling patients regarding realistic risks and expectations.

SMALL PROSTATE SIZE AND HIGH GRADE CANCER

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(Presentation to be made by Dr. Ngo)

Purpose: Several groups have reported an association between small prostate size and high grade cancer in radical prostatectomy series. Some have hypothesized that small prostate size signifies a hormonal milieu low in androgens that selects for less hormone dependent, more aggressive cancers. We recently showed in the Stanford Radical Prostatectomy Database that this association exists in those with clinical T1c but not T2 prostate cancer and suggested that this association resulted from ascertainment bias due to the performance characteristics of PSA rather than cancer biology. Nevertheless, a radical prostatectomy series contain a highly select group of patients who underwent prostate biopsy, had a positive finding, and elected to undergo surgical treatment. To better evaluate the relationship between prostate size and high grade prostate cancer in a more generalized population, we analyzed data from the Stanford Prostate Needle Biopsy Database (SPNDB).

Materials and Methods: The SPNDB 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 first time, extended scheme (12 cores or more) prostate needle biopsies that were positive for cancer. High grade prostate cancer was defined as having a Gleason score of 7 or higher. Clinical variables examined were patient age, race, PSA, Gleason score, clinical T stage, family history of prostate cancer. Prostate size was defined by TRUS volume determined at the time of prostate biopsy by the formula $V = \pi/6 \times \text{length} \times \text{width} \times \text{height}$ (in cm). Univariate and multivariate analysis were used to characterize the association between prostate size and high grade prostate cancer.

Results: Between 1998-2010, 1295 patients underwent a first time extended prostate needle biopsy scheme. Of these, 44.9% (N=582) were positive and 30.7% (N=398) had high grade prostate cancer. Of those with prostate cancer, 58.6% (N=341) were clinical T1c and 41.4% (N=241) were clinical T2 or greater. In univariate analysis, those with high grade prostate cancer had significantly smaller prostates (mean TRUS volume 50.3 mL vs. 41.1 mL, $p < 0.0001$). In multivariate logistic regression, smaller prostate size was associated with high grade disease when all patients were included in the model ($p = 0.0001$). However, when we stratified the analysis by clinical T stage, small prostate size independently predicted high grade prostate cancer only for those with clinical T1c prostate cancer ($p = 0.001$) but not for those with clinical T2 or greater prostate cancer ($p = 0.09$).

Conclusions: In a more generalized population, small prostate size does not consistently predict high grade cancer when stratified by clinical T stage. Therefore, this effect more likely resulted from ascertainment bias rather than an underlying biological process.

Sources of Funding: None

IMPACT OF NERVE PRESERVATION DURING PROSTATECTOMY ON LONG-TERM URINARY FUNCTION

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(Presentation to be made by Dr. O'Neil)

Purpose: The relationship between urinary continence and neurovascular bundle preservation after prostatectomy is controversial. Studies examining this association are often methodologically flawed. Limitations include the lack of validated quality of life (QOL) questionnaires, retrospectively collected data, and outcomes from multiple surgeons with different techniques for apical dissection. Further, most studies do not validate the degree of their nerve-sparing techniques with post-operative sexual function data. We examined the effect of neurovascular bundle preservation on post-operative urinary function addressing these aforementioned issues.

Material and Methods: Eight hundred and three consecutive patients undergoing radical retropubic prostatectomy (RRP) or Robotically-Assisted Laparoscopic Radical Prostatectomy (RALRP) were prospectively studied using the Expanded Prostate Cancer Index Composite (EPIC). Patients were evaluated preoperatively and post-operatively at 3, 6, 9, 12, 18 and 24 months. Statistical analysis adjusted for age and baseline sexual and urinary function.

Results: Of the patients who completed a questionnaire after 6 months (n=703), 340 underwent a bilateral nerve-sparing procedure, 241 a modified and 122 underwent a non-nerve-sparing (wide-excision) prostatectomy. The respective EPIC function scores were 77.5, 77.4 and 61.0 for urinary function and 48.7, 28.6 and 5.8 for sexual function. Urinary function was significantly different comparing any degree of nerve sparing to non-nerve sparing prostatectomy even after controlling for age and baseline sexual function scores ($p < 0.0001$).

Conclusion: Bilateral and unilateral nerve-sparing prostatectomy was associated with better urinary function rates than non-nerve-sparing prostatectomy.

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PROSTATE-SPECIFIC ANTIGEN SCREENING IN PATIENTS WITH END-STAGE RENAL DISEASE

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OBJECTIVES: Patients who are being evaluated for renal transplant (RT) must have non-cutaneous malignancy excluded in order to be eligible for RT. There is no agreed upon PSA cut point to prompt prostate biopsy (PB) in this patient population. The purpose of this study is to evaluate PSA cut points and PC detection in patients with end stage renal disease (ESRD) and pending RT.

METHODS: A retrospective review was conducted of 820 patients at a single institution who are or have been on the RT waiting list that had serum PSA measurement. After stratification by age at the time of screening, serum PSA levels from patients without evidence of PC were evaluated to determine a 95th percentile reference range for each age decade. Patients who underwent a PB (n=82) were reviewed to determine if the current screening indication is appropriate for patients with ESRD.

RESULTS: The serum PSA 95th percentile reference ranges for patients with ESRD is 0.0 to 2.1 ng/mL at 40-49 years, 0.0 to 3.5 ng/mL at 50-59 years, and 0.0 to 4.7 ng/mL at 60-69 years. Mean age of all patients evaluated was 55 (20-77), of patients biopsied was 61 (39-77), and of patients diagnosed with PC was 64 (49-77). In patients with PSA \geq 4 ng/mL (n=53), prostate biopsies detected PC in 41.5% of the patients, with an additional 5.8% of patients having pre-malignant changes (atypical small acinar proliferation ASAP or high-grade prostatic intraepithelial neoplasia HGPIN). For all patients with PSA between 2.5 and 4 ng/mL (n=26), the PC detection rate was 42.3%, with an additional 12% of patients having pre-malignant changes. Overall, prostate biopsy for PSA greater than 2.5 showed PC in 41.8% of patients, pre-malignant lesions in 7.7%.

