THE ROLE OF URODYNAMICS PRIOR TO HOLMIUM LASER ENUCLEATION OF THE PROSTATE IN MEN WITH BPH: A SERIES OF OVER 300 PATIENTS

Chinedu O. Mmeje, M.D., Rafael Nunez-Nateras, M.D., Meng-Ru Cheng, M.S.P.H., Yu-Hui Chang, M.P.H., Ph.D., Mitchell R. Humphreys, M.D.: Phoenix, AZ

(Introduction to be made by Dr. Mmeje)

Introduction and Objective: The role of urodynamics in aiding the decision for treating patients with lower urinary tract symptoms (LUTS) or urinary retention remains unclear. We reviewed our experience with Holmium laser enucleation of the prostate (HoLEP) to determine whether pre-operative multi-channel urodynamic study (UDS) may help predict short and long-term quality of life and functional outcomes after HoLEP.

Methods: A retrospective analysis was performed on 311 patients who underwent HoLEP for LUTS or urinary retention from August 2007 to June 2011. All patients were assessed pre-operatively with an American Urologic Association Symptom Score (AUA SS), Quality of Life score (QoL), post-void residual (PVR), and maximum flow (Qmax). UDS was obtained in select patients at the provider’s discretions. Quality of life (AUA SS, QoL) and functional outcomes (PVR, Qmax) were compared between patients receiving pre-op UDS versus those who did not undergo pre-op UDS at 6 weeks and 12 months after HoLEP. Multivariable regression analysis was used to determine predictors of improved quality of life, defined as a QoL < 3 or AUA SS < 8, and functional outcomes.

Results: Sixty-four patients underwent UDS prior to HoLEP, while 267 proceeded to surgery without pre-operative UDS. Patients who underwent UDS prior to surgery had smaller pre-operative prostate volumes (80.0 cm3 vs. 99.6 cm3; p = 0.02), and a higher prevalence of pre-operative urinary retention (57.8% vs. 27.9%; p = <0.01) and incontinence (27.0% vs. 12.6%; p < 0.01). Short term (6-weeks) and long-term (12-months) AUA SS and QoL after HoLEP was similar between both groups. At 12 months there was no significant difference in the amount of patients with an improved QoL (93.8%; vs. 79.6%; p = 0.17) or improved AUA SS (81.3% vs. 72.8%; p = 0.47) between the two groups. In terms of functional outcomes, Qmax was similar between the two groups at 6 week and 12 month follow up. Post-void residual was significantly higher in patients undergoing UDS prior to HoLEP at 6 weeks (88.9 mL vs. 40.8 mL; p < 0.01) and at 12 months (103.3 mL vs. 46.6 mL; p = 0.04). Multivariable regression analysis did not find pre-operative UDS to be a predictor of improved AUA SS, QoL, or functional outcomes at 6 weeks and 12 months.

Conclusion: There is no difference between short and long term quality of life outcomes after HoLEP in patients receiving pre-operative UDS compared to those proceeding straight to surgery. UDS prior to HoLEP is not predictive of quality of life or functional outcomes. Patients undergoing pre-operative UDS were associated with a higher PVR after HoLEP, this information can be used for patient counseling.

Source of Funding: None
MULTI-CENTER RANDOMIZED CONTROLLED BLINDED STUDY OF THE PROSTATIC URETHRAL LIFT: THE L.I.F.T. STUDY

Steven N. Gange, M.D., William G. Moseley, M.D., Shahram S. Gholami, M.D., Sheldon J. Freedman, M.D., Neal D. Shore, M.D., Kevin T. McVary, M.D., Alexis E. Te, M.D., Daniel B. Rukstalis, M.D., Claus G. Roehrborn, M.D.,

On behalf of the L.I.F.T. Study investigators: Salt Lake City, UT

(Presentation to be made by Dr. Gange)

Purpose: To report the results of a multi-center randomized blinded trial of the Prostatic Urethral Lift (PUL) in men with LUTS due to BPH. In the PUL small permanent UroLift® implants (NeoTract, Inc., Pleasanton, CA) are placed within the prostate to hold encroaching lobes in a retracted position and open the prostatic urethra.

