Gemcitabine Plus RT Offers Promising Results for MIBC

Phase II Study of Conformal Hypofractionated Radiotherapy With Concurrent Gemcitabine in Muscle-Invasive Bladder Cancer.


The combination of radiotherapy and concurrent gemcitabine offers excellent local control rates for patients with muscle-invasive bladder cancer.

**Objective:** To test the response of muscle-invasive bladder cancer (MIBC) to a combination of gemcitabine and radiotherapy.

**Design/Participants:** Prospective, phase II study involving 50 patients with MIBC.

**Methods:** Patients received 52.5 Gy radiotherapy in 20 fractions plus concurrent low-dose gemcitabine. Patients were assessed for response by cystoscopy, biopsy, and MRI. The primary end points of the study were primary tumor response, treatment-related toxicity, and overall survival.

**Results:** All patients were able to complete radiotherapy. All but 4 patients received all 4 cycles of gemcitabine. Of the 47 patients who underwent post-therapy cystoscopic evaluation, 88% achieved a complete tumor response. The median follow-up was 36 months, and, at last follow-up, 36 patients were alive. Of these, 32 patients had an intact, functional bladder. Fourteen patients died, 7 due to metastatic disease, 5 due to other causes, and 2 due to treatment-related complications. A total of 4 patients underwent cystectomy, 3 due to disease recurrence and a fourth for bladder toxicity. Estimated 3-year overall and cancer-specific survival rates were 75% and 82%, respectively.

**Conclusions:** Concurrent radiotherapy and gemcitabine is associated with a high response rate for MIBC and durable long-term local cancer control. Further phase III studies are warranted for this combination bladder-sparing treatment.

**Reviewer's Comments:** While the gold standard for managing MIBC has been radical cystectomy in most countries, if an alternative could be found that offered reliable, durable local control while retaining the patients’ native bladder and avoided the morbidity of cystectomy, it would be a major advance in the field. Many studies have explored the utility of radiotherapy in this context, and many have used differing radiosensitizing regimens. While some of these regimens have shown promise, none has replaced cystectomy as the standard of care, at least in the United States. This study by Choudhury and colleagues seeks to explore the potential of a novel combination of concurrent radiotherapy with gemcitabine as the radiosensitizer. This well-executed, prospective study demonstrates an impressive 88% local complete response rate among those evaluated after therapy. It also boasts good long-term overall and disease-specific survival rates at 3 years. It is important to bear in mind, however, that these results came at the cost of substantial toxicity, including 2 treatment-related deaths and 2 major surgeries due to toxicity. In addition, while control in the bladder was very good, there were failures in the locoregional lymph nodes that were not targeted by radiotherapy. Efforts to address these issues will require more carefully done trials like this one, as will the ultimate test by comparing one or more of these bladder-sparing regimens to the current gold standard, radical cystectomy. (Reviewer-Peter Clark, MD).

**Keywords:** Muscle-Invasive Bladder Cancer, Radiotherapy, Gemcitabine, Radiosensitizer

**Print Tag:** Refer to original journal article
Nephron-Sparing vs Radical Nephrectomy for Renal Masses

A Prospective, Randomised EORTC Intergroup Phase 3 Study Comparing the Oncologic Outcome of Elective Nephron-Sparing Surgery and Radical Nephrectomy for Low-Stage Renal Cell Carcinoma.

Van Poppel H, Da Pozzo L, et al:

Eur Assoc Urol 2011; 59 (April): 543-552

Nephron-sparing and radical nephrectomy for small renal masses have similar oncologic efficacy.

**Objective:** To compare overall and progression-free survival in patients undergoing nephron-sparing surgery (NSS) versus radical nephrectomy (RN) for a small renal mass.

**Design:** Prospective, randomized, multi-center trial.

**Participants/Methods:** 541 patients with a renal mass <5 cm were randomized to receive either NSS (n=268) or RN (n=273).

**Results:** Median follow-up was 9.3 years. On the intention-to-treat analysis, the estimated 10-year survival was lower for the NSS group (75.7%) than for the RN group (81.1%). However, no significant difference was found in disease-specific survival. In the analysis of clinically and pathologically eligible patients, the differences were no longer significant.

**Conclusions:** Both NSS and RN provide excellent oncologic efficacy. While in the intention-to-treat analysis, survival was better in the RN group, in the targeted population of renal cell carcinoma patients, this was no longer significant.

**Reviewer’s Comments:** For some time now, NSS has been a well-accepted alternative to RN in the management of small renal masses. Indeed, recently, there has been a growing call for NSS to be the preferred management. However, until this time, all the comparisons published in the literature have been based on retrospective cohort series. This study by Van Poppel and colleagues represents the first published, randomized, prospective trial to compare these approaches. The findings suggest that, oncologically, the 2 approaches are similar. However, the suggestion that NSS was associated with worse overall survival was surprising. While it would be easy to take this impression at face value, it is important to understand some of the acknowledged caveats regarding this study. One is that the trial was originally designed as a noninferiority trial, and when analyzed purely in that light, the difference between groups was not significant. The second is that the trial was designed to accrue 1300 patients, but had to be stopped early, with only 541 patients. Thus, the study is underpowered to test for both superiority and noninferiority. The third caveat is that, when the analysis is done by actual treatment received or restricted to those with proven renal cell carcinoma, all differences between the groups with regard to survival are no longer significant. Bearing in mind these limitations, the take-home message is that NSS is not inferior to RN for the management of small renal masses. It is not possible to state that either is superior based on this study. Therefore, based on the preponderance of evidence in other trials suggesting a benefit to NSS, in general, this still remains the preferred approach to the management of these patients. Larger-scale studies would be needed to address these points in more detail, but these will be hard to accomplish going forward. (Reviewer-Peter Clark, MD).