CONCLUSIONS: Patients with ESRD who are undergoing evaluation for RT have PSA reference ranges similar to those established for the non African-American US population. Clinical use of a PSA cutoff of 2.5 ng/mL results in a significant detection rate of PC and pre-malignant lesions (49.5%) which affect RT candidacy. Given that current best practice mandates cancer free status prior to RT, lower PSA cutoff values should be considered to improve the sensitivity of PC detection in this patient population.

SOURCE OF FUNDING: None.

DO REPEATED PROSTATE BIOPSIES WORSEN THE OUTCOME AMONG MEN WITH PROSTATE CANCER WHO HAVE A RADICAL PROSTATECTOMY? RESULTS FROM THE SEARCH DATABASE

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(Presentation to be made by Dr. Kopp.)

OBJECTIVES: Patients express concern over the risk posed by repeat prostate biopsy. It is of particular concern for patients who have repeat prostate biopsies as part of active surveillance follow-up. It is unclear if repeated biopsies may increase the risk of local or distant relapse. We sought to evaluate the impact of repeat biopsy sessions on biochemical recurrence among men who underwent radical prostatectomy using the Shared Equal Access Regional Cancer Hospital (SEARCH) cohort.

METHODS: Men undergoing radical prostatectomy between 1988 and 2010 with known data on number of prior biopsy sessions were evaluated. Number of prior biopsy sessions (range 1-8) was examined as a continuous and categorical (1, 2, 3-8) variable. Biochemical recurrence was defined as PSA > 0.2 ng/ml, 2 values at 0.2 ng/ml, or secondary treatment for an elevated PSA. The association between number of prior biopsy sessions as a categorical variable and clinical characteristics was tested using Kruskal-Wallis and chi-squared. The association number of prior biopsy sessions and PSA recurrence was analyzed using Cox-proportional Hazard models adjusted for demographic and clinicopathological characteristics at the time of diagnosis.

RESULTS: Of 2,297 men in the SEARCH database, 1,977 (86%) had only one biopsy, 217 men (9%) had two biopsy sessions, and 103 (4%) had 3 or more. More prior biopsy sessions was associated with higher PSA ($p=0.0001$), more recent year of surgery ($p=0.02$), and a trend toward lower Gleason scores ($p=0.06$). On multivariate analysis, there was a trend for more biopsy sessions as a continuous variable to be associated with lower risk of recurrence (HR 0.89, 95% CI 0.78-1.02, $p=0.09$). When examined as a categorical variable, relative to men with a single prior biopsy session, men with 2 sessions had similar recurrence risks (HR 1.07, 95% CI 0.83-1.39, $p=0.61$), while there was a suggestion men with 3 or more sessions had a reduced risk, which did not reach statistical significance (HR 0.71, 95% CI 0.47-1.07, $p=0.11$).

CONCLUSIONS: Multiple biopsy sessions are not associated with an increased risk of biochemical recurrence in men undergoing prostatectomy. Multiple biopsy sessions likely improve detection of low volume cancers and appear to select for a low risk cohort. Patients can be reassured that repeated biopsies do not appear to worsen prostate cancer outcomes after radical prostatectomy.

USE OF RECTAL CULTURE SPECIFIC ANTIBIOTICS FOR PATIENTS UNDERGOING TRANSRECTAL ULTRASOUND GUIDED PROSTATE NEEDLE BIOPSY

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(Presentation to be made by Dr. Santomauro)

Introduction and Objectives: The TRUS guided prostatic biopsy is one of the most common outpatient urologic procedure with some 800,000 performed annually in the United States. The risk of bacteremia and bacteriuria, and clinical infection has steadily increased in recent years with the advent of bacterial resistance. At our own institution, we have noted an increasing number of post procedure cases of bacteremia and frank urosepsis requiring hospitalization, extended courses of antibiotics, and associated morbidity. The aim of this study was to assess whether or not targeted antibiotic prophylaxis improved infection rates after biopsy.

Methods: From Oct 2010 until Mar 2011, we obtained rectal swabs on 130 patients who were scheduled for a transrectal ultrasound guided biopsy. The rectal swabs were cultured using selective media by the same laboratory with emphasis on fluoroquinolone resistance E-coli. Sensitivities were obtained and patients were given appropriate culture specific antibiotics for the procedure.

Results: Of the 130 patients who had rectal cultures obtained, 18 participants had documented culture positive fluoroquinolone resistant bacteria for an overall rate of 13.8%. Overall, 76 of the 130 patients had taken antibiotics within the last 12 months. Of the 18 who had resistant bacteria, 10 had taken antibiotics within the previous 12 months ($p=0.8$, OR 1.06). Of the patients who had no history of previous biopsy (75 of 130), approximately 20% had a resistant culture compared to 9.4% patients who had a prior biopsy (OR .41). Regarding ethnicity, Asians had the highest chance of resistance (OR 2.53). While using culture specific antibiotics for the procedure, there were no documented cases of post-biopsy fevers warranting admission.

Conclusion: Screening procedures in otherwise healthy men should be safe and associated with minimal adverse effects and/or complications. Our study shows that a recent history of antibiotic use or prior prostate biopsy does not seem to be associated with resistance and therefore cannot be used as surrogate for potential resistance. There seems to be an association with Asian cultural descent. This requires further study and verification. A direct comparative study is warranted, but difficult to perform in the face of apparent benefit of preemptive culture. Our study seems to have demonstrated that culture specific antibiotics for TRUS guided biopsy mitigates some of the infectious risks.

**RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED TRIAL OF
POLYPHENON E IN PROSTATE CANCER PATIENTS BEFORE RADICAL
PROSTATECTOMY: EVALUATION OF POTENTIAL
CHEMOPREVENTIVE ACTIVITIES**

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(Presentation to be made by Dr. Nguyen)

Purpose: Retrospective and in-vitro studies suggest that green tea may be effective in the chemoprevention of prostate cancer. The purpose of this study was to measure the bioavailability of green tea catechins in prostate tissue and to assess its effects on serum and tissue biomarkers of prostate cancer carcinogenesis, in men with prostate cancer given catechins in Polyphenon E pill form.