Methods: Men ≥50 years with LUTS due to BPH, an American Urological Association Symptom Index (AUASI) ≥13 and a peak flow (Qmax) ≤12 ml/s, and a prostate volume 30 to 80 cc, were randomized 2:1 between PUL and a sham procedure. Sham consisted of rigid cystoscopy conducted with a surgical screen in place and a biopsy device to mimic PUL sounds. The primary endpoint was comparison of AUASI reduction at 3 months (PUL vs. sham). While the surgeons were not blinded, a double blind was maintained with both patient and outcome assessor. PUL subjects were followed to 1 year with assessment of urinary symptoms, quality of life, flow and sexual function.

Results: 206 men were randomized (n=140 PUL, n=66 sham). In North America 99% procedures were conducted under local anesthesia; mean procedure time was 66 minutes. Adverse events were typically mild and transient, with most frequent being hematuria, dysuria, pelvic pain, urgency and urge incontinence. Mean postoperative catheterization was 0.9 days and mean return to preoperative activity was 8.6 days. The primary endpoint was met: AUASI reduction was 11.1±7.7 PUL vs. 5.9±7.7 sham, (p=0.003). PUL subjects experienced symptom relief by 2 weeks that improved to 3 months and was sustained to 1 year (AUASI reductions of 4.1, 11.1, 10.8, respectively, p<0.001). Improvements in quality of life score and BPH impact index tracked with AUASI changes. Qmax improved 4.4 ml/s at 3 months and was sustained to 4.0 ml/s at 1 year, p<0.001. Sexual function was preserved with no statistical difference from control at 3 months and no incidence of de novo sustained erectile dysfunction or loss of ejaculatory emission. Sexual Health Inventory for Men (SHIM) showed a 4 point improvement (p=0.011) at 12 months for men entering the study with ED. Ejaculatory bother score was 40% improved at 1 year, p<0.001.

Conclusions: The Prostatic Urethral Lift provides rapid and durable improvement in LUTS and urinary flow without compromising sexual function. The procedure can reliably be performed under local anesthesia with low morbidity. This minimally invasive treatment offers unique benefits for the treatment of BPH.

Source of Funding: NeoTract, Inc.
QUALITY OF LIFE OUTCOMES IN MEN UNDERGOING TREATMENT FOR PROSTATE CANCER: INITIAL RESULTS FROM THE KAISER PERMANENTE SOUTHERN CALIFORNIA REGION


(Presentation to be made by Dr. Kim)

**Purpose:** Various treatments are available for men diagnosed with localized prostate cancer demonstrating similar oncologic efficacy. Each treatment modality has varying associated morbidities affecting health-related quality of life (HRQOL) outcomes in patients. Therefore, HRQOL measurements are clinically important in these patients. We performed a multi-center, standardized, prospective study to evaluate and compare HRQOL differences in men undergoing prostate cancer treatment within a large managed-care organization.

**Materials and Methods:** Men with biopsy-proven prostate cancer were prospectively enrolled at 14 medical centers within the Kaiser Permanente Southern California medical region. Patients underwent radical prostatectomy (robotic, laparoscopic, or open), brachytherapy, external beam radiation therapy, hormone therapy, or active surveillance. Patients were given the Expanded Prostate Cancer Index Composite-26 (EPIC-26) HRQOL questionnaire at baseline and at 1, 3, 6, 12, 18, and 24 months after treatment. Treatment details and clinico-pathologic variables were also collected. The Kruskall-Wallis test was used to compare treatment groups.

