

Critical Discussion and Commentary

What Is the Most Accurate Way to Predict Erectile Function After Prostate Cancer Treatment?

Managing expectations for post-treatment erectile function can be made easier with this model, which provides realistic outcomes

By Steven E. Canfield, MD

Based on: Alemozaffar M, Regan MM, et al. Prediction of Erectile Function Following Treatment for Prostate Cancer. *JAMA* 2011; 306 (September 21): 1205–1214.

Authors of a recent article sought to assess erectile functional outcomes after common therapies for prostate cancer and develop an accurate prediction tool based on preoperative and treatment-

related factors. This was a prospective cohort study in men undergoing either radical prostatectomy, external beam radiotherapy or brachytherapy for localized prostate cancer. Preoperative patient characteristics, sexual quality of life and treatment details were collected from 1,201 men in the original study cohort of whom 1,027 had two-year follow-up data on sexual outcomes. These data were used to create the model, which was then externally validated in a community-based database cohort of 1,913 men. The primary outcome was erection suitable for intercourse two years after treatment. Factors useful in predicting sexual outcomes were found to include health-related quality-of-life score, age, preoperative PSA, race, BMI and treatment details such as nerve sparing. Overall at two years, 37% of men reported functional erections. This increased to 48% in men with functional erections prior to treatment. The model was fairly accurate for radical prostatectomy with an area under the curve of 0.77 and very accurate for radiotherapy 0.87 and brachytherapy 0.90.

These preoperative patient characteristics and treatment details can predict two-year erectile function with accuracy. Managing expectations for post-treatment erectile function can be made easier with this model, which provides realistic outcomes.

Men with newly diagnosed localized prostate cancer face a number of daunting and complicated decisions. As urologists, we are under the microscope now more than ever to guide men appropriately

through these decisions; to do so properly we need accurate information at our disposal with which to counsel these men.

Even more recently, Alemozaffar and colleagues reported on an update to the “Prostate Cancer Out-

comes and Satisfaction With Treatment Quality Assessment” PROST-QA study, which evaluated sexual function outcomes in this cohort with two-year follow-up after treatment with radical prostatectomy, radiotherapy or brachytherapy. The study authors looked at perioperative patient characteristics such as age, race, obesity and sexual quality-of-life scores, as well as treatment influences such as nerve sparing and hormonal therapy, all thought to play a role in this outcome. In the PROST-QA cohort, of the original 1,201 men enrolled, 86% or 1,027 men had information on sexual function at follow-up after two years. This includes 524 men who had undergone radical prostatectomy, 241 men who had undergone radiotherapy and 262 men who had undergone brachytherapy. Overall, only 37% of men still had functional erections after two years. This rose to 48% when considering men who had functional erections before treatment, which was a more practical number to consider. This entire range of function was from as low as 2% for non-nerve sparing surgery in a 70-year-old man whose PSA was greater than 10 and sexual

This model now represents the most accurate information we have to predict erectile function after treatment.

E-quiz code: **31663N**

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Media: Internet access to pdf.

Intended Audience: Urologists and Residents-in-Training interested in Urology.

Learning Objectives: At the conclusion of this activity, participants will demonstrate the ability to:

- Present controversial procedures in Urology.
- Discuss the advantages and disadvantages of common diagnosis and treatment procedures.
- Evaluate non-conventional principles and practices with conventional principles and practices.
- Review the latest basic science findings in Urology.
- Present the latest evidence-based medical procedures and methodologies in Urology.

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quality-of-life score was low, to as high as 98% for brachytherapy in a 60-year-old African-American man whose BMI was less than 25 and sexual quality-of-life score was high.

A preoperative erectile function prediction model was created, tested and validated using another large community-based registry database, the Cancer of the Prostate Strategic Urologic Endeavor (CaPSUR). The model was tested on 1,655 CaPSUR men with known preoperative characteristics and two-year sexual outcomes and was found to be very accurate in this population. The models appear simple to use and can be accessed in the tables presented in the paper. Various parameters are listed, and an individual patient can be plugged in to predict his probability of erectile function two years later. One caution is that the groups are not meant to be compared side-by-side, as this was not generated from randomized data. It is inevitable that direct comparisons will nonetheless be made by patients and physicians, and there is likely to be disagreement by physicians who feel the model does not do justice to their own results. However we see it, this model now represents the most accurate information we have to predict erectile function after treatment, and it would be wise to utilize this information for our patients.

Vitamin E Causes Prostate Cancer!

Men should be cautioned to avoid high-dose vitamin E supplementation due to the increased risk of prostate cancer

By Steven E. Canfield, MD

Based on: Klein EA, Thompson IM Jr, et al. Vitamin E and the Risk of Prostate Cancer: The Selenium and Vitamin E Cancer Prevention Trial (SELECT). *JAMA* 2011; 306 (October 12): 1549–1556.

The purpose of a study was to assess the risk of prostate cancer from Vitamin E supplementation in the SELECT trial. SELECT was a randomized controlled trial investigating the role of vitamin E, selenium, both or none in prostate cancer prevention. Thirty-five thousand five hundred and thirty-three men were randomized at over 400 sites in the United States, Puerto Rico and Canada between 2001 and 2004. This update included continued follow-up data to July 2011. The original trial was stopped early when interval analysis revealed the futility of the interventions to prevent prostate cancer. This update included follow-up data for a minimum of seven years after final enrollment and reported specifically on the increased risk of prostate cancer with these interventions.

Prostate cancer was found more often in each treatment group compared with placebo and was significantly increased in the vitamin E group by 17%. Vitamin E supplementation was associated with increased risk of prostate cancer in the SELECT trial. Men should be cautioned to avoid high-dose vitamin E supplementation due to the increased risk of prostate cancer. Observational data from earlier population-based epidemiological studies suggested

that vitamin E and selenium may reduce the risk of prostate cancer. The SELECT trial was designed to be the largest prostate cancer prevention trial ever to test this hypothesis. The trial was stopped after a median of 5.5 years of follow-up for futility. Additionally, concern existed over a nonsignificant observed increase risk of prostate cancer in patients in the vitamin E arm. The data monitoring and safety board requested a follow-up analysis to further assess this risk.

In a recent article, Klein and colleagues report on the final analysis at full follow-up. The trend in increased prostate cancer continued steadily and at this analysis reached statistical significance with a hazard ratio of 1.17 and a 95% confidence interval of 1.004 to 1.36, suggesting a true increased risk ranging from less than 1% up to possibly 36%. Other noteworthy items from this update included the consistent trend in increased prostate cancer over time in the vitamin E group, suggesting a true effect rather than a result due to chance alone. Additionally, selenium appeared to mitigate the risk caused by vitamin E whereby the risk was no longer significant in the combination group.

The results from this update are another reminder of the potential pitfalls in observational study data. Once again, an exciting natural intervention has been shown to be harmful rather than helpful when taken at super therapeutic levels. Often, when observational studies have shown potential benefit of a supplement such as vitamin E, most participants may have been deficient in that vitamin, unhealthy in general, smokers or obese, for example. When the supplement is then studied directly, the participants may be different. People who sign up for a vitamin study are likely to be healthier, to eat well, to exercise and to start out with normal vitamin levels. It is not that surprising when high levels of vitamins then become toxic in unexpected ways. Another major study has demonstrated that the hopeful intervention may actually be harmful, and prostate cancer prevention continues to elude us.

Nocturia Linked With Decreased Quality of Life, Depression

This report shows a strong association of nocturia with depression in both men and women, with a significant trend in increased odds of depression with more voids nightly and in younger age groups

By Karl J. Kreder, MD

Based on: Kupelian V, Wei JT, et al. Nocturia and Quality of Life: Results From the Boston Area Community Health Survey. *Eur Urol* 2012; 61 (January): 78–84.

A recent study was designed to investigate the association of nocturia with quality of life and the presence of depressive symptoms. The data for this study came from the Boston Area Community Health (BACH) Survey. This is a population-based epidemiologic survey of urologic

symptoms and risk factors. To be eligible, patients had to speak English or Spanish and have the cognitive ability to provide informed consent.

A multi-stage stratified design was used to randomly recruit approximately equal numbers into different age-decade groups — 30s, 40s, 50s, and 60 to 79 — and also have equal representation between gender, race and ethnic groups including black, Hispanic and white. Five thousand five hundred three subjects were recruited — approximately 2,300 men and 3,200 women. Data were obtained during a two-hour in-person interview conducted by a trained interviewer. This was usually conducted in the subject's home.