Materials and Methods: The study was a randomized, double-blind, placebo controlled intervention trial. Patients with a diagnosis of prostate cancer who were scheduled to undergo radical prostatectomy were randomly assigned to receive either Polyphenon E or placebo for 3-6 weeks before surgery. Catechin levels were measured in serum and prostate tissue to assess bioavailability. Serum biomarkers measured included PSA, 8-hydroxydeoxyguanosine to deoxyguanosine ratio (8OHdG/dG ratio), serum Insulin-like growth factor 1 levels (IGF1), and Insulin-like growth factor-binding protein 3 levels (IGFBP3). Tissue biomarkers included Ki-67 for proliferation, cleaved caspase 3 for apoptosis, and microvessel density for angiogenesis. Change in Gleason's score between biopsy and surgical specimens was also assessed.

Results: Serum levels of catechins were achieved in the Polyphenon E intervention subjects but tissue bioavailability was low to undetectable for all measured catechins. Systemic biomarker endpoints demonstrated a favorable trend but no statistical significance for PSA (-0.66 versus -0.08 ng/ml, $p=0.26$), 8OHdG/dG ratio (-0.79 versus 1.81, $p=0.17$), IGF1 (-6.89 versus -1.20 ng/ml, $p=0.53$) and IFGBP3 levels (20.38 versus 74.76 ng/ml, $p=0.24$) for Polyphenon E versus placebo subjects, respectively. Tissue biomarkers did not differ between the treatment and control arms for Ki67 (5.65 versus 4.37%, $p=0.68$), cleaved caspase 3 (0.39 versus 0.46%, $p=0.29$), and microvessel density (22.43 versus 23.04 microvessels per 40X field, $p=0.89$) respectively. The proportion of subjects who had a decrease in Gleason score between biopsy and surgical specimens was greater in those on Polyphenon E but this was not statistically significant (20.8 versus 8.3%, $p=0.22$).

Conclusions: Prostate tissue catechin concentrations were low or undetectable after 3-6 weeks of oral intervention, suggesting activity, if occurring, is through indirect means. Trends observed in serum biomarkers suggest potential efficacy of Polyphenon E for prostate cancer chemoprevention but the short duration of intervention and small sample size of this trial may have precluded detection of statistically significant changes in serum or tissue biomarkers.

Source of funding: This work was supported by a contract (N01-CN35158) from the National Cancer Institute.

UPGRADING AT RADICAL PROSTATECTOMY BETWEEN COMMUNITY AND ACADEMIC UROLOGISTS

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(Presentation to be made by Dr. Lee)

Objective: Gleason upgrading from biopsy to radical prostatectomy (RP) is an important event as treatment decisions are made based on the biopsy score. Factors thought to explain discordant Gleason scores between biopsy and RP are interobserver variability in biopsy pathologic interpretation and sampling error, potentially through inadequate sampling. Recent studies of upgrading have primarily been limited to men undergoing both biopsy and RP at a single institution. Differences in upgrading between men diagnosed at referral centers vs. community centers has not been explored. We determine the factors associated with Gleason upgrading at a referral center where many RPs are performed following initial diagnosis from biopsies obtained from a community setting.

Material and Methods: We reviewed our database of men undergoing RP for Gleason 3+3 or 3+4 disease at our regional academic referral center. Outside pathology slides were centrally reviewed and Gleason score assigned. Multivariate logistic regression was used to determine factors associated with Gleason upgrading, including where the biopsy was performed, age, PSA, year of RP, total and positive cores, prostate weight and secondary biopsy pattern (3 vs. 4).

Results: Data were available from 1,375 men. There was no difference in upgrading at RP by whether the biopsy was performed at our referral center or outside community (OR 1.0, 0.7 – 1.3). An increased risk of upgrading was seen in those with > 1 positive core, those treated in more recent years, in older men and those with higher PSAs. Compared to those aged < 60, the risk of upgrading was increased in those aged 60-69 (OR 1.4, 1.1 – 1.9) and those ≥ 70 years (OR 3.3, 2.1 – 5.2). Secondary biopsy pattern 4 and larger prostate size were associated with a lower risk of upgrading. Compared to the smallest quartile of prostate size (< 35g), those in the highest quartile (> 56g) had a 40% reduction in risk of upgrading (OR 0.6, 95% CI 0.4 – 0.8). Limiting the analysis to those with only Gleason 3+3, those treated after the year 2000, or those with > 10 cores did not significantly change the results.

Conclusions: There was no difference in upgrading between where the biopsy was performed, suggesting comparable prostate sampling between community and academic urologists. Several factors are significantly associated with Gleason upgrading at RP such as older men, smaller prostates and higher PSAs. These data can be used to identify those at greatest risk of upgrading. With an increasing number of patients on active surveillance protocols, these data can help select those who may benefit from early rebiopsy or extended-biopsy schemes.

Source of Funding: None

SELECTIVE INTRA-ARTERIAL TARGETING OF THE HUMAN PROSTATE.

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(Presentation to be made by Dr. Moore)

Background and Objective: Prostate disease, both benign and malignant, causes a significant healthcare burden. The incidence of both increase with aging, with over 50% of men over 50 yrs having symptoms of benign prostate hypertrophy (BPH), and 30% of men having prostate cancer (PCa). As life expectancy increases the other significant disease affecting survival and quality of life is cardiovascular disease, with 50% of men succumbing to this disease. Experimental targeted therapies have been exploring embolization of the prostate for treatment of BPH and intra-arterial (IA) delivery of photosensitizer for photodynamic therapy (PDT) and liposomal encapsulated nucleic acid for gene therapy of PCa. In the patient population undergoing coronary angiography we wished to determine the ability to target the prostate gland intra-arterially. We have previously published our preclinical studies on canine IA targeting of the prostate.

Methods: Following institution ethics approval, patients undergoing coronary angiography were consented to additionally undergo IA delivery of ^{99m}Tc Macro Aggregated Albumin (^{99m}Tc MAA) either unilaterally or bilaterally in a serial fashion. IA access was gained using a standard femoral Seldinger technique and a 3F tracker angiocatheter floated to the prostatovesical artery. After a confirmatory blush of low ionic contrast; 200 mega Becquerel (MBq) of ^{99m}Tc MAA (2mg/ml) in 1 ml of normal saline (NS) was delivered per side. Immediately following delivery the patients were imaged with single photon computed tomography (SPECT)/CT scan. The amount and location (inside and outside of the prostate) of drug and the percentage of prostate labeled were determined by region of interest (ROI) analysis. PSA and voiding symptoms were monitored pre and post delivery of ^{99m}Tc MAA. The study remains ongoing.