Keywords: Kidney Cancer, Nephron-Sparing Surgery, Radical Nephrectomy, RCC

Print Tag: Refer to original journal article
NBI Digital Flexible Ureteroscopy Increases Tumor Detection


Traxer O, Geavlete B, et al:

J Endourol 2011; 25 (January): 19-23

Narrow-band imaging with the Olympus digital ureteroscope improves the detection of urothelial tumors by 23%.

Background: The Olympus digital ureteroscope (URF-V) provides a larger image size and narrow-band imaging (NBI) and is an alternative light-wavelength capture system that detects altered blood vessel morphology of urothelial mucosa.

Objective: To determine if NBI using the Olympus digital flexible ureteroscope improves the cancer detection rate when used in conjunction with white light.

Participants: 27 patients. Half of the patients underwent follow-up for known upper tract transitional cell carcinoma, and half underwent initial evaluation.

Methods: Lesions were identified on NBI as having either increased vasculature or having dotted, tortuous, or large-caliber vessels.

Interventions: Full inspection of the upper collecting system was performed first with white-light and then with NBI. All suspicious lesions were biopsied with Piranha biopsy forceps and then fulgurated with the holmium laser.

Results: NBI resulted in improved endoscopic visualization of the lesions. Additional tumor detection (14%) and extended limits of ablation (9%) led to significant improvement in cancer detection and changes in management in 23% of patients. Insufficient biopsy samples were obtained in one fourth of patients. The lower calyces could not be inspected in their entirety in 7% of patients.

Conclusions: NBI is superior to white light imaging for the detection of upper tract urothelial malignancy.

Reviewer’s Comments: NBI utilizes an optical image enhancement technology that enhances the contrast between capillaries and tissue surfaces. This study establishes superiority in the ability to identify lesions and define the limits of disease. Others have reported its value over standard cystoscopy for bladder tumor detection. One of the most important findings of this study was that, in 3 patients (11%), traditional white light imaging would have detected no cancer while NBI provided the true diagnosis. The impact of improved detection and definition of margins on recurrence and progression of disease warrants further long-term investigation. (Reviewer-Manoj Monga, MD).

Keywords: Ureteroscopy, Instrumentation, Transitional Cell Cancer

Print Tag: Refer to original journal article
Objective: To evaluate the impact of early (<48 hours) shockwave lithotripsy (SWL) for proximal ureteral calculi.

Design: Prospective, randomized, clinical trial.

Participants: 160 patients with a single radio-opaque proximal ureteral calculi <1 cm in size.

Methods: Patients were randomized to SWL <48 hours after onset of renal colic versus >48 hours after onset of renal colic. Final outcome was determined by noncontrast CT at 3 months.

Interventions: SWL was performed with the Dornier Alpha Compact (electromagnetic) lithotripter with oral analgesia and local anesthesia. Patients were treated at a rate of 100/minute to a maximum of 3000 shockwaves. Repeat SWL was performed every 24 hours if residual fragments were noted on KUB; up to 4 sessions. Patients were hospitalized through the treatment course.

Results: The mean stone size was 7.5 mm. Stone fragmentation was comparable (90%) between the 2 groups, as was the stone-free rate (86% vs 80%). However, the time to stone clearance was shorter (10 days) for early SWL than for late SWL (21 days). There was no difference if patients were treated within 24 hours versus 48 hours. Retreatment rates (16% vs 26%) and auxiliary procedures (16% vs 33%) were significantly lower in the early treatment group. On average, delayed SWL patients required 3 SWL sessions, while the early SWL patients required 1 session. Steinstrasse was more common with delayed SWL (13%) than with early treatment (6%).

Conclusions: Early SWL is more efficacious than delayed SWL for proximal ureteral calculi.

Reviewer's Comments: This intriguing study lends support to the theory that early management of obstructive ureteral calculi should be considered. Indeed, for a 7-mm proximal ureteral stone that would have only a 30% chance of spontaneous stone passage, in situ SWL on an urgent basis is an excellent alternative. Ease of scheduling and insurer authorization would likely be a limiting factor for implementation of such a protocol. The impact on time to stone passage and the development of steinstrasse is clear. What is less clear is the impact on retreatment rates and the algorithm followed by the authors of reimage and retreat every 24 hours as an inpatient diverges from current practice in the United States. Outpatient therapy and reimaging in 2 weeks might allow more patients the opportunity for spontaneous stone passage after just one therapy. Similarly, the addition of an alpha-blocker after SWL to promote stone expulsion could change the findings of this study. Last, treating at a slow rate (60/minute) may have resulted in smaller fragments and improved outcomes. Despite these limitations, the study provides food for thought -- that early intervention before the development of ureteral edema and mucosal hyperplasia -- may improve outcomes. (Reviewer-Manoj Monga, MD).
Background: Ultrasound (US) is increasingly being utilized by pediatricians in the preoperative evaluation of nonpalpable testes (NPT).

Objective: To evaluate the diagnostic performance of US in localizing NPTs in pediatric patients.

Methods: A literature review was performed that included studies of subjects aged <18 years with preoperative US for nonpalpable testes and surgical confirmation of the position or absence of the testes. US performance characteristics were derived, and a meta-analysis of 12 studies (591 testes) was performed.

Results: US is associated with a sensitivity of 45% and a specificity of 78%. The positive and negative likelihood ratios are 1.5 and 0.8, respectively. Significant heterogeneity limited the precision of these estimates related to variability in reporting the selection criteria, ultrasound methodology, and differences in the proportion of intra-abdominal testes.