Nocturia was defined by two questions: During the last month, how often have you had to get up to urinate more than once during the night? In the last seven days, on average, how many times have you had to go to the bathroom to empty your bladder during the night after falling asleep? If the subjects responded to question 1 with "fairly often," "usually" or "almost always" or if the response to question 2 was a report of two or more episodes of voiding during the night, nocturia was considered to be present. To measure quality of life, the 12-item Short Form Survey (SF-12), the 12-item Physical Component Score (PCS-12) and the 12-item Mental Health Component Score (MCS-12) were used.

The overall prevalence of nocturia was 25.3% in men and 31.3% in women. The prevalence increased to almost 40% in men and women over the age of 60. A significant trend of decreasing quality-of-life scores was observed, with the largest drop in mean scores observed in those with between one and two voids nightly. The overall prevalence of depression was 14% in men and 20% in women and did not seem to vary with age. A higher prevalence of depression with nocturia was observed in younger groups; however, this difference decreased with age. Nocturia was associated with increased odds of depression with statistically significant trends with a higher number of voids. Among men, an association of nocturia and depression was observed at ages less than 65 years, and in women, an association of nocturia and depression was observed only in ages less than 50. The results of the BACH study demonstrate a significant association of nocturia with decreased quality of life and interference with daily activities in both men and women. The presence of nocturia was associated with an increased likelihood of depression, especially among younger men and women.

The potential limitations of this study are the self-reported nature of the study with its potential biases and the fact that the BACH study did not include a neurologic assessment or data on life events, sleep apnea and other sleep-related conditions. The strength of the study is that it includes a community-based random sample of a broad age range, which included both genders and the black, white and Hispanic ethnic groups.

The take-home message is that this study shows nocturia is associated with decreased quality of life, increased symptom bother and increased prevalence of depression, especially in younger men and women, and that significant trends in decreased quality of life and increased odds of depression are observed as the number of voids per night increased.

Ethical Experience With Postmortem Sperm Retrieval

Postmortem sperm retrieval is a rare event with many ethical entanglements that bear consideration prior to being called upon

By Tobias S. Kohler, MD, MPH

Based on: Laborde E, Sandlow J, Brannigan RE. Postmortem Sperm Retrieval. *J Androl* 2011; 32 (September–October): 467–469.

If you received a request from a grieving wife to extract sperm from her husband who was just killed, how would you respond? Authors of a recent study help to clarify this issue. Postmortem sperm retrieval (PMSR) is an infrequent but often ethically challenging scenario presented to the urologist. This article was an androlog discussion and summary of this controversial topic. Participants of the discussion included several urologists who submitted their opinions via androlog, and additional background on the subject matter was added by the authors of this article. Several issues were discussed in the article. The key take-home point was that the ethics committee of the American Society of Reproductive Medicine (ASRM) specifically states that PMSR requests need not be honored without signed consent or known wishes of the deceased.

Several key points were brought up. Dr. Jay Sandlow from the University of Milwaukee has already put this issue through the Institutional Review Board (IRB), and their policy is that — without explicit written consent from the deceased, which is quite unlikely — the procedure is never performed. Again the ethics committee of the ASRM echoes this sentiment and makes it acceptable for urologists to simply refuse PMSR requests by specifically stating that they need not be honored without the signed consent or the known wishes of the deceased. However, in contrast, Dr. Cappy Rothman, affiliated with UCLA, has performed 50 posthumous extractions and sites the duty of easing pain and suffering of the grieving family from the Hippocratic Oath as one of his rationale. Importantly, only two of these 50 have gone on to have children from this retrieved sperm. Dr. Arnold Belker states it is imperative to have already put this topic through one's IRB before performing PMSR. He also recommends a one-year quarantine period of the frozen tissue before it can be used and the potential requirement of psychological counseling for the widow, again before the sperm can be utilized.

Cost of harvest, long-term freezing and who has long-term rights to the tissue must also be discussed. Issues of whether the child has rights to things such as Social Security have also come to trial in the United States. Most believed only the request of the wife of the deceased could be honored — not the parents.

Geography tends to help determine the laws. In Germany, it is illegal to use gametes from a dead person to procreate. In the United Kingdom, posthumous insemination is forbidden without the expressed consent of the father, and in Israel there are guidelines from the Attorney General, though it

appears they are seldom honored. In the United States, unfortunately, there are no absolute laws on the subject. It was suggested that the IRB be involved in the creation of a plan of action should postmortem retrieval be desired. In the end, I think it is important to remember that the wishes of the deceased must be considered, as he typically has the least pronounced voice and representation.

In conclusion, PMSR remains a controversial subject when a patient is dying or dead. Time pressure does not allow for adequate consideration of ethical implications of PMSR. It behooves all urologists to have preemptively considered the scenario along with its relevant associated issues and factors involved. Knowledge of appropriate contact numbers for the area's medical ethics committee is imperative. This is an excellent summary of a complex issue. This is a nonstandard article, but I thought important for all urologists to consider.

Caffeine May Reduce Risk of Depression in Women

Caffeine and even coffee consumption could be recommended to potentially improve quality of life

By Mark Moyad, MD, MPH

Based on: Lucas M, Mirzaei F, et al. Coffee, Caffeine, and Risk of Depression Among Women. *Arch Intern Med* 2011; 171 (September 26): 1571–1578.

The world's most frequently consumed central nervous stimulant is caffeine, and the vast majority is from coffee. However, few prospective studies of caffeine and coffee and depression have ever been completed. In a recent study, authors sought to evaluate the impact of caffeinated coffee on the risk of depression in women.

A prospective cohort from the Nurses' Health Study that included >50,000 women with a mean age of 63 years that did not have depressive symptoms at baseline was evaluated. Coffee consumption was estimated from validated questionnaires. During 10 years of follow-up, >2,600 cases of depression were found. Women consuming two to three cups of coffee a day or ≥ 4 cups compared to ≤ 1 per week had a significant ($P < 0.001$) reduction in the risk of depression, and a similar finding occurred for just caffeine consumption. No relationship was found for decaffeinated coffee and the risk of depression.

The authors conclude that caffeinated coffee consumption may reduce the risk of depression.

First, keep in mind that this epidemiologic study is arguably one of the best conducted in the world. Second, the results of this study are awesome (note: that is a word my teenager would say, but it precisely describes my feelings, folks)! And, I say this only because I am so sick and tired of the day-to-day assault on wonderful quality-of-life benefits of some foods and beverages by bone-headed experts — remember

eggs? You could not eat them, and now they provide benefits! Remember chocolate? Could not eat it, and now provides benefits! The micro-dissection of our diets has become somewhat absurd, because it causes a person to contemplate and analyze every single food or beverage without being able to consume comfort foods. The end result is stressed out and anxiety-prone obsessive-compulsive human beings that do not have time for general lifestyle changes because they are told to become fixated on minutiae. It is time to encourage patients to consume coffee and caffeine. What is also not well-known by some clinicians from past studies is the fairly consistent inverse relationship between suicide and coffee consumption. Moderate coffee and caffeine are simply associated with greater attention, energy, memory and probably mood. It is time for practitioners to encourage coffee and caffeine for most individuals (okay, I understand that some have bladder, etc, issues but this is a minority). I have one more thing to say and that is "VIVA Diet Mountain Dew!"

Weight Loss From Dietary Changes Produces Improvements in Obese Diabetic Men

Reducing 600 calories a day from your diet may be equivalent or even superior to diets allowing only 1,000 total calories per day

By Mark Moyad, MD, MPH

Based on: Khoo J, Piantadosi C, et al. Comparing Effects of a Low-Energy Diet and a High-Protein Low-Fat Diet on Sexual and Endothelial Function, Urinary Tract Symptoms, and Inflammation in Obese Diabetic Men. *J Sex Med* 2011; 8 (October): 2868–2875.

The objective of a recent study was to determine the effects of diet-induced weight loss and maintenance on sexual and endothelial function, lower urinary tract symptoms and inflammatory markers in obese diabetic men. This was initially an eight-week study of 31 obese (mean body mass index [BMI] 35 and waist circumference of 49 inches) men with type 2 diabetes (mean age 60 years) who received a 1,000 calorie/day meal replacement low-calorie

(LC) diet (n=19), or a high-protein (HP), low-fat, reduced carbohydrate (n=12) diet that cut total daily caloric intake by approximately 600 calories per day. After the eight weeks, all subjects were placed on the HP (–600 calories per day) diet for 44 weeks.