Results: To date we have accrued 15 patients to the study. Two were excluded from analysis, with 1 patient not injected due to angiography difficulty and the other had anomalous anatomy with the fiducial markers erroneously moved making SPECT and CT fusion impossible. Of the remaining 13 patients, 3 patients had bilateral MAA injections (still accruing). The bilateral injection cases demonstrated more activity within the prostate but greater activity within extra prostatic structures as well. Two of the unilateral only injections had no prostate activity. Unlike the canine studies there was midline cross-over with 6/13 patients having bilateral prostatic activity. No extra prostatic activity was observed in 4/13, while 9/13 had extra prostatic activity including the following sites: unilateral seminal vesicle (4 patients), bilateral seminal vesicle (1 patient), bladder neck wall (3 patients), rectal wall (2 patients), and space of Retzius (2 patients). Some patients more than 1 site. Although the volume of the prostate varied greatly, the measured distribution on average was 50% of the gland for unilateral delivery. Consistent with the pioneering micropaque blood supply work of E. J. Clegg (J. Anat. 89:p209; 1955) the anatomy was variable especially at the origin of the prostatovesical artery. No patient had sequelae and only 2 had a minor elevation in serum PSA.

Conclusions: This unique approach for mapping IA vascular distribution to target organs confirms our prior canine studies that it is possible to selectively target the prostate in this population. The process of dual targeting as proposed for PDT may be more desirable given the extra prostatic distribution. However, pro-apoptotic drug therapy could be repeatedly or continuously administered for targeted effect. Furthermore, this labeling technique could be used to map the IA distribution in other organs and assist in planning targeted drug delivery.

Source of Funding: Alberta Innovates Health Solutions/Mr. Lube Foundation/ H. Gusse Foundation

PERFORMANCE CHARACTERISTICS OF PSA IN PATIENTS UNDERGOING RADICAL PROSTATECTOMY

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(Presentation to be made by Jen-Jane Liu)

Purpose: The performance characteristics of PSA are improved for predicting the *presence* of high grade prostate cancer. We assessed the performance characteristics of PSA for predicting the *volume* of cancer or *volume* of high grade cancer in men undergoing radical prostatectomy.

Materials and Methods: We identified 1307 patients from the Stanford Radical Prostatectomy Database with clinical stage T1c (n=658) and T2 (n=549) disease who underwent surgery between 1988 and 2002 and had detailed morphometric mapping by a single pathologist. We generated receiver operating characteristic (ROC) curves for PSA based on total tumor volume and volume of Gleason 4 or 5 disease and compared the areas under the curve (AUC) for different cut points of total and high grade cancer volume.

Results: For patients with T1c disease, the AUC for the PSA ROC curve increased in a stepwise fashion as total cancer volume increased. Specifically, the AUCs for 0.5 cc, 1 cc, 2 cc, 3 cc, and 5 cc were 0.62, 0.66, 0.72, 0.72, and 0.79, respectively, with significant differences noted in the AUC between 0.5, 2, and 5 cc of total cancer volume. For high grade cancer volume the AUC for the PSA ROC curve for 0 cc, 0.2 cc, 0.5 cc, 1 cc, 2 cc, and 3 cc was 0.66, 0.67, 0.68, 0.69, 0.72 and 0.76, respectively, with significant differences in AUC for low volumes of high grade disease (0, 0.2, and 0.5 cc) compared to high volumes (3 cc). For T2 disease, AUCs for predicting high grade cancer volume were generally higher than the corresponding AUCs for T1c disease but no incremental increase was observed.

Conclusions: In T1c patients, where PSA was the driving force for biopsy, PSA performance improved in a stepwise fashion with higher total and high grade cancer volumes as evidenced by improved receiver operating characteristics. Prior studies show that PSA performs better for detecting the *presence* of high grade disease; here, we show that PSA performs better in predicting *volume* of high grade disease in radical prostatectomy specimens.

Source of Funding: None

DO ALL PATIENTS WITH GLEASON 8 PROSTATE CANCER DIE OF THEIR DISEASE?

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(Presentation to be made by Dr. Koo)

Objective: Until very recently, patients with Gleason 8 prostate cancer were considered poor surgical candidates and were treated with external beam radiation therapy with or without androgen deprivation therapy. Some studies suggest that patients may be cured by multimodal therapy including radical prostatectomy (RP). Thus, we explored the natural history of a cohort of patients with Gleason 8 prostate cancer and attempted to ascertain predictors of prostate cancer specific-survival.

Methods: We retrospectively analyzed charts of patients who had pathologic Gleason 8 at time of RP. We then used Cox regression to evaluate clinical and pathologic variables that may predict prostate cancer-specific survival. We determined pathologic outcomes and rates of recurrence, survival, and cancer-specific survival using Kaplan-Meier analysis. Biochemical recurrence (BCR) was analyzed in patients operated after 1988, since systematic PSA follow up was instituted at that time and was defined at 0.1ng/ml.

Results: The cohort consisted of 117 patients. The median age was 65 years (range 49-93). The median PSA and median tumor volume were 9.60 (2-48) and 5.33 cc (0-50), respectively. Of all patients, 27.6% had a family history of prostate cancer, 68.1% were stage pT3 or higher, and 55.9% had positive margins. Of all patients, 40.7% had biochemical recurrence (BCR), 12.7% had metastatic disease, and 13.6% of patients died of prostate cancer. On both univariate and multivariate analysis, only margin status was a significant predictor of prostate cancer-specific survival, and patients were 4 times more likely to die of prostate cancer (HR 4.006; $p=0.038$). PSA, pathologic stage, family history, and secondary Gleason score were not significant. Kaplan-Meier estimated mean times to BCR and metastases were 16.8 years (14.5-19.1) and 22.7 years (21.0-24.4), respectively. Overall mean actuarial prostate-cancer specific survival was 21.6 years (19.6 -23.7). Patients with positive margin status had significant shorter mean actuarial time to prostate cancer death (19.4 vs. 22.0 years, $p=0.016$).