Conclusions: US does not reliably localize nonpalpable testes and does not rule out intra-abdominal testes. Eliminating US from the preoperative evaluation of NPT will not change management, but it will decrease cost.

Reviewer’s Comments: This article could not be timelier in the face of increasing health care costs and immense pressure to reduce health care spending. This is a situation ripe for reform. The authors perform an elegant analysis that, if anything, overestimates the performance of US in localizing NPT. Were it more accurate, it would potentially spare a child an operation for absent testes or possibly limit the extent of surgery. However, simply put, US is inadequate to obviate the need for surgical exploration for the nonpalpable testes and does not have the diagnostic power necessary to change the standard surgical algorithm. (Reviewer-John Gatti, MD).

Keywords: Nonpalpable Testes, Ultrasound

Print Tag: Refer to original journal article
As age increases, germ cell counts decrease in intra-abdominal testes, with 93% of boys having no germ cells by age 3 years.

**Objective:** To study the histology of intra-abdominal testes obtained by biopsy at the time of orchiopexy and to correlate findings with age at the time of orchiopexy.

**Participants/Methods:** 57 boys underwent laparoscopy for nonpalpable testes from 2002 to 2005. Testicular biopsies were taken from 42 intra-abdominal testes in 32 boys. Biopsies were examined for testicular histology with regard to mean diameter of seminiferous tubules (MTD) and germ cells per tubule.

**Results:** Testicular biopsies from 29 boys were included in the analysis. Histology revealed decreased MTD compared to historical controls. Germ cells were absent in 55%. As age at orchiopexy increased, germ cell counts decreased. The absence of germ cells was noted in biopsies in boys aged >1 year and was noted in 93% of boys by age 3 years. Microlithiasis was noted in 7% of boys overall.

**Conclusions:** As age at orchiopexy increases, histological abnormality in germ cell numbers increases, with 93% having an absence of germ cells after 3 years of age. Whether earlier orchiopexy would improve this finding remains to be proven.

**Reviewer's Comments:** It is clear that undescended testes, especially intra-abdominal testes, have worsening histologic parameters over time. This article describes the findings of worsening MTD and germ cell counts as boys age, implying an increasing risk for infertility as adults. The study is limited by historical controls and uses surrogate parameters for paternity. Nonetheless, "no germ cells" can't be good. The million-dollar question is, "What can be done to modify this?" Is earlier surgery the answer, or is additional hormonal modulation required to salvage this course? These last questions have dampened enthusiasm for testicular biopsy in general, since, at this point, the results are more academic than useful in modifying the management of cryptorchidism. This article contributes to the cause, and the information may ultimately support answers to these vital questions. (Reviewer-John Gatti, MD).

**Keywords:** Intra-Abdominal Testis, Histopathology

**Print Tag:** Refer to original journal article
Anterior graft kits used for recurrent prolapse appear, in some hands, to have efficacy, but this must be balanced with postoperative symptomatic response and mesh exposure rate.

**Objective:** To assess 2-year outcomes associated with the use of a particular anterior compartment mesh kit repair (Prolift™) for women who had undergone prior anterior vaginal prolapse repair and repeat surgery.

**Design:** Prospective observational study.

**Participants:** 36 consecutive women at a referral institution in Northern England.

**Methods:** Women were assessed at baseline, 6 months, and 2 years and completed the Prolapse Quality of Life Questionnaire, the Prolapse and Incontinence Sexual Function Questionnaire-Short Form, and, postoperatively, the Global Impression of Improvement Questionnaire. Women underwent evaluation with Pelvic Organ Prolapse Quantification System staging, and anatomical success was defined as less than or equal to stage 1 prolapse postoperatively in the anterior compartment. Other outcome measures included quality of life domains and mesh exposure rate. Preoperatively, stage 2 or greater anterior vaginal wall prolapse was noted in 34 of 36 cases (the other 2 cases had less than stage 2). At a mean follow-up of 24.6 months, 19 patients (53%) had stage 1 or less anterior prolapse; these cases were considered anatomical successes. Fifteen women had a stage 2 anterior prolapse, and 2 women had a stage 3 prolapse. Of the group, 29 patients had an improvement in symptoms. Sixteen patients were sexually active preoperatively, and 7 reported dyspareunia postoperatively, which was significant. As noted in prior studies, poor correlation exists between anatomical and functional outcomes. Mesh exposure was seen in 18% of patients (7), and 5 patients needed surgical revision for mesh exposure or recurrent prolapse.

**Conclusions:** There was poor functional outcome correlation with symptomatic success. A slight majority of patients had achieved anatomical success by surgical criteria identified in this paper. However, the mesh exposure rate of 18% was concerning, and 7 patients required re-intervention for problems related to their mesh.

**Reviewer’s Comments:** Again, aspects of mesh compartment repairs remain to be answered. This paper looks at a group of women undergoing recurrent prolapse repair with a mesh kit. As noted in many papers, there is a poor correlation between anatomical evaluation and functional outcomes. This is critical in prolapse because functional outcomes historically have not been well categorized and studied. Functional outcomes are very important to patients and are problematic to deal with. Patients had almost a 20% exposure rate, but, more worrisome was that dyspareunia was possibly related to exposed mesh and/or relative nonelasticity of the mesh when in place. Dyspareunia remains a significant consequence of prolapse repair under any circumstance. This study lacks a comparison group, but the authors are well experienced and the findings are representative of results that might be obtained by accomplished surgeons. (Reviewer-Roger R. Dmochowski, MD).

**Keywords:** Prolapse, Anterior Wall, Mesh, Prolift, Recurrent, Erosion

**Print Tag:** Refer to original journal article
Postpartum Urinary Retention Can Produce Long-Term Voiding Dysfunction

Objective: To assess the risk factors and prevalence for protracted urinary retention after childbirth occurring from postpartum day 3 forward.