After eight weeks, the total weight and waist size of men in the LC diet was reduced by 10% compared to 5% in the HP diet. Both diets caused significant improvement in glucose, LDL, sex hormone binding globulin, IIEF-5, Sexual Desire Inventory (SDI), IPSS scores and endothelial function as measured by brachial artery flow-mediated dilatation and reduced soluble E-selectin. Erectile dysfunction, sexual desire and urinary symptoms improved by a similar degree with both diets. C-reactive protein and interleukin-6 were reduced with the HP diet. At 52 weeks, metabolic benefits were maintained and sexual and urinary parameters continued to improve.

The authors concluded that weight loss from dietary and caloric changes caused rapid improvement in sexual, urinary, metabolic and endothelial function in obese diabetic men. And, an HP diet may allow these benefits to continue over one year.

The men in this study were not small (politically correct terminology alert), but their weight and waist loss was impressive, and this caused dramatic changes in their lives in just eight weeks (sounds like a commercial). And, by switching to a more moderate diet after the eight-week challenge, the results were sustainable up to a year. Losing 20 pounds (average loss) and keeping it off is not easy. The biggest lipid drop was in triglycerides, as expected with a low-carbohydrate and high-protein diet. The mean IPSS score dropped from 9 to 4 in the HP group (moderate to mild) after 52 weeks. The mean SDI score increased over 20 points. IIEF-5 was 11 and improved to 18. Interestingly, the changes in total and free testosterone were not significant, but the average man in this study was not hypogonadal.

What can really be gleaned from this study? Regardless of weight or waist size, it is time to give some patients the opportunity to make diet and lifestyle changes to improve their heart and urologic health. I can appreciate throwing numerous supplements and prescriptions at these men because the results tend to be faster and easier for the patient and clinician. However, it is time to recognize that even moderate lifestyle changes can profoundly improve the lives of many patients. I realize you will never see these results emphasized in most television commercials, but that is precisely why we need to spend more time mentioning these things.

Preop PCNL Urine Culture Status Does Not Necessarily Predict Postop SIRS



Bladder Infections

Take Home Pearl:

Positive renal pelvis urine cultures and stone cultures are more predictive of post-percutaneous nephrolithotomy systemic inflammatory response syndrome.

Objective: To determine the correlation between preoperative bladder urine cultures, intraoperative renal pelvis cultures, and stone cultures in patients undergoing percutaneous nephrolithotomy (PCNL), and to examine post-procedure risk factors for systemic inflammatory response syndrome (SIRS).

Design: Prospective database review.

Participants: 198 patients undergoing 204 PCNLs.

Methods: Urine samples from the bladder, renal pelvis, and extracted stones were sent for culture analysis. Postoperatively, patients were closely monitored for any signs of SIRS. The concordance of urine and stone cultures across different sites was examined. Regression analysis was done to identify clinical variables associated with SIRS.

Results: 20 of 204 (9.8%) PCNLs had evidence of SIRS, including 6 of 20 (30%) requiring ICU care. The

concordance between stone, renal pelvic, and preoperative urine cultures was 64% to 75%, with the highest concordance between renal pelvic urine and stone cultures. In multivariate analysis, multiple access tracts and a stone burden ≥ 10 cm² were significant predictors of SIRS.

Conclusions: Even appropriately treated preoperative urinary infections may not prevent infected renal pelvis urine at PCNL. Renal pelvic urine and stone cultures may be the only way to identify the causative organism and direct antimicrobial therapy. The authors recommend collecting pelvic urine and stone cultures to identify the offending organism in patients at risk for sepsis, particularly those with large stone burden requiring multiple access tracts.

Reviewer's Comments: SIRS after PCNL can be very frustrating, especially in patients that you have treated preoperatively based on urine cultures with an extended course of culture-specific antibiotics. The authors here demonstrate that, while 24% of patients had positive preoperative urine cultures, 10% still had positive renal pelvis cultures, of which one-third had negative bladder urine cultures. Overall, 16% of patients had positive stone cultures including 49% of those with negative preoperative urine cultures and 75% with negative renal pelvis urine

cultures. The concordance rate of specific bacteria was relatively high at approximately 70%. Obviously, bacteria can avoid the effects of culture-specific antibiotics. These cultures are significant for predicting SIRS on univariate analysis, in which female gender, multiple renal punctures, struvite calculi, and positive renal pelvis and stone cultures were predictive of SIRS. However, on multivariate analysis, the renal pelvis and stone cultures did not hold significance and only stone size and multiple access tracts were statistically significant. This suggests that bacteria status may not be as important as the endotoxin load of the stone and the number of areas (tracts) in which endotoxins can enter the blood. Therefore, even some of our best antimicrobial treatment may not prevent SIRS in certain patients. I believe renal pelvis and stone cultures may be useful in certain situations to more accurately identify the bacteria involved, but they can be somewhat tricky to accurately obtain and may not ultimately affect treatment.

Reviewer: David A. Duchene, MD

Article Reviewed: Korets R, Gravarsen JA, et al. Post-Percutaneous Nephrolithotomy Systemic Inflammatory Response: A Prospective Analysis of Preoperative Urine, Renal Pelvic Urine and Stone Cultures. *J Urol* 2011; 186 (November): 1899–1903.

Renal Function Significantly Affects Kidney Stone Composition



Chronic Renal Failure

Take Home Pearl:

Renal function may be an under-appreciated factor that affects kidney stone composition and urinary mineral excretion.

Objective: To determine effect of renal function on urinary mineral stone excretion and composition of kidney stones in patients undergoing surgical intervention for nephrolithiasis.

Design: Retrospective chart review.

Participants: 158 patients undergoing endourologic intervention for nephrolithiasis.

Methods: 158 patients with 193 stones were grouped by the estimated glomerular filtration rate (eGFR). Kidney stone composition and results of 24-hour urinalysis were reported for each group.

Results: Kidney stone composition profile differed significantly between the groups, with uric acid stones associated with a lower eGFR and calcium phosphate stones associated with a

greater eGFR. A lower eGFR correlated with lower urine pH, lower calcium excretion, and greater oxalate excretion. Excretion of uric acid and body mass index did not differ between the groups.

Conclusions: Different degrees of renal function correlated with certain composition of kidney stones. Urine pH was lower in patients with impaired renal function. Renal function may be an under-appreciated factor that affects kidney stone composition and urinary mineral excretion.

Reviewer's Comments: The authors of this study take a unique approach to evaluate the difference in stone composition based on the accepted stages of chronic kidney disease. It has been well-accepted that one condition predisposes the patient to the other. This study shows that decreased renal function patients are more likely to have uric acid stone composition. A few important points in this manuscript, however, are that calcium oxalate stones still comprised two-thirds of stones regardless of eGFR. eGFR

also significantly correlated with age, so that the increased calcium phosphate stone distribution in better renal function may be a reflection of younger patients having more calcium phosphate stones, rather than a reflection of kidney function. The main emphasis in the manuscript is that urine pH lowers as renal function deteriorates, thus increasing uric acid stones. Uric acid nephrolithiasis risk is multifactorial, however, to include insulin resistance, obesity, hypertension, and atherosclerosis — co-factors that were

not assessed in the study. Therefore, it is difficult to determine how much renal function alone affects stone composition. Nonetheless, I think renal function does deserve more recognition and study on its contribution to uric acid nephrolithiasis.

Reviewer: David A. Duchene, MD
Article Reviewed: Kadlec AO, Greco KA, et al. Effect of Renal Function on Urinary Mineral Excretion and Stone Composition. *Urology* 2011; 78 (October): 744–747.

Ureteral Access Sheaths Facilitate Evaluation of Upper Tract Urothelial Carcinoma



Endourologic Procedures

Take Home Pearl:

Ureteral access sheaths are safe for use in the diagnoses and treatment of upper tract urothelial carcinoma.

Objective: To describe the authors' experience with ureteral access sheaths in the diagnosis and treatment of upper tract urothelial carcinoma.

Design: Retrospective chart review.

Participants: 64 patients undergoing 85 procedures with use of ureteral access sheath.

Methods: Records were reviewed for demographic information, comorbidity data, operative complications, and pathology results. The histologic grade of ureteroscopic biopsies and nephroureterectomy specimens was evaluated for concordance.

Results: 125 patients underwent 235 procedures for upper tract urothelial carcinoma, but only 64 patients with 85 procedures had significant lesions in the proximal upper urinary tract and had access sheaths utilized. Sheath deployment was successful in 83 of 85 (98%) procedures. Biopsies yielded specimens adequate for histopathological diagnosis in 75 of 83 (90%)

cases. No ureteral access sheath-related complications were noted. Of 34 patients eventually undergoing nephroureterectomy, the concordance of tumor grade between biopsy and final specimen was 89%.