Conclusions: In this study, patients with very aggressive prostate cancer had acceptable rates of biochemical recurrence and only 13.6% of patients died of their disease. Moreover, patients that had positive margins were 4 times more likely to die of prostate cancer. This emphasizes the importance of meticulous surgical technique.

Source of funding: None

DO PATIENTS WITH GLEASON 6 PROSTATE CANCER DIE OF THEIR DISEASE?

Sandra J. Koo, MD, Dan J. Lewinshtein, MD, Christopher R. Porter, MD:
Seattle, WA

(Presentation to be made by Dr. Koo)

Objective: Very recently, a large study showed that patients with Gleason 6 prostate cancer will not die of their disease; however, our institutional prostate cancer database suggests that these patients may die of prostate cancer. Thus, we explored the clinical and pathologic characteristics of patients with Gleason 6 prostate cancer that died of their disease.

Methods: We retrospectively analyzed charts of patients who had pathologic Gleason 6 at time of RP and died of prostate cancer. We determined pathologic outcomes, and estimated rates of metastatic disease, overall- and cancer-specific survival using Kaplan-Meier analysis. BCR was analyzed in patients operated after 1988, since systematic PSA follow up was instituted at that time and was defined at 0.1ng/ml.

Results: The cohort consisted of 28 patients. The median age was 62.5 years (range 52-75). The median tumor volume was 13.5 cc (8-15). Median follow-up time was 12.3 years. Of all patients, 70.4% were stage pT3 or higher, and 50% had positive margins. All patients died of their disease. Kaplan-Meier estimated mean time to distant metastases was 9.3 years (6.9-11.6). Actuarial mean overall survival and prostate-cancer specific survival were identical at 13.5 years (11.1-15.9).

Conclusions: In our nested case series, all 28 patients with Gleason 6 cancer did die of their disease with a mean time to death of 13.5 years. These data suggest that patients with low-grade prostate cancer may, in fact, experience adverse clinical outcomes.

DO MULTIPLE PROSTATE NEEDLE BIOPSIES CAUSE PERSISTENT LOWER URINARY TRACT SYMPTOMS?

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(Presentation to be made by Dr. Koo)

Objective: Patients undergoing active surveillance for prostate cancer may be subject to multiple prostate biopsies. Two prior studies suggest that prostate needle biopsy (PNB) may cause transient lower urinary tract symptoms (LUTS). We explored whether multiple PNB may increase the risk for persistent LUTS.

Methods : We reviewed a prospectively organized database of 890 patients who underwent transrectal ultrasound (TRUS)-guided PNB. LUTS were modeled as a categorical variable as either moderate-severe or severe based on American Urological Association Symptom Score (AUASS). Moreover, we analyzed AUASS quality of life (QOL) as a categorical variable with those patients having mostly dissatisfied or worse QOL as impaired urinary QOL. Logistic regression was used to analyze the predictive ability of multiple PNB, which was adjusted for age, PSA, and prostate volume.

Results: Median age and PSA were 63 years (30-97) and 4.47 ng/ml, respectively. According to AUASS, 2.6%, 46.7%, 43%, and 7.8% had no, mild, moderate, and severe LUTS, respectively. Of all patients, 10.7% had impaired QOL and the median prostate volume was 42.6 cc. On multivariate analysis, prostate volume (HR=1.012; $p<0.001$) and age (HR=1.107; $p=0.033$) were predictive of moderate to severe AUASS. Only prostate volume was predictive of severe AUASS on multivariate analysis (HR=1.007; $p=0.003$). Predictors of impaired urinary QOL were prostate volume (HR=1.007; $p=0.031$) and age on multivariate analysis. History of previous PNB was neither predictive of AUASS ($p=0.09$) nor impaired urinary QOL ($p=0.447$).

Conclusions : Age and prostate volume were strong predictors of LUTS and impaired urinary QOL. Prior PNB did not increase the risk of increased AUASS or impaired urinary QOL. Patients should be reassured that PNB does not appear to directly cause LUTS.

Source of funding: None

STATUS OF ROBOTIC ASSISTED SURGERY AMONG CANADIAN UROLOGY RESIDENTS

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(Presentation to be made by Dr. Michael Robinson)

Purpose: Robotic-assisted surgery (RAS) has been rapidly adopted in Urology, especially in the United States. Although less prevalent in Canada, RAS is a growing and controversial field that has implications for resident training. We report on the status and perception of RAS among Canadian Urology residents.

Methods: All Canadian Urology residents from Anglophone programs were contacted by email and asked to participate in an online survey. Current resident exposure to, and perception of RAS was assessed with this survey.

Results: Fifty of 128 (39%) residents completed the survey. Fifty-two percent have been involved in RAS. Those who have not been involved in RAS express lower interest and lesser knowledge regarding RAS. Ninety-two percent of respondents feel the use of RAS will increase, although only 29% feel it is feasible in Canada. Just 24% and 36% feel RAS to be superior to open and laparoscopic techniques, respectively. Sixty-eight percent of residents in programs with a robot viewed it as detrimental to training, whereas 81% of residents in programs without one viewed its absence to either have no impact, or even be beneficial. Both groups expressed a desire for more experience with RAS.

Conclusion: The resident experience with respect to RAS is mixed. Overall, residents view RAS as an expanding field with potentially negative impacts on their present training, although they appear to desire the acquisition of more experience in RAS. We plan to monitor the evolution of these perceptions over next four years.

SILODOSIN FOR MEN WITH MODERATE OR SEVERE CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME: RESULTS OF A DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 STUDY

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(Presentation to be made by Kim E. Caramelli)

Purpose: Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is associated with debilitating lower urinary tract symptoms (LUTS) and urogenital pain in the absence of urinary tract infection. Silodosin, a roselective alpha-blocker, is an established therapy for LUTS of benign prostatic hyperplasia. In this double-blind, placebo-controlled, phase 2 study, the safety and efficacy of two different doses of silodosin were evaluated in patients with moderate to severe CP/CPPS.