Design: This was an observational study of 30,757 women delivering over a 3-year time frame from June 2006 to June 2009 in a large Israeli teaching hospital.

Methods/Results: Patients were identified in a cohort of women undergoing delivery at a large referral hospital. Those with voiding dysfunction after day 3 postpartum were considered to have protracted postpartum urinary retention. Of this large group of patients, 55 patients were identified who fulfilled the diagnostic criteria as labeled above. These patients were matched to a contemporaneous cohort of 110 women for both age and parity delivering at the same time who did not develop urinary symptoms. Of the 55 women who developed voiding dysfunction, 41 were first delivery patients and 14 were patients who had had multiple deliveries. The overall incidence of postpartum urinary retention was 0.18%. Multivariate logistic regression analysis performed for a variety of demographic and labor-related criteria revealed that the duration of the second stage of labor and vacuum delivery were found to be significant independent risk factors for the development of postpartum urinary retention. Of those who developed urinary retention, 36 (65%) achieved normal voiding by 14 days postpartum, and 19 (35%) required time frames from 15 to 28 days. There was a tendency for high post-void residual retention at 72 hours after delivery to be predictive of increased risks for the late recovery of voiding. Of the initial patients identified, 48 were then contacted at a longer time frame from surgery (3 to 39 months). Five of these women (10%) had stress urinary incontinence, and 4 (8.3%) had de novo overactive bladder symptoms. Three women (6.3%) had other subjective voiding difficulties without urodynamic evidence. These rates were lower than those seen in the controlled population.

Conclusions: Protracted urinary problems related to retention after delivery is uncommon. One of the factors found to be predictive of this problem was high post-void residual at day 3 after delivery. No patients developed long-term urinary retention.

Reviewer's Comments: The woman who presents with urinary problems post-delivery is unusual but problematic. Data regarding these patients are not well identified, and this study presents interesting data to assess this population. Obviously, partum-related factors clearly have a predictive value for longer-term problems. Additionally, these women appear to be at a small increased risk for longer-term lower urinary tract issues such as incontinence and overactive bladder. Given the observational nature of this study, it is well done; however, follow-up at other institutions using different delivery techniques and assessment of cesarean section patients as comparators would also be noteworthy. (Reviewer-Roger R. Dmochowski, MD).

Keywords: Labor & Delivery, Postpartum, Puerperium, Urinary Retention, Voiding Dysfunction

Print Tag: Refer to original journal article
Improvement in EF Can Occur More Than 2 years After Prostate Surgery

Time Course of Recovery of Erectile Function After Radical Retropubic Prostatectomy: Does Anyone Recover After 2 Years?
Rabbani F, Schiff J, et al:
J Sex Med 2010; 7 (December): 3984-3990

Prolonged spontaneous recovery of erectile function may affect the recommendation concerning non-reversible procedures such as the insertion of penile prosthesis.

Background: Given the lack of reliable literature on the time course of erectile function (EF) recovery after radical prostatectomy (RP), many physicians guide patients and suggest that recovery beyond 24 months is unlikely.

Objective: Using a large database, the authors sought to determine the time course of EF recovery after RP.

Methods: EF was scored prospectively on a 5-point scale (with 1 being a full erection and 5 being no erection); 136 men who were potent preoperatively underwent bi-lateral nerve-sparing RP without prior treatment. They had not recovered EF at 24 months and, therefore, had further follow-up regarding EF. The mean follow-up after the 2-year visit was 36 months.

Results: The actuarial rates for further recovery of EF to level 1 to 2 in those with level 3 EF at 2 years was 8% (at 3 years), 20% (at 4 years), and 23% (at 5 years); these rates for further recovery of EF to level 1 to 3 in those with level 4 to 5 at 2 years was 5% (at 3 years), 17% (at 4 years), and 21% (at 5 years).

Conclusions: Younger age was predictive of a greater likelihood of recovery beyond the 2-year mark. The authors also concluded that there was continued improvement in EF beyond 2 years, and this prolonged time of recovery may allow patients to have a more realistic time expectation in terms of spontaneous recovery. This may affect recommendations concerning nonreversible procedures for EF such as insertion of a penile prosthesis.

Reviewer's Comments: Weaknesses in this study include the use of a 5-point scale for EF recovery rather than more sophisticated EF scaling methods. Why the authors preferred this is not clear. Also, the surgeon was interviewing the patient for EF recovery rather than a more accepted measure, which could account for a "report bias" limitation in this study. Men may feel obligated to tell the surgeon that their erections are working well when, in fact, they are not, because they do not want to appear ungrateful or disappoint the surgeon. There is no validated way to measure nerve-sparing efficacy; therefore, some men may have had a non-nerve-sparing procedure. The cohort consists of <50%, as a majority of men did not recover sexual function at the 2-year mark. (Reviewer-Kevin T. McVary, MD, FACS).

Keywords: Erectile Function, Erectile Dysfunction, Radical Prostatectomy

Print Tag: Refer to original journal article
Vacuum Therapy Can Improve or Stabilize PD Curvature

The Role of Vacuum Pump Therapy to Mechanically Straighten the Penis in Peyronie’s Disease.

Raheem AA, Garaffa G, et al:

BJU Int 2010; 106 (October): 1178-1180

In this study of patients with Peyronie’s disease, penile curvature was corrected surgically in 15 patients; the remaining 16 patients were sufficiently satisfied with the vacuum therapy results to avoid surgery.