Conclusions: Ureteral access sheaths are safe for use in the diagnoses and treatment of upper tract urothelial carcinoma. Sheath placement facilitated the acquisition of multiple biopsy specimens adequate for histopathological evaluation. The technique precludes need for repeat ureteroscopy to establish a diagnosis. Biopsies are highly predictive of final pathological grade in nephroureterectomy specimens.

Reviewer's Comments: With the availability of ureteroscopes, upper tract urothelial carcinoma usually requires visual and biopsy evidence prior to proceeding with nephroureterectomy. Likewise, organ-preserving approaches for upper tract urothelial carcinoma are becoming more common and are often based upon accurate grading on biopsy. Biopsies through a ureteroscope can be challenging for getting an adequate sample size and number. Traditionally, ureteral access sheaths have not been employed during the diagnostic evaluation of upper tract

lesions due to the mild trauma that they may cause during placement, which can cause false-positive appearing areas in the upper tract. It is important not to use an access sheath prior to a full evaluation without a sheath in place. The authors describe this technique very nicely in the methods section of the paper. Essentially, a non-traumatic and non-access sheath evaluation is taken of the entire upper tract. Only if proximal lesions are noted is an access sheath placed. Once placed, the access sheath provides numerous advantages of better continuous flow, ability to take multiple biopsies, less chance of losing a biopsy specimen during scope removal, and ability to treat different areas of urothelial carcinoma. This paper confirms that using an access sheath is beneficial in that 90% of patients had adequate tissue yield for diagnosis. The correlation between high- and low-grade specimens was also acceptable at 89%. I routinely use an access sheath in appropriate proximal lesion tumors and find it extremely useful.

Reviewer: David A. Duchene, MD
Article Reviewed: Gorin MA, Santos Cortes JA, et al. Initial Clinical Experience With Use of Ureteral Access Sheaths in the Diagnosis and Treatment of Upper Tract Urothelial Carcinoma. *Urology* 2011; 78 (September): 523–527.

Adverse Events Are Common After Midurethral Sling

Take Home Pearl:

The data in this report are unique in that the TOMUS adverse event (AE) data were collected prospectively and as part of a large, randomized surgical trial. Quality controls included a predefined list of AEs to monitor.

Objective: To describe surgical complications in 597 women who were randomized to retropubic or transobturator slings over a 24-month follow-up period.

Design/Methods: The patients in this report came from the Trial of Midurethral Slings (TOMUS) study. Uniform definitions of adverse events and serious adverse events were established before trial initiation at all participating sites. Neurologic symptoms were defined as new paresthesias or alterations in motor function that developed within the first 6 weeks after surgery. Reporting of urinary tract infections was based on the time from surgery. Within the first 6 weeks

postoperatively, bother from presumed (not necessarily culture-proven) and/or culture-proven urinary tract infections (UTIs) was reported. In the interval between 6 weeks and 1 year postoperatively, only recurrent UTIs were considered as adverse events (AEs) and were defined as ≥ 3 episodes of symptoms characteristic of urinary tract infection that resulted in antibiotic treatment regardless of culture results.

Results: Of 597 women who were randomly assigned in the TOMUS trial (298 retropubic and 299 transobturator), one-fourth had concomitant procedures, most often to repair pelvic organ prolapse. The distribution of adverse events differed by sling type. Intraoperative bladder perforation occurred only in the retropubic group. Intraoperative blood loss of >100 mL was the second most common intraoperative complication in both study groups but occurred twice as frequently in the retropubic group. In women without concomitant surgery, postoperative neurologic symptoms were the most common. Neurologic adverse events were more common in the transobturator group

regardless of concomitant surgery. Most neurologic symptoms were mild and self-limited. The most common serious AE was vaginal epithelial perforation, and UTIs were common in both groups but occurred with increased frequency in the retropubic group.

Conclusions: Adverse events vary by procedure but are common after midurethral sling. Most events resolve without significant sequelae.

Reviewer's Comments: In the first 2 years after midurethral sling surgery, $>40\%$ of women undergoing a midurethral sling experienced at least 1 adverse event. Complications differ by surgical approach, with bladder perforation and voiding dysfunction and UTI occurring more commonly in the retropubic group and neurologic symptoms occurring more commonly in the transobturator group.

Reviewer: Karl J. Kreder, MD
Article Reviewed: Brubaker L, Norton PA, et al. Adverse Events Over Two Years After Retropubic or Transobturator Midurethral Sling Surgery: Findings From the Trial of Midurethral Slings (TOMUS) Study. *Am J Obstet Gynecol* 2011; 205 (November): 498.e1–498.e6.

Ajust Is Safe, Feasible for Female Stress Urinary Incontinence

Take Home Pearl:

The present report establishes the feasibility and acceptability of carrying out a single-incision mid-urethral sling under local anesthesia.

Objective: To determine whether an adjustable single-incision mini-sling is a safe and effective treatment for female stress urinary incontinence.

Design/Methods: The patients in this report came from the Trial of Mid-Urethral Slings study (TOMUS). This study is a multi-center prospective cohort study. All patients admitted for mid-urethral slings in 6 centers in Scotland between May and December 2009 who met inclusion criteria were asked to participate. Surgeons were 3 urogynecologists and 3 gynecologists, all with experience in performing the procedure. The inclusion criteria were urodynamic stress incontinence or urodynamic mixed urinary incontinence. All patients had and had failed

or declined conservative management. Patients were excluded if they had pelvic organ prolapse greater than stage 2 on the POP-Q or predominant overactive bladder symptoms or were to undergo a concomitant surgery. The primary outcome measure was patient-reported success defined as “very much improved” or “much improved” on the Patient Global Impression of Improvement at 12 months. Secondary outcomes included the ability to satisfactorily perform the procedure under local anesthesia.

Results: 214 eligible patients were asked to participate in the study, and 90 women (42%) were recruited during the study period. All patients were offered local anesthesia. Age, parity, body mass index, percentage of patients with stress incontinence versus urge incontinence, smoking history, and hormone replacement therapy were not significantly different between the whole group versus those who got general versus those who had local anesthesia. There were no major

complications. No patients had urinary tract injuries or required blood transfusion. The patient-reported success rate of the single-incision mid-urethral sling using the Ajust system was 80% at 12-month follow-up. With regard to the secondary outcome measure, 71% of patients who were offered local anesthesia accepted. Of those who did accept, 97% were successfully completed under local anesthesia.

Conclusions: Ajust appears to be a safe procedure, which is feasible under local anesthesia.

Reviewer's Comments: At 12-month follow-up, the single-incision mid-urethral sling with Ajust had an 80% patient-reported success rate. Longer follow-up will be needed to see if these success rates are durable or fade.

Reviewer: Karl J. Kreder, MD
Article Reviewed: Abdel-Fattah M, Agur W, et al. Prospective Multi-Centre Study of Adjustable Single-Incision Mini-Sling (Ajust®) in the Management of Stress Urinary Incontinence in Women: 1-Year Follow-Up Study. *BJU Int* 2011; August 26 (); epub ahead of print.

Take Home Pearl:

Increased cigarette use degrades semen quality, with higher levels of oxidative stress and apoptotic markers being noted in the semen of heavy smokers.

Background: Smoking is well-known to have a large detrimental effect on female fertility. Its effect on male fertility is controversial.

Objective: To look at semen parameters, sperm apoptotic markers, and seminal cotinine levels in fertile and infertile smokers.

Design: Prospective trial.

Participants: 160 total men, 40 each of 4 groups: fertile smokers, fertile non-smokers, infertile smokers, and infertile non-smokers.

Methods: A semen sample was collected from each man after 4 to 5 days abstinence. Routine semen analysis

was carried out on each sample. Additionally, percent DNA fragmentation, Smac/DIABLO, caspase-9, and seminal plasma cotinine were assessed in each sample. Each of those were analyzed for correlations with average cigarette use (<10 per day, 10 to 20 per day, >20 per day), and total number of smoking years.

Results: Increased cigarette use was positively correlated in both the fertile and infertile groups with age, seminal cotinine, seminal Smac/DIABLO levels, caspase-9 levels, and DNA fragmentation. Increasing cigarette use was negatively correlated with sperm counts, motility, and morphology. Data on non-smokers were not reported.

Conclusions: Increased cigarette use degrades semen quality, with higher levels of oxidative stress and apoptotic markers being noted in the semen of heavy smokers.