Materials and Methods: Men aged ≥ 18 years with National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) total score ≥ 15 , NIH-CPSI pain score ≥ 8 , and pelvic pain for ≥ 3 months before screening were randomized to received silodosin 4 mg or 8 mg per day, or placebo. The primary efficacy endpoint was change from baseline to week 12 (last observation carried forward) in NIH-CPSI total score. Bonferroni correction was used to adjust for multiple comparisons of continuous variables between active and placebo treatments. A significance level of .025 was used for categorical variable comparisons.

Results: Of 151 participants (median age, 48.2y), 80.1% of patients had experienced pain for ≥ 1 year; 76.2% completed the study. Decrease from baseline to week 12 (mean \pm standard deviation) in NIH-CPSI total score was significantly greater with silodosin 4 mg (-12.1 ± 9.3) than placebo (-8.5 ± 7.2 ; $P=.022$). Silodosin 4 mg vs placebo also provided significant improvement in NIH-CPSI urinary symptom score (-2.2 ± 2.7 vs -1.3 ± 3.0 ; $P=.010$), NIH-CPSI quality of life impact score (4.1 ± 3.1 vs 2.7 ± 2.5 ; $P=.010$), and Medical Outcomes Study Short Form 12 physical component score (4.2 ± 8.1 vs 1.7 ± 9.0 ; $P=.049$). In addition, 55.8% of patients receiving silodosin 4 mg versus 29.4% receiving placebo ($P=.007$) reported marked or moderate improvement in global response assessment, with early termination counted as nonresponse. Silodosin 4 mg was well tolerated, with treatment-related incidences of dizziness and headache lower than those for placebo; 26.9% of patients receiving silodosin 4 mg experienced retrograde ejaculation (placebo, 1.9%). Treatment with silodosin 8 mg rather than 4 mg provided no additional clinical benefit.

Conclusions: Silodosin 4 mg may be an effective treatment option for patients with CP/CPPS.

Source of Funding: Watson Laboratories, Inc.

CONCURRENT AND PREDICTIVE VALIDITY OF A NOVEL ROBOTIC SURGERY SIMULATOR

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(Presentation to be made by Dr. Hung)

Purpose: To evaluate the concurrent and predictive validities (correlation of simulator performance with present and future actual robotic performances) of a novel robotic surgery simulator that utilizes the da Vinci Si Surgeon Console.

Materials & Methods: Robotic surgery trainees (experience ≤ 10 console cases) were recruited in this prospective, institutional review board-approved study. Participants performed a series of simulator exercises to capture baseline simulator performance. Expert robotic surgeons then evaluated baseline robotic performance of participants on three ex-vivo animal tissue exercises (bowel handling/resection, cystotomy & repair, partial nephrectomy) using validated laparoscopic assessment metrics. Study participants were randomized to simulator training or no simulator training with groups matched for baseline tissue scores. Participants in the training group underwent a 10-week curriculum on the novel da Vinci Skills Simulator (Intuitive Surgical, Mimic Technologies). Repeat of animal tissue exercises at study conclusion for all participants assessed potential improvement in performance. Spearman's correlation analysis evaluated the extent baseline simulator performance correlated with beginning of study robotic performance (concurrent validity) and end of study performance (predictive validity) on the animal tissue models. Kruskal-Wallis test compared performance between study arms.

Results: Participants in the simulator training and no simulator training groups were comparable in age, overall surgical experience, and robotic experience ($p > 0.05$). Baseline simulator performance significantly correlated with baseline performance (concurrent validity) and final tissue performance (predictive validity) on animal tissue exercises ($r = 0.7$ and 0.7 , respectively $p < 0.0001$). At baseline, the two arms had similar overall scores on the simulator and with animal tissue exercises ($p > 0.05$). Simulator training significantly enhanced tissue performance in the subgroup of trainees that had lower (below 50th percentile) baseline scores over their counterparts who did not receive simulator training ($p < 0.05$). The overall simulator-trained group outperformed the non-trained group on final tissue performance, although the difference was not significant ($p > 0.05$).

Conclusions: The da Vinci Skills Simulator has demonstrated significant concurrent and predictive validities. The benefit of simulator training appears to be more significant in trainees with low baseline surgical performance.

Source of funding: Intuitive Surgical

CONTEMPORARY TRENDS IN IMAGING USE AMONG MEN NEWLY DIAGNOSED WITH CLINICALLY LOCALIZED PROSTATE CANCER

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For the Urologic Disease of America Project. San Francisco, CA.

(Presentation to be made by Dr. Porten)

Background: Recent studies have found an ongoing over-use of imaging for clinical staging of low-risk prostate cancer. We aimed to determine updated trends of imaging utilization in three large cohorts of men diagnosed with various stages of disease.

Methods: We analyzed imaging trends of men with prostate cancer who were a part of Cancer of the Prostate Strategic Urologic Research Endeavor CaPSURE (1998-2006), were insured by Medicare (1998-2006), or were privately insured men (Ingenix database, 2002-2006). The rates of computerized tomography (CT), magnetic resonance imaging (MRI), and bone scan (BS) were determined in each cohort and time trends were analyzed by linear regression. For men in CaPSURE, demographic and clinical predictors of test use were explored using a multivariable regression model.

Results: Since 1998, there was a significant downward trend in BS (10.2%) use in the CaPSURE cohort. MRI and CT use had a slight downward trend in use (2.1% and 0.2% respectively). Among 54,322 Medicare patients, BS, CT, and MRI use increased by 2.1%, 10.8%, and 2.2% and in 16,161 privately insured patients, use increased by 7.9%, 8.9%, and 3.7% from during each study period respectively. In CaPSURE, the use of any imaging test was greater in men with higher risk disease (BS OR 1.57, CT OR 1.27, MRI OR 1.38). Men with Veteran's Affairs coverage were less likely to have a BS (OR 0.29, 0.18-0.47) or CT (OR 0.35, 0.20-0.61). Treatment type was found to affect the use of imaging modality, with men undergoing brachytherapy and EBRT having significantly greater odds of BS (OR 1.64 and 1.49) and CT (OR 1.72 and 1.39) compared with men treated with ADT (OR 0.42 and 0.53) and WW/AS (0.53 and 0.24) who were less likely to have imaging using these two modalities. In men who were imaged with MRI, only those treated with brachytherapy were significantly more likely to undergo imaging (OR 1.83). Age at diagnosis, race, level of education, and income were not significantly associated with a specific imaging pattern.