**Background/Objective:** This interesting article looks at the role of vacuum therapy to assist in the correction of Peyronie’s disease (PD). It has long been noted that modeling by manual manipulation can correct defects in the tunica albugenia during penile implantation. The authors have applied this principle as an alternative conservative therapy in men with PD who refused more invasive therapy.

**Participants:** 31 patients with PD for an average duration of 9.9 months and a mean age of 51 years completed the study.

**Methods:** The study was performed for a 12-week period using various vacuum devices for only 10 minutes twice a day. The assessments at entry and completion after 12 weeks included the International Index of Erectile Function and another assessment of pain and intensity, as well as measurement of the penile length and the angle of deformity after intra-cavernous injection with prostaglandin-E1.

**Results:** The authors reported a clinically and statistically significant improvement in penile length, angle of curvature, and pain after only 12 weeks of using the vacuum device. Of these 31 patients, 21 had a reduction in the angle of curvature by 5 to 25 degrees, 3 had a worsening of the curvature, and no change in the balance was noted in 7 patients. The curvature was corrected surgically in 15 patients, and the 16 remaining patients were sufficiently satisfied with the outcome to avoid surgery.

**Conclusions:** Vacuum therapy can improve or perhaps stabilize PD curvature, is likely to be safe in all stages of the disease, and may reduce the incidence of required surgery.

**Reviewer’s Comments:** Unfortunately, the authors did not include a control group. It is not clear what percentage of these patients would improve spontaneously regardless of treatment? PD, especially in those with more acute disease, have a known resolution rate; therefore, some of the attributes related to the vacuum device may have actually been resolution of the disease by spontaneous recovery. It is interesting that investigators in PD appear particularly adverse to appropriate control groups. (Reviewer-Chris T. McVary, MD, FACS).

Keywords: Peyronie’s Disease, Vacuum Therapy

Print Tag: Refer to original journal article
A variety of cost-effective dietary supplements are immediate potential candidates to improve sperm quality.

**Background:** A large percentage of male subfertility issues are believed to be the result of oxidative stress on sperm quality and quantity. Numerous antioxidant studies have been completed in urology, but a large meta-analysis has been needed.

**Objective:** To evaluate the impact of a variety of antioxidant dietary supplements on fertility issues for men/couples undergoing assisted reproduction techniques (ART).

**Design/Methods:** 34 randomized trials involving 2876 couples were used for this analysis. Any type of antioxidant supplement intervention was included, whether single or multiple compound products. The clinical outcomes evaluated were live birth, pregnancy, miscarriage, stillbirth, sperm DNA damage, sperm concentration and motility, and side effects. Two review authors independently evaluated these studies for proper criteria.

**Results:** No serious side effects were reported in any of the clinical trials. A significantly ($P=0.0008$) higher rate of live births occurred in 3 trials compared to controls; this finding was based on 214 couples and 20 live births. A significant ($P<0.00001$) increase in pregnancy rates compared to controls was found in 15 trials that included 964 couples and 96 pregnancies.

**Conclusions:** Oral antioxidant supplements may improve the chances of conception during fertility treatment.

**Reviewer's Comments:** I think it is really easy for many in medicine (including urology) to dismiss the impact of dietary supplements for all kinds of conditions. However, I contend that dietary supplements occupy a beautiful place in medicine when benefits outweigh risks, and these supplements are especially utilized for a specific condition (like a prescription drug) that does not have an ocean of opportunity available for the patient. This review is one of the most positive for the use of a variety of dietary supplements to improve a specific urologic condition. Yet, some researchers will continue to want more data before using this method with ART. This would be foolish. We have to be honest that, if this review really involved a low-cost prescription drug, many of us would recommend that patients take it, along with other conventional treatments. It is easy to make fun of alternative medicine, but it is hard to acknowledge that benefit outweighs risk in certain situations and that some alternatives should be considered conventional medicine right now. If a desperate couple comes into your office about to pay a fortune for a reproductive technique and asks if they can take a certain quantity of vitamin C, L-carnitine, or coenzyme Q10 during the process, what are you going to say? I hope you will not let a stuffy callous "expert" from some urologic journal article or presentation convince you that we need "more randomized trials" (which is true of everything in medicine)! That answer stinks about as bad as a new dog (without tomato juice) that decided to wrestle for a while with the neighborhood skunk! (Reviewer-Mark A. Moyad, MD, MPH).

**Keywords:** Antioxidants, Male Subfertility

**Print Tag:** Refer to original journal article
Aspirin Has Anti-Cancer Properties

Effect of Daily Aspirin on Long-Term Risk of Death Due to Cancer: Analysis of Individual Patient Data From Randomized Trials.
Rothwell PM, Fowkes FGR, et al:
Lancet 2011; 377 (January 1): 31-41

Low-dose aspirin may make sense for colorectal cancer mortality prevention but is not yet recommended for urologic cancers.

**Background:** There have been numerous clinical trials for cardiovascular primary and secondary prevention over several decades that may provide some insight into the ability of aspirin to reduce the risk of mortality from cancer. However, specific cancers that have been affected more than others have not been recently evaluated.

**Objective:** To determine the impact of daily aspirin use on overall and cancer-specific mortality.

**Design/Methods:** This analysis of 8 clinical trials included >25,500 participants and 674 recorded cancer deaths. Trials of ≥4 years were included, and gastrointestinal as well as nongastrointestinal causes of death were determined.

**Results:** Allocation to aspirin was associated with a significant ($P = 0.003$) 21% reduction in the risk of cancer death. The benefit was observed after at least 5 years of use, and larger reductions were observed with longer use (up to 20 years). The largest reduction was observed for colorectal cancer (-59%; $P = 0.0001$). A benefit against cancer was not related to dose, gender, or smoking status, but the effect increased with age, especially for those aged ≥65 years. Deaths from urologic cancers (bladder, kidney, and prostate) were nonsignificantly reduced, especially with a longer duration of aspirin use.