Reviewer's Comments: While the effects of smoking on female fertility are clearly detrimental, the effects of

smoking on male fertility are controversial. While the study included 80 non-smokers in its design, these men are not reported on. The analysis of the effects of smoking on semen parameters is marred by the issue of increased age in the heavy infertile smoker group; they were 16 years older than the light infertile smoker group. Though age alone has not been shown to have significant effects on male fertility, it does increase the likelihood of comorbid conditions that do have effects on male fertility, and there was no analysis of these potential confounding factors in this paper. Smoking clearly has many detrimental effects on health and should be stopped in the interest of general health, but this paper, unfortunately, does not provide convincing evidence of major effects on semen quality.

Reviewer: Tobias S. Kohler, MD, MPH
Article Reviewed: Tawadrous GA, Aziz AA, Mostafa T. Effect of Smoking Status on Seminal Parameters and Apoptotic Markers in Infertile Men. *J Urol* 2011; 186 (November): 1986–1990.

Treatment of Childhood ALL Can Result in Long-Term Infertility

Take Home Pearl:

Chemotherapy with high doses of cyclophosphamide or testicular radiation results in large decreases in fertility.

Background: Chemotherapeutic agents damage rapidly proliferating cells, and as such, damage spermatogenic cells.

Objective: To determine the long-term effects of chemotherapy on semen quality and fertility in survivors of acute lymphoblastic leukemia (ALL).

Design: Prospective study.

Participants: 51 long-term male survivors of ALL treated at Helsinki University Hospital between 1970 and 1995 and 56 age-matched controls.

Methods: Each participant was evaluated by questionnaire, physical exam, semen analysis, and serum hormone levels. Participants were evaluated between October 2004 and June 2005. ALL survivors were subdivided by treatment regimen: no cyclophosphamide or

testicular irradiation (no CTI), low-dose (<10 g/m²) cyclophosphamide (LDC) without testicular irradiation, high-dose (>20 g/m²) cyclophosphamide (HDC) without testicular radiation, and testicular irradiation (TI). These different survivor groups were compared with the control group to determine which regimens had the greatest effect on long-term fertility.

Results: Follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone (T), free T, testicular size, and sperm counts all showed aberrations in the treatment group. FSH levels were significantly increased in the cyclophosphamide and TI groups but most elevated in the HDC and TI groups at 11.1 and 10.8 IU/L as compared to 3.2 IU/L in the control group. LH was significantly higher only in the TI group. Testosterone was significantly lower in the TI group (1.4 vs 18.4 nmol/L). Free T was significantly lower than control for all treatment groups. Free T was 296 pmol/L in the control group compared to 206, 213, 187, and 169 pmol/L, respectively, in the no CTI, LDC, HDC, and TI groups.

Sperm counts for the no CTI and LDC groups were not significantly different from the control group. Median sperm concentrations from the HDC and TI groups were 1 million and 0, respectively. Paternity rates among survivors were lower than the control group (14% vs 43%). None of the 6 survivors who achieved paternity had HDC or TI.

Conclusions: Testicular radiation and high-dose cyclophosphamide (>20 g/m²) demonstrated the most severe long-term effects on fertility and testosterone production.

Reviewer's Comments: Short-term effects of cancer treatments on seminal parameters and hormonal levels are well-documented in the literature, but little data exist on long-term effects on fertility. This article provides insight on the long-term ramifications of treatment of childhood ALL on the male reproductive system. Important conclusions can be made as a result of this article. The first is that alternative regimens to cyclophosphamide and testicular radiation should be used whenever feasible in childhood ALL,

with the aim of preserving future fertility. Second, barring alternative treatment options, efforts should be made to preserve sperm prior to treatment with cyclophosphamide or radiation to the testes. Finally, testosterone levels

should be carefully monitored after ALL treatments, particularly testicular irradiation.

Reviewer: Tobias S. Kohler, MD, MPH
Article Reviewed: Jahnukainen K, Heikkinen R, et al. Semen Quality and

Fertility in Adult Long-Term Survivors of Childhood Acute Lymphoblastic Leukemia. *Fertil Steril* 2011; 96 (October): 837–842.

Infertility Does Not Alter the Sex Ratio of Offspring



Take Home Pearl:

This study did not detect any noticeable effect of overall or male or female factor infertility on the sex ratio of offspring.

Background: The proportion of male to female births has been declining over recent years. Previous studies have proven inconclusive as to whether infertile couples aided and unaided with ART produce offspring with an altered sex ratio.

Objective: To determine whether male and female subfertility is associated with the gender ratio.

Design: Retrospective cohort study.

Participants: 6,178 children born to women evaluated/treated for infertility and 9,131 children born to a random sample of parents, age matched for child and mother, and matched for multiplicity of births.

Methods: The 2 populations were selected and analyzed for demographic characteristic trends, trends in the sex ratio as influenced by overall infertility, as well as male and female factor infertility.

Results: Infertile couples were more advanced in age and were more commonly white. Sex ratio was not noted to be different between the 2 populations. Neither male nor female factor infertility specifically affected the sex ratio. The sex ratios for the fertile and infertile groups were 51.0% and 51.6% male, respectively. The sex ratio in couples with male factor infertility was 50.3% male, and it was 51.3% male in couples with female factor infertility.

Conclusions: This study did not detect any noticeable effect of overall or male or female factor infertility on the sex ratio of offspring.

Reviewer's Comments: This study looked at a large population of children

of infertile couples and their matched counterparts in the general population. Contrary to previous European studies, the sex ratio in this study was not found to be affected by infertility in general or male or female factor infertility. While the control group was not a purely "fertile" population, the large numbers involved in the study should compensate and these numbers are believable. Overall, this study demonstrates again the relative effectiveness of modern fertility treatments in as far as returning the couple toward normal fertility with minimization of effects on the offspring.

Reviewer: Tobias S. Kohler, MD, MPH
Article Reviewed: Eisenberg ML, Schembri M, et al. Fecundity and Sex Ratio of Offspring in an Infertile Cohort. *Fertil Steril* 2011; 96 (October): 833–836.

Novel Suture Material — Faster Urethrovessel Anastomosis



Take Home Pearl:

Using barbed polyglyconate suture compared to standard monofilament suture during urethrovessel anastomosis can increase efficiency during robot-assisted radical prostatectomy.

Objective: To compare the perioperative and functional outcomes of patients who undergo urethrovessel anastomosis with barbed polyglyconate suture or monofilament polyglactone suture during robot-assisted radical prostatectomy.

Design/Participants: This was a prospective, randomized controlled trial involving 64 patients; anastomosis was performed with barbed suture in 33 and standard monofilament suture in 31 patients.

Methods: In the barbed suture arm, the periurethral tissue and Denonvilliers' fascia were reapproximated using 3-0 barbed suture. Then, a double-armed suture with bidirectional barbs was used for the urethrovessel anastomosis. When the barbed suture was cinched, the tissue remained approximated without slippage. Both arms of the suture were used as in the standard Van Velthoven technique, but upon completion no knot tying was required because the barbs held the anastomosis intact. Unless a large bladder neck reconstruction was performed or significant hematuria was present, a 14F percutaneous suprapubic catheter was placed. The control arm using standard monofilament suture was performed in a similar fashion except attention was devoted to maintaining suture tension throughout the anastomosis and knot tying at the conclusion of the

anastomosis. Cystography was performed 6 to 8 days postoperatively followed by catheter removal.

Results: No baseline patient characteristics were significantly different between the groups. The mean anastomosis time (including posterior reconstruction) with the barbed suture was 13.4 minutes compared to the standard monofilament suture at 18.1 minutes. The bladder neck reconstruction rate was the same between groups. One patient in the standard suture group had a cystogram leak at 1 week. The 6-week functional outcome was assessed with a modified Expanded Prostate Cancer Index Composite questionnaire. No difference between the groups was recorded in terms of pad use or bother. However, the barbed suture group had a significantly greater 6-week AUA Symptom Score. No

difference in AUA Symptom Score was found in either group at 6 weeks compared to relative preoperative scores.

Conclusions: Vesicourethral anastomosis with the barbed suture can be performed safely and more quickly compared to standard monofilament suture with no difference in functional outcomes.

Reviewer's Comments: I commend the authors on the presentation of their evidence drawn from their randomized

controlled trial. These expert surgeons decreased their anastomosis time by 27% or 4.7 minutes by using the barbed suture. This may account for a more significant time savings for novice surgeons with longer average anastomosis times. Concern for fibrotic reaction to the barbed suture is minimized because the authors found no increased incidence of bladder neck contractures and equivalent functional outcomes with the barbed suture.