Conclusions: There is widespread misuse of imaging tests in men with low-risk prostate cancer, specifically for computerized tomography. These findings highlight the need for examination of incentives and other factors that drive over-use of imaging.

Source of Funding: Urologic Diseases of America

MULTIINSTITUTIONAL VALIDATION OF UCSF CANCER OF THE PROSTATE RISK ASSESSMENT-POSTSURGICAL SCORE FOR PREDICTION OF RECURRENCE POST RADICAL PROSTATECTOMY

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(Presentation to be made by Dr. Punnen)

Introduction: The UCSF cancer of the prostate risk assessment – postsurgical (CAPRA-S) is a novel risk assessment tool that uses postoperative pathological data to predict the risk of recurrence post radical prostatectomy. The objective of this study was to validate its use in a large external database.

Methods and Materials: The Shared Equal Access Regional Cancer Hospital (SEARCH) database is a registry of men who underwent radical prostatectomy at 4 Veterans Affairs and 1 active military medical center. Of the 2,211 men in the SEARCH database, 2078 (94%) had full data available to calculate a CAPRA-S score. The CAPRA-S is determined by adding up to 3 points each for PSA and pathological Gleason score, 2 points each for positive surgical margins and seminal vesicle invasion and 1 point each for extra-capsular extension and lymph node involvement. Performance of the CAPRA-S score was assessed and compared to the Stephenson nomogram using proportional hazards regression, the concordance (c) index, calibration plots and decision curves analysis.

Results: Among this cohort, the mean age was 62 (SD 6.3) years and 33.3 % of the men recurred. The median follow up time of men who did not recur was 60.7 months. The hazard ratio (HR) for each one-point increase in the CAPRA-S score was 1.42 (95%CI 1.37-1.46). The 5-year recurrence free survival for those patients with a CAPRA-S score of 0-2, 3-6 and 7-10 were 74%, 45%, and 18%, respectively. The CAPRA-S c-index was 0.74 in this validation set, compared to a c-index of 0.77 for the original development set and 0.73 for the Stephenson nomogram. The CAPRA-S score performed better than the Stephenson nomogram on both calibration plots and decision curves analysis.

Conclusion: The CAPRA-S score accurately predicted recurrence after radical prostatectomy in this large cohort of men. This validates its use as an effective prognostic tool to stratify men with prostate cancer for risk of recurrence post surgery.

DOES NEOADJUVANT HORMONAL THERAPY BEFORE SALVAGE CRYOTHERAPY IMPROVE TREATMENT OUTCOMES?

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(Presentation to be made by Dr. Schlaifer)

INTRODUCTION AND OBJECTIVES: Neoadjuvant Hormonal Therapy (NHT) in prostate cancer patients has previously been studied when combined with radiation therapy or radical prostatectomy (RP). It has been shown in high risk prostate cancer patients that NHT prior to external beam radiation therapy (EBRT) improves cause-specific and overall survival compared to EBRT alone. Conversely, NHT prior to RP decreases positive margins and early biochemical failure but by 3 years biochemical failure is equivalent in the group treated with NHT compared to patients treated with RP alone. In patients suffering local failure after EBRT we sought to determine if treatment with NHT prior to salvage cryotherapy improved functional or biochemical outcomes when compared to similar patients treated with salvage cryotherapy alone.

METHODS: Using the Cryo On Line Database (COLD) the records of 567 men treated with cryotherapy for biopsy proven recurrent prostate cancer following full dose radiation therapy were reviewed. All patients studied had NHT or no hormonal therapy (HT). Patients who received post-treatment HT were excluded. Pre-treatment parameters, complications, functional outcomes and biochemical failure using the Phoenix criteria were analyzed. The patients were stratified using D'Amico criteria into low, intermediate and high-risk groups.

RESULTS: 222 patients had NHT and 345 patients did not have HT. Freedom from biochemical failure at 5 years using the Phoenix criteria was 41.5% vs 41.0% ($p=0.47$) for NHT and no HT patients, respectively. Stratification into low, intermediate and high-risk groups also showed no significant difference between NHT and no HT groups using the Phoenix criteria ($p= 0.27$, 0.38, 0.87). Functional outcomes comparing NHT to no HT at 12 months were: incontinence 4.8% vs 7.3%, pad usage 9.5% vs 14.3%, urinary retention 7.2% vs 15.4%.

CONCLUSIONS: This retrospective study of salvage cryotherapy found no difference in biochemical free survival between the NHT and no HT groups, even when stratified by risk groups. There was minimal improvement in incontinence and pad usage with NHT. There was also a decreased likelihood of urinary retention in the group treated with NHT, probably due to prostate size reduction.

SOURCE OF FUNDING: The Cold registry is sponsored by an unrestricted research grant from Endocare. Data are held and analyzed by Watermark, an independent research company under the direction of an independent physician board.

CENTRAL VENOUS CATHETER UTILIZATION DURING THE IMPACT (D9902B) TRIAL: A REVIEW OF CENTRAL VENOUS CATHETER INCIDENCE AND ASSOCIATED ADVERSE EVENTS

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(Presentation to be made by Dr. Corman)

Objectives: Sipuleucel-T is an autologous cellular immunotherapy designed to stimulate an immune response against prostate cancer. Here we describe the frequency of central venous catheter (CVC) use and the incidence of infections associated with venous access in the Phase 3 IMPACT study of men with asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer.

Methods: 512 subjects were randomized 2:1 to sipuleucel-T or control administered Q2 weeks x3. Control was non-activated autologous peripheral blood mononuclear cells. The safety population comprised 506 subjects. 23.3% of subjects in the safety population had CVCs at some point during their study participation. To determine the incidence of AEs likely related to venous access, the Medical Dictionary for Regulatory Activities (MedDRA) category "Infections and Infestations" was searched. Selected terms included bacteraemia, bacterial infection, catheter bacteraemia, catheter related infection, catheter sepsis, catheter site infection, cellulitis, sepsis, staphylococcal bacteraemia, staphylococcal sepsis, and staphylococcal skin infection. Events occurring from registration until 30 days following last infusion or leukapheresis were analyzed.