**Results:** From March 2011 to April 2013, 5,262 patients were detected to have prostate cancer and were enrolled in the study. At the time of analysis, 2,897 patients returned baseline surveys and 876 completed 12-month follow up surveys. Patients in the radiation group had poorer irritative urinary and bowel quality of life outcomes after treatment, but had the least changes in their sexual and urinary incontinence domains. Patients undergoing radical prostatectomy had the greatest declines in their sexual function and urinary incontinence domain scores, whereas bowel, irritative urinary, and hormonal domain scores remained relatively constant. Robot-assisted radical prostatectomy patients had significantly better sexual domain scores than men undergoing open surgery.

**Conclusions:** Each prostate cancer treatment modality is associated with its own unique pattern of HRQOL changes. These differences will be important in counseling patients contemplating these options. Long-term follow up of these results is being accrued.

**Source of Funding:** Intuitive Surgical Inc.
DISPARITIES IN SURVIVAL FOR CALIFORNIA MEN WITH PROSTATE CANCER ARE MORE ASSOCIATED WITH SOCIOECONOMICS THAN EITHER RACE OR INSURANCE STATUS

Thenappan Chandrasekar, M.D., Kari M. Fish, M.P.H,
Christopher P. Evans, M.D., Ralph W. deVere White, M.D.,
Marc A. Dall’Era, M.D.: Sacramento, CA
(Presentation to be made by Dr. Chandrasekar)

Introduction: The racial and socioeconomic disparities for men with prostate cancer (PC) are well described. Under-insured men and those of low socioeconomic status (SES) have been shown to have greater PSA values and higher risk features at the time of diagnosis. We sought to determine whether these features are associated with disparities in overall survival (OS) and cause specific survival (CSS), and to quantify the degree of association.

Materials and Methods: We identified all men older than 45 who presented with prostate cancer within the California Cancer Registry between 1988-2009. OS was the primary outcome measured with prostate cancer CSS measured as a secondary endpoint. Mortality rates were calculated per 100,000 men at risk. Multivariate COX Proportional Hazard models were constructed to assess the association between socioeconomic status, insurance status, and race with the primary and secondary outcomes while adjusting for other covariates.

Results: We identified 364,014 men presenting with prostate cancer in California from 1988 to 2009. The age adjusted prostate cancer mortality rate has declined over time. On univariate analysis, low SES, African American race, and absent/public insurance status were significantly associated with worse overall and cause specific survival. Adjusting for race and insurance type, socioeconomic status was the most important predictor of overall and prostate cancer specific survival, particularly for men with localized and regional disease. Men of low economic means show 30-40% increased hazard of all cause and prostate cancer specific mortality for localized and regionally advanced disease.

Conclusions: Socioeconomic status is an important predictor of OS and CSS for men with prostate cancer. The disparity based on economics is most profound for men with localized and regional disease and greater than either race or insurance status.

Source of Funding: None
RISK STRATIFIED TRENDS IN PROSTATE CANCER SURVIVAL USING THE SEER REGISTRY: 1983-2002
Ross E. Anderson*, B.S., Brian Cox*, M.D., Yiyi Chen*, Ph.D.,
Steven McNamara*, M.P.H., Jeffrey C. LaRochelle, M.D.,
Christopher L. Amling, M.D., Theresa M. Koppie, M.D.: Portland, OR
(Presentation to be made by Ross Anderson)

Background and Objective: High grade localized and locally advanced prostate cancer (CaP) are less common forms of prostate cancer, but with an increased risk of cancer specific mortality. We sought to determine risk-based differences in prostate cancer survival using data from the Surveillance, Epidemiology and End Results (SEER) registry.

Methods: Using the SEER registry, we identified patients diagnosed with prostate cancer from 1983 to 2002, with at least 5 year follow up (2008). Patients were stratified into 4 risk groups: 1. Organ Confined, well/moderately differentiated; 2. Organ Confined, poorly differentiated; 3. Locally Advanced/Regional with any Gleason Grade (GG); 4. Metastatic disease. We also grouped the cohort by year of diagnosis and prostate specific antigen (PSA): 1. the pre-PSA period (1983-87); 2. transitional-PSA period (1987-1992); 3. post-PSA period (1993-2002). The primary outcome measured was the 5-year CaP specific mortality, estimated using the Kaplan-Meier methods. Log-rank test was used to compare the distributions of CaP specific survival between pre- and post-PSA periods, and a supplemental z-test was also conducted to compare the 5-year CaP specific survival rate.