Reviewer: Kyle J. Weld, MD

Article Reviewed: Sammon J, Kim T-K, et al. Anastomosis During Robot-Assisted Radical Prostatectomy: Randomized Controlled Trial Comparing Barbed and Standard Monofilament Suture. *Urology* 2011; 78 (September): 572–579.

Prostate Cancer Reduces Quality of Life



Prostate Tumors

Take Home Pearl:

Patients diagnosed with prostate cancer will live a long time with or without their disease, and there are significant long-term consequences that go along with this diagnosis.

Objective: To assess functional and quality-of-life (QOL) outcomes with long-term follow-up in men treated with radical prostatectomy (RP) or watchful waiting (WW) for localized prostate cancer.

Participants/Methods: Men were enrolled in the Scandinavian Prostate Cancer Group Study Number 4 (SPCG-4) between 1989 and 1999, which randomized men with localized prostate cancer to RP versus WW. In total, 400 of these men were included for analysis of long-term functional and QOL outcomes and compared to 281 matched controls with no prostate cancer.

Results: Compliance with the questionnaire ranged from 76% to 88%. After a median follow-up of >12 years, highly rated QOL and lower anxiety was reported by 10% more control

men than study men. Erectile dysfunction was much more common after RP (84%) and WW (80%) than in the control group (46%). Urinary leakage was much more common after RP (41%) than with WW (11%) or in the control group (3%). Overall, men in the study reported much greater distress and lower QOL over time and when compared to the control group.

Conclusions: Erectile dysfunction was a common finding in men with prostate cancer — whether treated with surgery or not — over the long term. Urinary leakage was common after RP. Distress and lower QOL in general appeared to be consequences of prostate cancer as well, regardless of treatment.

Reviewer's Comments: The SPCG-4 QOL study presents very long-term data on functional and QOL items after RP and WW. Of the original 695 study participants, 400 men were still alive at the time of this follow-up study and were contacted to provide survey information. Additionally, 281 control men were age and region matched to provide comparison for functional and QOL outcomes. The information gathered represents over 12 years of follow-up. Findings from the study

include the higher rates of urinary leakage after RP (41%), which is not surprising, and the equivalent rates of erectile dysfunction after either RP (84%) or WW (80%) compared to controls (46%), which may be surprising to some. QOL scores in general were lower for study participants, and anxiety and distress were greater in these men, even over the long term. Concerns with the methodology exist. There is no baseline functional or QOL data from the study men. There were some men who did not answer the questionnaire, and many men were already dead. The control group was not randomized with the study group and may include imbalances. In the end, this study should remind us that prostate cancer is a long-term disease, which influences QOL whether treated with RP or not, and men who are diagnosed with it have a long time to live with those consequences.

Reviewer: Steven E. Canfield, MD

Article Reviewed: Johansson E, Steineck G, et al. Long-Term Quality-of-Life Outcomes After Radical Prostatectomy or Watchful Waiting: The Scandinavian Prostate Cancer Group-4 Randomised Trial. *Lancet Oncol* 2011; 12 (September): 891–899.

Pad Usage After Catheter Removal Predicts Timing of Continence After RARP



Prostate Tumors

Take Home Pearl:

Time to continence after robot-assisted radical prostatectomy is predicted by pad requirements 4 to 7 days after catheter removal.

Background: Most men experience post-prostatectomy incontinence after

catheter removal. Predictive models for when continence will return after robot-assisted radical prostatectomy (RARP) are needed.

Objective: To develop an outpatient method to predict time to return of continence after RARP.

Participants/Methods: 207 patients underwent RARP, and 172 patients

completed follow-up requirements necessary for the study. Preoperative patient demographics, prostate cancer characteristics, and uroflow parameters were collected. The RARP technique for these patients included a running Van Velthoven anastomosis, no use of cautery during the pedicle and neurovascular bundle portions of the procedure, a Rocco reconstruction,

and local endorectal hypothermia. The catheter was removed on postoperative day 7. Continence was defined as the need for no pads. Patients reported the day they stopped using pads by returning a postcard. Information on pad use (number of pads, thickness of pads, and percentage of wetness) during the first week after catheter removal was collected by telephone interview and patient-submitted data. The urinary continence was monitored closely throughout the first year after surgery by survey, telephone interview, and follow-up visits.

Results: No baseline characteristics including preoperative uroflow parameters or perioperative factors such as nerve-sparing status predicted time to

continence after surgery. Continence was variable and generally improved quickly during the first 4 days after catheter removal. In general, continence was more stable during days 4 through 7 after catheter removal and correlated well to time to pad-free status. For men using ≥ 3 pads, 2 pads, and 1 pad during days 4 to 7 after catheter removal, the median time to continence was 73 days, 42 days, and 35 days, respectively. Any of days 4 to 7 after catheter removal strongly predicted these outcomes.

Conclusions: Pad requirements during days 4 to 7 after catheter removal predict time to continence and can be used to counsel patients for expectations or possibly directing early intervention for incontinence.

Reviewer's Comments: This study reaffirms the difficulty of predicting continence based on preoperative and operative factors. Most other studies that have tried to predict time to continence have relied on data collected immediately after catheter removal. This study suggests that the continence level during the latter part of the first week after catheter removal is more predictive of time to continence. The study also suggests that patient estimates of pad requirements are sufficient for predictive purposes instead of having to ask patients for pad weights.

Reviewer: Kyle J. Weld, MD

Article Reviewed: Skarecky D, Morales B, et al. Simple Method to Predict Return of Continence After Robot-Assisted Radical Prostatectomy. *J Endourol* 2011; 25 (September): 1451–1455.

Metabolic Syndrome Is Independent Risk Factor for Nephrolithiasis



Take Home Pearl:

Metabolic syndrome is significantly associated with increased risk of developing urine acidification, which changes as the status of metabolic syndrome changes with time.

Objective: To examine the independent effect of metabolic syndrome (MS) on nephrolithiasis including assessing effect on nephrolithiasis with changes in status of metabolic syndrome over time.

Design: Prospective cohort study.

Participants: 3,872 Korean men aged 20 to 59 years participating in a comprehensive health examination at Hani General Hospital in Seoul, South Korea.

Methods: Examination was on an annual or biannual basis from 2002 to 2009. Evaluation included anthropometric measurements, biochemical measurement, and kidney ultrasonography (US). Participants were stratified based on observed or developed MS.

Results: After adjusting for age, baseline glomerular filtration rate, and uric acid level, MS at baseline was associated with a significantly increased risk of nephrolithiasis (HR, 1.77). MS over

time as a time-dependent variable also predicted the development of nephrolithiasis after adjusted baseline covariate (HR, 1.678). A significant stepwise increase in risk of nephrolithiasis was identified with each additional MS trait compared to those with no traits of MS at baseline and follow-up. As the number of MS traits increased at baseline and follow-up, the urine pH of participants at baseline and follow-up decreased significantly ($P < 0.01$). The prevalence of nephrolithiasis in participants with continual MS (6.6%) was higher than those with resolved MS (1.7%), and continual MS was an independent factor to predict nephrolithiasis.

Conclusions: Metabolic syndrome is significantly associated with increased risk of developing urine acidification, which changes as the status of metabolic syndrome changes with time.

Reviewer's Comments: MS is associated with an increased risk of diabetes, cardiovascular disease, chronic renal disease, and nephrolithiasis. Metabolic syndrome is defined as an elevated blood pressure of $>130/85$ mm Hg, an elevated fasting plasma glucose level >110 mg/dL, high serum triglyceride levels >150 mg/dL, and low HDL cholesterol levels <40 mg/dL. Waist circumference

is the other variable usually reported, but the current study substituted body mass index >25 kg/m² as the obese range variable. MS was defined as the presence of ≥ 3 of the above metabolic traits. MS is thought to increase the predisposition to kidney stones due to urine acidification, but the cause is likely multifactorial. The unique aspect about this study was the longitudinal aspect and changing status of MS in the patients that were examined. The authors also stratified by number of MS traits present to determine if it impacted stone development. The findings showed a very high correlation with MS and risk of nephrolithiasis. The data also suggested (although more difficult to demonstrate) that modifying MS traits (ie, through exercise and diet) may reduce the risk of nephrolithiasis to near baseline. More studies will need to be done to elucidate all the factors involved with stone risk and metabolic syndrome, but this study offers data that stone risk can be modified by improving metabolic syndrome status.

Reviewer: David A. Duchene, MD

Article Reviewed: Chang IH, Lee YT, et al. Metabolic Syndrome, Urine pH, and Time-Dependent Risk of Nephrolithiasis in Korean Men Without Hypertension and Diabetes. *Urology* 2011; 78 (October): 753–758.