Results: For the overall population, the risk of these infection types was 3.8% (19/506): 11.9% (14/118, 9 sipuleucel-T and 5 control) for subjects with CVCs and 1.3% (5/388, 3 sipuleucel-T and 2 control) for subjects without CVCs. For the majority of subjects with CVCs the events were Grade 3/4 (57.1% Grade 3, 14.3% Grade 4), and resolved with appropriate outpatient management, such as antibiotic therapy or CVC removal, without long-term sequelae (median AE duration 14 days, range 6 to 63 days). Subjects who had previously received chemotherapy had a higher rate of CVC use in this study (29.3% vs. 22.0%).

Conclusions: Most subjects treated with sipuleucel-T in this study did not require central venous access. For those subjects who did receive a CVC, there was an increased but manageable risk of infections associated with venous access. Clinical personnel should carefully evaluate venous access and the need for a CVC, especially for those with previous chemotherapy. The risks and benefits of CVC use should be addressed during this evaluation.

CAN ULTRASOUND PERFORMED DURING TRUS BIOPSY OF THE PROSTATE ENHANCE OUR ABILITY TO PREDICT VARIOUS PATHOLOGICAL OUTCOMES AT TIME OF RADICAL PROSTATECTOMY?

Sandra Koo, MD, Dan Lewinshtein, MD, Christopher Porter, MD:
Seattle, WA

(Presentation to be made by Dr. Koo)

Introduction and Objective: Studies have demonstrated that the presence of suspicious lesions on ultrasound (US) do not enhance our ability to predict whether a patient will have prostate cancer found on prostate biopsy. However, the ability of US to enhance prediction of pathological outcomes at time of radical prostatectomy (RP) is not presently elucidated. Thus, we explored the ability of suspicious lesions on US to predict higher Gleason grade and higher pathologic stage in a cohort of patients who had undergone transrectal ultrasound (TRUS) guided prostate biopsy and RP.

Methods: We retrospectively reviewed the charts of all patients who had been referred to Virginia Mason Medical Center for TRUS biopsy and who had undergone radical prostatectomy (RP) at our institution. We defined a suspicious US lesion as one that led the surgeon to biopsy in that location. Predictive variables included an abnormal digital rectal exam, preoperative PSA, suspicious lesion at time of TRUS biopsy, and biopsy Gleason sum. We used logistic regression and receiver operator curve (ROC) analysis to evaluate the ability of these variables to predict pathologic Gleason sum and stage at time of RP.

Results: The cohort consisted of 113 patients. Median age was 61 years and median PSA was 4.6 ng/ml. Of all patients, 69.9% and 42.5% had suspicious DRE or US lesion, respectively. At time of RP, 67.3% and 16.8% were Gleason 7 or higher and stage pT3 or higher, respectively. On multivariate analysis for Gleason 7 or higher at time of RP, only biopsy Gleason score was a significant predictor ($p=0.009$). On multivariate analysis for stage pT3 or higher, there was a trend for US ($HR=3.107$; $p=0.098$) and biopsy Gleason ($p=0.088$) to be predictive. On ROC analysis, the inclusion of US with the base model (PSA, DRE, and biopsy Gleason) increased the accuracy of predicting Gleason 7 or higher (80.7% vs. 81.0%) and stage pT3 or higher (87.1% vs. 85.8%) at time of RP.

Conclusions: Adding US findings to our traditional predictive model of pathologic outcomes at time of RP significantly increased our predictive accuracy of final pathologic stage; however, its ability to predict final pathologic Gleason sum was less robust.

PROSTATE CANCER IN VIETNAMESE MEN

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(Presentation to be made by Dr. Ngo)

Purpose: Although prostate cancer is the most common malignancy and is the second leading cause of cancer mortality in US men, little is known about its natural history among minority groups. Even less is known about prostate cancer in Vietnamese Americans. Although some studies have shown that the incidence of prostate cancer is lower among Asians, some new evidence suggests that these patients often present with more severe disease. Additionally, Asian Americans have been shown to undergo cancer screening at rates much lower than the general population, and a recent study from the California Health Interview Study found that only 15% of Vietnamese American men eligible for prostate cancer screening underwent PSA testing. However, it is unclear whether decreased screening is associated with worse clinicopathologic outcomes. Therefore, we reviewed our institutional experience with prostate cancer to characterize the pathologic and clinical features of prostate cancer in Vietnamese men.

Materials and Methods: Santa Clara Valley Medical Center, a safety net institution that provides care to under and uninsured patients, serves a large ethnically diverse population that includes approximately 900 adult Vietnamese men annually. We retrospectively reviewed the charts of all patients who underwent a prostate needle biopsy from 1999-2010 and selected all patients who self-identified as Vietnamese. Baseline demographics, medical histories, and prostate cancer specific characteristics were tabulated. Specifically, the PSA at the time of diagnosis, prostate needle biopsy information, pathologic grade, clinical stage, treatment modalities used, and survival information were extracted.

Results: We identified 891 men who underwent prostate needle biopsy within the study period. Of these, 144 were Vietnamese and 46 had prostate cancer. At the time of diagnosis, the median age was 65.4 years (IQR 62.8-68.0) and the median PSA was 12.2 ng/ml (IQR 6.8-19.3). Approximately half of these patients had clinical T1c prostate cancer. Two-thirds had high grade cancer (defined as having a Gleason score of 7 or higher). The median TRUS volume was 29.6 (IQR 22.2-45.3) and the median PSAD was 1.48 ng/ml² (IQR 0.18-0.57). Although the cancer specific mortality was only 2%, the median follow up was only 43 months. The PSA performance characteristics for these patients resembled that of the general population with an area under the AUC curve of 0.655 and 0.701 for prostate cancer and high grade prostate cancer detection, respectively.

Conclusions: Vietnamese American men make up a significant proportion of the Asian American population in the US. At the time of diagnosis, they present with higher grade and more advanced cancers compared to the general population. This may be due to differences in the screening of prostate cancer or tumor biology. However, it remains unclear whether they experience worse clinical outcomes in terms of biochemical recurrence or mortality. Long term follow up is required to accurately define these outcomes.

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