**Conclusions:** Daily aspirin reduces the chance of dying from several cancers.

**Reviewer’s Comments:** Heart health=urologic health! Say this 20 times fast! However, aspirin increases the risk of ulcers and serious internal bleeding (like the kind that could cause you to miss a lifetime of work). Also, this risk increases with age. The use of aspirin to prevent the risk of dying from urologic cancers is compelling, but one would have to take it for many years to apparently get even a slight nonsignificant reduction in risk, according to this analysis. This fact was missed by many media sources that ran wild with these positive findings. Still, selective cancer risk reduction may make some sense, and aspirin could be a part of that equation. For example, I am more likely to encourage baby aspirin use in an individual who has a strong genetic/family history of gastrointestinal cancer prevalence and mortality or someone who was previously treated. I would probably be more inclined to recommend statin use for those with a strong history of urologic disease mortality, especially prostate cancer deaths. Triaging preventive care is challenging, but aspirin is working its way up the ladder and makes a lot more sense compared to selenium, vitamin E, or some new hyped up multivitamin, especially for gastrointestinal cancers. Heart-healthy changes are the best potential pathway to prevent urologic cancer and other overall cancer deaths. I love it! Dang, this stuff is fun! (Reviewer—Mark A. Moyad, MD, MPH).

**Keywords:** Aspirin Use, Cancer, Death

**Print Tag:** Refer to original journal article
Higher socioeconomic status is associated with better cancer-specific survival for multiple cancers, including bladder and prostate cancer.

**Objective:** To determine the impact of individual socioeconomic factors on racial disparities in survival after treatment for cancer.

**Methods:** Data were acquired from the linked National Longitudinal Mortality Study and Surveillance, Epidemiology, and End Results (SEER) datasets on 13,234 patients diagnosed with the top 8 cancers (breast, colorectal, prostate, lung, cervical, ovarian, melanoma, and bladder) from 1973 to 2003. Survival outcomes were compared across racial groups on univariate analysis and after correcting for individual socioeconomic factors such as health insurance, income, education, and poverty status.

**Results:** Overall, lower socioeconomic status was associated with worse survival across all cancers. Similarly, Blacks were less likely to receive first-course cancer-directed therapy and were more likely to die from cancer than whites. However, after correction for individual socioeconomic factors, stage, and treatment, these differences were no longer present for most cancers. The 2 exceptions were breast and prostate cancer, where racial disparities persisted even after correcting for these factors.

**Conclusions:** Higher socioeconomic factors are associated with improved survival after a cancer diagnosis. Racial disparities in survival persisted after correction for these factors only for breast and prostate cancer.

**Reviewer’s Comments:** There is a large body of literature arguing whether racial disparities in cancer outcomes are due to differences in socioeconomic factors or due to some difference in the biology of the tumors. The epidemiologic literature has typically addressed this question by assigning socioeconomic factors based on the zip code in which the person lives. This approach averages the typical education status, income, health insurance access, and poverty level across an entire zip code and then assumes all individuals inside that zip code are essentially equal. This leads to the obvious potential for bias and has hampered much of the literature in this regard. The key point to this study by Du et al is that it uses, for the first time, a linked dataset that combines the ability to determine socioeconomic factors for each individual patient via the National Longitudinal Mortality Study, with the cancer-related data available through SEER. Thus, this study is the first to study at the individual level how socioeconomic factors impact racial disparities in cancer survival. The interesting finding is that in many cancers, much of the disparities disappear once socioeconomic, treatment, and cancer stage information is taken into account. This suggests that modifications at the societal level and in health care delivery can improve outcomes in these cancers. However, for breast and prostate cancer, racial disparities remain, suggesting that there is more to the story and that perhaps there may be biologic differences underlying these disparities. The challenge now will be independently validating these findings and working to determine what exactly is driving these differences. (Reviewer-Peter Clark, MD).

Keywords: Prostate Cancer, Socioeconomic Status, Racial Disparities, Bladder Cancer

Print Tag: Refer to original journal article
Behavioral Therapy Can Improve Postprostatectomy Incontinence

Behavioral Therapy With or Without Biofeedback and Pelvic Floor Electrical Stimulation for Persistent Postprostatectomy Incontinence: A Randomized Controlled Trial.

Goode PS, Burgio KL, et al:

JAMA 2011; 305 (January 12): 151-159

Eight weeks of behavioral therapy can improve postprostatectomy incontinence; the addition of biofeedback or pelvic floor electrical stimulation did not have added benefit.

Objective: To evaluate the effectiveness of behavioral therapy to improve persistent postprostatectomy incontinence and to assess the utility of adding biofeedback and pelvic floor electrical stimulation to behavioral therapy.

Design/Participants: Prospective, randomized 3-armed trial of 208 men (age range, 51 to 85 years) with postprostatectomy incontinence of at least 1 year duration.

Methods: The men were randomized to receive 8 weeks of behavioral therapy alone, behavioral therapy plus biofeedback and home pelvic floor electrical stimulation, or delayed treatment (control group). The primary outcome measure was the reduction of mean incontinence episodes based on a 7-day voiding diary. The men were followed for 12 months after therapy to assess durability of the intervention.

Results: Men randomized to behavioral therapy had a 55% reduction in mean incontinence episodes, which was significantly lower than the 24% reduction in men assigned to the delayed therapy arm (controls). These reductions were durable out to 1 year. The addition of biofeedback or pelvic floor electrical stimulation did not have any added benefit over behavioral therapy alone.