Key NSAIDs Increase the Risk of Renal Cell Carcinoma

Take Home Pearl:

There appears to be a small but significant increased risk of renal cell carcinoma in long-term NSAID users. Such patients should be monitored with this in mind.

Objective: To assess the association between analgesic use and the development of renal cell carcinoma (RCC).

Design/Methods: Retrospective analysis of 2 large, prospective, longitudinal cohort databases — the Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS). The NHS included 16 years of follow-up in 77,525 women, and the HPFS included 20 years of follow-up in 49,403 men, with aspirin, NSAIDs, and acetaminophen usage tracked every 2 years.

Results: There were 333 cases of RCC diagnosed over that time period in the 2 studies. While no association was found for acetaminophen and aspirin,

use of NSAIDs was significantly linked to RCC, with a relative risk of 1.51 (95% CI, 1.12 to 2.04) after multivariate analysis. The risk was “dose dependent” such that it increased steadily with increased NSAID usage over time. The absolute risk increases for women and men were 9.15 and 10.92 per 100,000 patient-years, respectively.

Conclusions: Data from 2 large, comprehensive longitudinal cohort studies showed an association between increasing NSAID usage and increasing risk for developing RCC.

Reviewer's Comments: Small observational studies with limited follow-up have suggested an association between RCC and analgesic use. Data from these types of studies are interesting but unreliable and often found to be untrue after large prospective or randomized studies are undertaken. The current study looks at the association between RCC and analgesics by combining data from 2 very large, prospectively collected longitudinal studies —



the Nurses' Health Study and the Health Professionals Follow-up Study. These studies provide higher quality data due to the prospective collection and careful follow-up. Details on analgesic use were recorded every 2 years and follow-up was between 16 and 20 years. Authors found a significant association between NSAIDs and RCC, which increased with increasing NSAID usage in a dose-dependent manner. Such a finding can raise the quality of evidence in an observational study, which makes this finding even more likely to be true. The patients at highest risk were those who took NSAIDs for >10 years. Applying these results to our own patients suggests that we may consider monitoring those patients who are taking chronic NSAIDs more closely for the development of RCC.

Reviewer: Steven E. Canfield, MD
Article Reviewed: Cho E, Curhan G, et al. Prospective Evaluation of Analgesic Use and Risk of Renal Cell Cancer. *Arch Intern Med* 2011; 171 (September 12): 1487–1493.

BioGlue Reduces Hemorrhage During Laparoscopic Renal Cryoablation

Take Home Pearl:

BioGlue application on the surface of the renal tumor and surrounding tissue prior to laparoscopic cryoablation reduces post-ablation hemorrhage.

Objective: To evaluate whether the application of BioGlue to the renal surface just prior to cryoablation from a laparoscopic approach would decrease the risk of iceball fracture and subsequent hemorrhage.

Methods: The upper and lower poles of 10 kidneys in 5 pigs were subjected to laparoscopic cryoablation, for a total of 20 cryolesions. Cryolesions were created with 3 Icerods (1.47 mm) placed percutaneously 2.5 cm into the kidney and 1.5 cm apart from each other in a triangle formation. In the 10 cryolesions with BioGlue, 5 mL of purified bovine albumin glutaraldehyde tissue adhesive (BioGlue) was placed around the Icerod formation with a laparoscopic BioGlue tip applicator just prior to cryoablation. One pole was randomly selected in each kidney for the

cryolesion with BioGlue while the other served as a control without BioGlue. The BioGlue was allowed to dry for 2 minutes prior to starting the cryoablation. A 10-minute double freeze cycle was performed with intervening and subsequent 5-minute active thaw sessions. After the second active thaw, the Icerods were removed under direct laparoscopic vision, and the ablation sites were observed for bleeding.

Results: Fracture between the iceball and normal renal parenchyma was not observed in the BioGlue cryolesions, and no bleeding was observed in 70% of the BioGlue cryolesions. The mean estimated blood loss in the BioGlue group was 6 mL. In total, 70% of control cryolesions demonstrated fracture, and the average fracture length among control cryolesions was 1.9 mm. The average estimated blood loss among control lesions was 24.5 mL. There was not a statistically significant difference in mean blood loss between the control and BioGlue lesions ($P=0.06$).

Conclusions: BioGlue application reduced the incidence of fracture and the amount of post-ablation bleeding.



Reviewer's Comments: The normal renal parenchyma surrounding a renal tumor is typically compressed, and there may be a natural propensity for fracture between the tumor and normal parenchyma or within the compressed normal parenchyma. Iceball formation beyond the tumor and into the normal parenchyma may further serve to weaken this cleavage plane, making fracture a distinct possibility. This study presents encouraging data for the utility of BioGlue to stabilize this plane and minimize fracture and bleeding for cryolesions in normal porcine kidneys with no tumor. Clinical studies are needed to further evaluate BioGlue's ability to stabilize the potential fracture plane in the presence of renal tumor. If the success in iceball stabilization observed in this animal model is demonstrated in clinical studies, laparoscopic cryoablation of renal tumors will become even safer with application.

Reviewer: Kyle J. Weld, MD
Article Reviewed: Mues AC, Graversen JA, et al. BioGlue Iceball Stabilization to Minimize the Risk of Hemorrhage During Laparoscopic Renal Cryoablation. *Urology* 2011; 78 (August): 353–356.

Many Laparoscopic Pyeloplasty Failures Can Be Managed By Endopyelotomy

Take Home Pearl:

Primary laparoscopic pyeloplasty failure is uncommon and salvage with endoscopic repair is likely.

Background: Laparoscopic pyeloplasty has a high success rate of approximately $\geq 90\%$. Because of this high success rate, the literature is sparse with management recommendations for failure.

Objective: To discuss strategies for managing failures after laparoscopic pyeloplasty.

Participants/Methods: Of 128 patients who underwent laparoscopic pyeloplasty, the charts for 102 patients were available for retrospective review. Ureteropelvic junction obstruction was diagnosed by diuretic renal scan and retrograde pyelography. The procedure was performed transperitoneally and a ureteral stent and drain was placed in each case. The stent was removed 2 to 6 weeks after the case. The follow-up consisted of diuretic renal scan at 3 weeks and 1 year. If the 3-week scan was equivocal, a repeat scan was obtained at 3 months.

Results: In general, success was defined as a $T_{1/2}$ of ≤ 20 minutes and improvement in symptoms. In total, 84 (82%) patients were successfully treated with primary laparoscopic pyeloplasty and 18 (18%) patients failed. Patients with primary failure were more likely to have diabetes mellitus, longer length of stay, higher ASA score, stent placement at time of pyeloplasty, or ureteral stent malfunction. Of the 18 failures, 13 presented within the first year and 5 beyond the 1-year follow-up. Median time to failure was 2.5 months. Salvage treatment consisted of 2 treated conservatively, 10 with endopyelotomy, and 6 with nephrectomy. Of the 10 treated endoscopically, 7 were successfully treated while 3 failed. Patients with salvage failure were more likely to have a stent malfunction or body mass index >30 kg/m². Multivariate analysis revealed stent placement at the time of pyeloplasty (as opposed to stent placement previously) and ASA score >2 to be associated with failure. The overall primary and salvage success rate was 90%.

Conclusions: Primary laparoscopic pyeloplasty failure is uncommon, and salvage with endoscopic repair is likely.

Reviewer's Comments: It is important to note that most failures occur early, but some did not present until more than a year after surgery. This possibility of late failure should be remembered when following patients after laparoscopic pyeloplasty. Many authors have discussed the association of high ASA score and body mass index with laparoscopic complications. I find it interesting that the authors associated a history of diabetes with pyeloplasty failure. Diabetes can negatively affect the microvasculature that surgeons rely on for success in reconstructive procedures. Also interesting is the link between stent placement at the time of pyeloplasty and failure, which suggests that prior stent placement may be optimal. The early stent placement may be due to better chances of success with symptomatic or severe obstruction, partial dilation of the obstruction making the reconstructive effort easier, or there may be other unknown reasons for this finding.

Reviewer: Kyle J. Weld, MD

Article Reviewed: Tan H-J, Ye Z, et al. Failure After Laparoscopic Pyeloplasty: Prevention and Management. *J Endourol* 2011; 25 (September): 1457–1462.

Botox Reduces Incontinence in Patients With Neurogenic Detrusor Overactivity

Take Home Pearl:

OnabotulinumtoxinA 200 U and 300 U significantly reduced incontinence and improved urodynamic parameters and quality of life in patients with urinary incontinence secondary to neurogenic detrusor overactivity.