Results: During our study period 314,930 men were diagnosed with CaP. 5-year survival improved in all 4 risk groups with each subsequent PSA era, as shown in the figure. When evaluated by risk group, patients with locally advanced/regional disease improved the least between pre and post-PSA periods, with a 6.23% increase in 5-year survival. Patients with high risk, organ confined disease (OCD+Poor), showed the most significant improvement between pre and post-PSA periods (17.34%, p< .001). From a treatment standpoint for this subgroup, the patients who received radiation showed the most significant improvement between pre and post-PSA periods (20.01%, p < .001).

Conclusions: Prostate Cancer survival has improved in the last 25 years, presumably secondary to increased PSA screening, stage migration and changes in prostate cancer treatment. This improvement has been minimal among patients with low risk prostate cancer. Patients with high risk organ confined, for whom survival is sensitive to subtle variations in diagnosis and treatment, have seen more significant survival improvements during this time interval.

Source of Funding: None
Purpose: The inability to visualize prostate cancer (CaP) during prostatectomy may contribute to surgical side effects and positive margins. Optical imaging using a fluorescent probe may enable visualization of cancer in real-time. However, current pre-clinical methods employing intact antibodies (~155 kDa) require >1 day from probe administration to imaging. We sought to develop a probe using a humanized anti-prostate stem cell antigen (α-PSCA) antibody fragment (diabody, Db, 55 kDa) labeled with a fluorescent dye to enable more rapid cancer imaging.

Materials and Methods: The Db was engineered with C-terminal cysteine residues that enable site-specific labeling without interfering with PSCA binding. The Db was labeled with the far-red fluorescent dye Cy5 following reduction using tris(2-carboxyethyl)phosphine (TCEP). SDS-PAGE and size exclusion experiments confirmed Db purity, correct size, and Cy5-Db conjugation. Binding specificity and affinity were analyzed in vitro using flow cytometry. The ability of the fluorescently labeled Db to image CaP in vivo was evaluated using xenograft mouse models (22Rv1 and LAPC9). PSCA+ and PSCA- 22Rv1 xenografts were implanted in opposite shoulders of 8-week old nude mice. At 2 weeks, mice were intravenously administered 25μg of the Cy5-Db probe and imaged serially at 30 min, 2 hrs, 4 hrs, 6 hrs, 8 hrs, and 24 hrs using the IVIS-200 Optical Imaging System. The mice were then sacrificed and reimaged after skin removal. After optimization of the imaging protocol, surgical resection of xenografts in mice was performed. Immediately following conventional white light resection, real-time fluorescence imaging was used to guide removal of residual tumor tissue using the Leica M205 FA fluorescence dissecting microscope.

Results: The Cy5-Db probe was reproducibly conjugated (dye:protein ratio = 1.3:1). Flow cytometry of 22Rv1 PSCA+ vs. PSCA- cells incubated with Cy5-Db demonstrated specific binding to PSCA+ cells. In vivo imaging showed maximal signal to noise by 6 hours. After sacrificing the mice, the skin was removed while leaving tumors in situ to minimize autofluorescence and more closely replicate the goal of surgical guidance. Repeat imaging showed a PSCA+ to PSCA- mean fluorescence ratio of 4.4:1 for 22Rv1 and 4.5 for LAPC9 (Figure). In the surgical resection experiments, residual tumors < 1mm in size after conventional white light resection were identified and removed using fluorescence guidance.

Conclusions: We developed an antibody fragment labeled with a fluorescent dye that enables same day in vivo imaging of prostate cancer xenografts in mice. The small size of the diabody enables rapid imaging. Real-time fluorescence image-guided surgery enables more complete tumor removal than use of conventional white light surgery alone.

Source of Funding: None