Conclusions: Eight weeks of behavioral therapy significantly reduced persistent postprostatectomy incontinence in men 1 year out from surgery. The addition of biofeedback or pelvic floor electrical stimulation did not have any added benefit.

Reviewer's Comments: The main long-term morbidity that occurs with increased frequency in men treated by radical prostatectomy, relative to other active treatment modalities, is postprostatectomy stress urinary incontinence. Goode et al have conducted a well-executed randomized trial in men with persistent incontinence 1 year after surgery. Their study nicely demonstrates that an 8-week session of behavioral therapy can improve continence, and the results are durable, lasting at least 1 year. This study adds a measure of hope for those men who are suffering from postprostatectomy incontinence, particularly since the intervention has little risk associated with it and relatively low cost. This is especially true since biofeedback and electrical stimulation do not appear to add much to therapy and therefore are probably not needed. Some important things to bear in mind regarding these results are that the men enrolled in the study had moderate incontinence. These were not men with severe incontinence who would typically be considered for an artificial sphincter. This might represent an alternative or first-line therapy prior to proceeding to a male sling procedure and offers an alternative to men who have milder degrees of incontinence. It also opens up the intriguing question about the potential for a more aggressive behavioral therapy regimen in the immediate postoperative period and whether this would improve the results for men undergoing surgery. Another challenge will be setting up systems in urologists' offices to offer behavioral therapy in a cost-efficient manner to men who may benefit from it. (Reviewer-Peter Clark, MD).

Keywords: Prostate Cancer, Behavioral Therapy, Incontinence, Prostatectomy

Print Tag: Refer to original journal article
A 2-cm stone diameter should be considered a cutoff for retrograde ureteroscopy and laser lithotripsy, unless multiple procedures are anticipated.

**Objective:** To evaluate treatment outcomes of flexible ureterorenoscopy (URS) for intrarenal calculi.

**Design:** Retrospective case series.

**Participants:** 185 patients who presented between May 2005 and September 2008 for flexible URS and holmium laser lithotripsy were retrospectively analyzed.

**Methods:** Flexible ureteroscopy was performed, with the patient under general anesthesia, by introducing the ureteroscope over a safety guidewire under fluoroscopic guidance. Ureteral access sheaths and ureteral Nottingham dilators were used in only 3% of patients with difficult access. Stone dusting was performed without active basket extraction of fragments. Stents were left in 72% of patients. Success was defined as <2-mm fragments on noncontrast CT scan imaging and no requirement for secondary procedures.

**Results:** The 185 patients (median age, 51 years; age range, 18 to 83 years) included in the study underwent 236 treatments for renal calculi. Stone clearance was accomplished with only 1 treatment in 214 of the 236 treatments. The overall success rate was 91%. The success rate was 97% for stones ≤20 mm in size and 58% for stones >20 mm in size. With a second URS, the success rate increased to 86% for patients with stones >20 mm in size. Hounsfield units and stone location did not impact outcomes.

**Conclusions:** A 20-mm stone size should be considered the upper limit for single-procedure URS.

**Reviewer's Comments:** The authors report excellent outcomes with dusting of intrarenal calculi without active basketing. Their results are superior to the few other studies that have utilized CT scan imaging for primary outcome measures. In addition, 30% of patients avoided the morbidity of a ureteral stent. However, no outcomes are reported for this subgroup. How many required readmission for pain control or delayed stenting? The authors suggest a cutoff of 20 mm in stone size for flexible URS management of intrarenal calculi. Other investigators suggest a cutoff of 15 mm. Indeed, in this study, there was a drop-off in success as the 15-mm cutoff was passed, with stones 11 to 15 mm in size having a 98% success compared to stones 15 to 20 mm in size with a success rate of only 83%. (Reviewer-Manoj Monga, MD).

**Keywords:** Ureteroscopy, Renal Calculi

**Print Tag:** Refer to original journal article
This large global study establishes contemporary complication rates for percutaneous nephrolithotomy.

**Background:** The Clinical Research Office of the Endourological Society was established to organize, structure, and facilitate a global network of endourologic research.

**Objective:** To evaluate outcomes of percutaneous nephrolithotomy (PCNL).

**Design:** A global registry was established, and surgeons reported their data over a 1-year period.

**Participants:** 5800 patients undergoing PCNL at 96 centers across the world. Approximately 30% of the patients treated had staghorn calculi.

**Methods:** Surgeons used their "standard practice" for patient selection, surgical technique, and follow-up.

**Results:** 80% of patients had no complications. The major complications were significant bleeding (8%), renal pelvis perforation (3%), hydrothorax (2%), and fever >38.5°C (11%). The transfusion rate was 6%. The stone-free rate was 76%, with only 14% of patients undergoing postoperative CT imaging. The retreatment rate was 15%.

**Conclusions:** PCNL has a high success rate and a low complication rate.

**Reviewer's Comments:** The great value of this study is the establishment of contemporary guidelines for complication rates after PCNL. As the patient selection, surgical technique, and follow-up were not standardized, it is somewhat harder to draw firm conclusions regarding efficacy outcomes. However, the stone-free rate of 76%, despite relying primarily on KUB for follow-up, suggests that in the “real world,” PCNL is not as efficacious as the literature may suggest. Is this the "real world?" Access was obtained by urologists in 90% of cases. Twenty percent of the procedures were performed in a supine position, which suggests a unique skill set for most of the physicians. Ninety percent of the patients had an American Society of Anesthesiologists score of 1 or 2. Only a small portion of patients had a body mass index >35. This may not reflect the common patient population seen in the United States. Lastly, only 9% of patients were treated in a tubeless manner, which is a trend that will hopefully increase as the registry continues. (Reviewer-Manoj Monga, MD).