Objective: To evaluate the safety and efficacy of onabotulinumtoxinA (Botox®) in doses of 200 U and 300 U for the treatment of urinary incontinence due to neurogenic detrusor overactivity.

Design: Large, randomized placebo-controlled trial.

Participants/Methods: To be eligible, subjects had to be between the ages of 18 and 80 years with >14 urinary incontinence episodes per week due to neurogenic detrusor overactivity from a spinal cord injury or multiple sclerosis (MS). OnabotulinumtoxinA was administered via a cystoscope as 30 intradetrusor injections (1 mL each) approximately 1 cm apart and to a depth of 2 mm, sparing the trigone. Injections were performed without

anesthesia after bladder instillation and drainage with local anesthesia, or under general anesthesia if necessary. Study visits occurred at weeks 2, 6, and 12 after treatment and every 6 weeks thereafter. Patients were followed for 1 year. If retreatment was necessary, they were followed for an additional 12-week time period.

Results: 275 patients were randomized: 92 to placebo, 92 to onabotulinumtoxinA 200 U, and 91 to onabotulinumtoxinA 300 U. At week 6, the mean weekly urinary incontinence episodes were significantly reduced in both the onabotulinumtoxinA 200 U and 300 U groups compared to placebo ($P < 0.01$). There were no clinically relevant differences between onabotulinumtoxinA dose groups; however, the 200 U group had a more favorable safety profile. Significant benefits were observed in patients by week 2, and the proportion of patients who achieved a $\geq 50\%$, $\geq 75\%$, or 100% reduction in weekly urinary incontinence episodes was significantly higher with onabotulinumtoxinA than placebo ($P < 0.001$). The most common adverse event during the first 3 months was urinary tract infection. In patients

not using clean intermittent catheterization at baseline, most of whom were MS patients, post-void residual (PVR) significantly increased following onabotulinumtoxinA treatment in a dose-dependent manner. The percentage of patients with a PVR over 200 mL was highest in the 300 U group.

Conclusions: OnabotulinumtoxinA significantly reduced urinary incontinence and improved urodynamics and quality of life in MS and spinal cord injury patients with neurogenic detrusor overactivity.

Reviewer's Comments: It is interesting that this paper seems to have found a dose ceiling effect for onabotulinumtoxinA whereby no clinically significant additional benefit was observed with a 300 U dose compared to the 200 U dose.

Reviewer: Karl J. Kreder, MD

Article Reviewed: Cruz F, Herschorn S, et al. Efficacy and Safety of OnabotulinumtoxinA in Patients With Urinary Incontinence Due to Neurogenic Detrusor Overactivity: A Randomised, Double-Blind, Placebo-Controlled Trial. *Eur Urol* 2011; 60 (October): 742–750.

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E-quiz code: 31663N

1. A recent study found that in men with functional erections prior to treatment, the rate of functional erections 2 years after treatment was 48%.
Practice: T F **Answer Submitted: T F**
2. A recent trial found that vitamin E supplementation increased the risk of prostate cancer by 17%.
Practice: T F **Answer Submitted: T F**
3. Appropriately treated preoperative urine cultures eliminate positive renal pelvis urine or positive stone cultures.
Practice: T F **Answer Submitted: T F**
4. Ureteral access sheaths should not be used in the diagnosis of upper tract urothelial carcinoma.
Practice: T F **Answer Submitted: T F**
5. In a recent study by Tan et al, all of the primary laparoscopic pyeloplasty failures presented within the first year after surgery.
Practice: T F **Answer Submitted: T F**
6. Vesicourethral anastomosis with barbed suture can be performed safely and more quickly compared to standard monofilament suture with no difference in functional outcomes.
Practice: T F **Answer Submitted: T F**
7. Nocturia is associated with decreased quality of life and increased prevalence of depression in both men and women.
Practice: T F **Answer Submitted: T F**
8. A recent study found that intraoperative blood loss >100 cc occurred more frequently in the retropubic group compared to the transobturator group.
Practice: T F **Answer Submitted: T F**
9. According to the Ethics Committee of the American Society for Reproductive Medicine, the urologist is required to honor the wishes of the power of attorney and harvest sperm from a deceased man.
Practice: T F **Answer Submitted: T F**
10. High-dose cyclophosphamide and testicular radiation result in severe, long-term infertility.
Practice: T F **Answer Submitted: T F**
11. Decaffeinated coffee appears to be as effective as caffeinated coffee for reducing the risk of depression.
Practice: T F **Answer Submitted: T F**
12. Low-calorie or high-protein diets can improve multiple aspects of sexual and urinary health within 8 weeks.
Practice: T F **Answer Submitted: T F**
13. Men treated with radical prostatectomy have significantly worse erectile function in the long term compared to men treated with watchful waiting.
Practice: T F **Answer Submitted: T F**
14. Patients who take NSAIDs long term have an increased risk of renal cell carcinoma over time.
Practice: T F **Answer Submitted: T F**
15. Uric acid stones are associated with a lower estimated glomerular filtration rate.
Practice: T F **Answer Submitted: T F**
16. Metabolic syndrome is an independent risk factor of nephrolithiasis.
Practice: T F **Answer Submitted: T F**
17. Time to return of continence after robot-assisted radical prostatectomy is reliably predicted based on preoperative uroflow parameters.
Practice: T F **Answer Submitted: T F**
18. In a recent study, fracture between the iceball and normal parenchyma was not observed when BioGlue was applied to the cryolesion.
Practice: T F **Answer Submitted: T F**
19. A recent study found that the ideal dose of onabotulinumtoxinA in neurogenic detrusor overactivity patients appears to be 200 U.
Practice: T F **Answer Submitted: T F**
20. The single-incision mid-urethral Ajust sling has a success rate at 1-year follow up of approximately 80%.
Practice: T F **Answer Submitted: T F**

1. **T** Neoadjuvant cisplatin, methotrexate, and vinblastine chemotherapy improves overall survival in patients undergoing cystectomy or radiation therapy for muscle-invasive bladder cancer.
2. **T** Preoperative intravesical electromotive mitomycin is superior to postoperative passive diffusion mitomycin and transurethral resection of bladder tumor alone for primary nonmuscle-invasive bladder cancer.
3. **T** Ureteral avulsion can occur with withdrawal of a semirigid ureteroscope, even if a stone is not basketed and extracted.
4. **F** More than 25% of patients undergoing percutaneous nephrolithotomy for a staghorn calculus will require a blood transfusion.
5. **F** Although CT scans impart increased radiation exposure, it is justified by the inadequacy of ultrasound in imaging stones in children.
6. **F** In patients with unilateral Wilms tumor, partial nephrectomy has higher local recurrence than radical nephrectomy for similar stage disease and is not recommended.
7. **F** Percutaneous nerve evaluation may be a more sensitive screening method than first-stage timed-lead placement testing for the identification of patients eligible for sacral neuromodulation therapy.
8. **T** Because women undergoing prolapse surgery tend to hold a wide variety of expectations for both negative and positive outcomes, these considerations should be a vital part of preoperative counseling.
9. **F** Men who successfully quit smoking display enhancements in sexual function and show a differential improvement compared to unsuccessful quitters.
10. **T** Between 16 and 30 minutes postdosing, the onset of action of vardenafil is >65% for both the orodispersible tablet and the film-coated formulation.
11. **T** Metformin and lifestyle changes can significantly reduce weight, waist circumference, body mass index, and systolic blood pressure in men who are on androgen deprivation therapy for prostate cancer.
12. **F** For the treatment of benign prostatic hyperplasia, saw palmetto is slightly (nonsignificantly) more effective compared to a placebo when using 960 mg a day.
13. **F** A combination of soy, selenium, and vitamin E does not reduce the progression of high-grade prostatic intraepithelial neoplasia to prostate cancer but does result in a lower detection rate of high-grade cancer.
14. **T** According to a recent study, objective radiographic response may be a predictor of overall survival in men with metastatic castrate-resistant prostate cancer who undergo chemotherapy.
15. **T** Ultrasonic lithotrites can fragment a basket wire but take longer to do so than the holmium laser.
16. **F** Real-time visualization of cystoscopy by patients on the endoscopic monitor is important only if they have not had a cystoscopy in the past.
17. **F** A large mound on postoperative ultrasound correlates with a low risk of persistent vesicoureteral reflux.
18. **F** Compared to the V-flap, the VQZ flap has a higher complication rate related to the complexity of the skin flap.
19. **T** Neuromodulation may have a role in the treatment of chronic bladder pain.
20. **F** Patients with overactive bladder tend to regard treatment efficacy and side effects of equal magnitude when making decisions regarding treatment.

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