Keywords: PCNL, Nephrolithotomy, Complications

Print Tag: Refer to original journal article
Split-Appendix Technique Good Option When Anatomy Permits

Split-Appendix Technique for Simultaneous Appendicovesicostomy and Appendicocecostomy.
VanderBrink BA, Cain MP, et al:

J Pediatr Surg 2011; 46 (January): 259-262

Often, anatomy will not permit splitting the appendix into 2 stomas, but when feasible, outcomes are good and an additional bowel anastomosis is potentially avoided.

**Objective:** Appendicovesicostomy (AV) for urinary continence and appendicocecostomy (AC) for fecal incontinence are frequently utilized, but generally, the appendix can only be used for one or the other. The authors review their experience utilizing a "split-appendix" technique, using the appendix for both purposes simultaneously.

**Methods:** A retrospective review was performed from 1999 to 2009 identifying patients in whom the split-appendix technique was utilized. The proximal end was kept in continuity with cecum for the AC, and the distal end was used for the AV. Appendiceal length, continence status, and need for subsequent revision were noted.

**Results:** 394 patients underwent creation of a Mitrofanoff stoma over the 10-year period. Of these, 43 patients (11%) underwent the split-appendix technique. All 43 ACs and 41 of 43 AVs were patent with a mean follow-up of 40 months. Sixteen of 86 channels (19%) required surgical revision.

**Conclusions:** Although this technique is feasible to use in a minority of children undergoing surgery for incontinence, the outcome and revision rates make the split-appendix technique a viable option comparable to other techniques.

**Reviewer’s Comments:** The split-appendix technique is a clever adjunct to reconstructive surgery. When the appendix is lengthy, both AV and AC can be performed without an additional bowel anastomosis to harvest tissue for the second channel. Its real utility is in patients who are not undergoing simultaneous bladder augmentation, since in that scenario, little benefit is achieved because a segment of bowel adjacent to that harvested for the augment can be utilized for stomal construction with little down-side. (The authors performed simultaneous augmentation in 13 of 43 patients.) The reasonable revision rate certainly validates that this is a good technique when the anatomy permits. (Reviewer-John Gatti, MD).

Keywords: Stoma, Appendicovesicostomy, Appendicocecostomy, Reconstruction

Print Tag: Refer to original journal article
Age Is Risk Factor for Kidney Stone Dz in Children

Medical Comorbidities Associated With Pediatric Kidney Stone Disease.
Schaeffer AJ, Feng Z, et al:
Urology 2011; 77 (January): 195-199

Kidney stone disease is significantly associated with age in all children, and with both hypertension and diabetes mellitus in younger children.

Objective: To characterize the association of pediatric kidney stone disease with other comorbidities including hypertension, diabetes mellitus, and obesity. These associations have been made in the adult population, but not generally in children.

Methods: From 2003 to 2006, the Kids' Inpatient Databases were assayed for children treated as inpatients for kidney stone disease based on ICD-9 codes. The comorbidities were also assessed. Risk of stone disease was assessed using multivariate and logistic regression.

Results: 6,115,443 subjects were evaluated with 14,245 (0.2%) having a diagnosis of upper tract calculus (4092 boys and 10,045 girls). Age was the greatest independent predictor of stone risk. With subset analysis, hypertension and diabetes mellitus were associated with an increased risk of kidney stone disease in children less than 10 years of age and 6 years of age, respectively. Obesity did not appear to be a risk factor.

Conclusions: Kidney stone disease is significantly associated with age in all children, and with both hypertension and diabetes mellitus in younger children.

Reviewer's Comments: This article is interesting in that it draws on associations previously noted in adult populations. The database that the study draws upon represents only inpatients, which presumably omits the majority of children treated for stone disease on an outpatient basis. Additionally, the database does not discriminate repeat admissions by the same patient. In other words, repeat visits by the same patient appear as different data sets. Finally, the assessment is limited to diagnoses coded, and as no laboratory or clinical objective parameters such as blood pressure or weight are included, the assessment for comorbidity may be incomplete. As limited as this assessment is, it does draw a correlation that may benefit from prospective assessment of this growing population of stone formers. (Reviewer-John Gatti, MD).

Keywords: Pediatric, Kidney Stone Disease

Print Tag: Refer to original journal article
Thyroid Disease May Affect Lower Urinary Tract

Lower Urinary Tract Symptoms and Urinary Flow Rates in Female Patients With Hyperthyroidism.

Ho C-H, Chang T-C, et al:

Urology 2011; 77 (January): 50-54

Thyroid function, specifically, hyperthyroid conditions, may have a greater association with lower urinary tract symptoms.

**Objective:** To investigate lower urinary tract symptoms (LUTS) and voiding function in a group of women with known hyperthyroidism.

**Design/Participants:** Prospective analysis of 65 women with previously untreated hyperthyroidism.

**Methods:** The participants were matched against 62 age-matched healthy female volunteers who served as contemporaneous controls. Patients underwent demographic assessment as well as assessment of LUTS using the International Prostate Symptom Score (IPSS). In addition, thyroid-based symptomatology, urinary flow rates, and serum level of thyroid hormones were recorded. All tests were done before and after stabilization on medical therapy.

**Results:** 62 patients were entered into each group for purposes of analysis. The hyperthyroid patients had a higher mean symptom score compared to controls with regard to frequency, incomplete emptying, straining, voiding symptoms, and overall total symptoms. Only 12 (18.5%) of the 65 hyperthyroid patients had an IPSS ≥8, while the majority (81.5%) had an IPSS <8. In addition, peak flow rates were lower in women with untreated thyroid disease. After therapy, LUTS and flow rates improved substantially. Therapy improved not only lower urinary tract symptoms but also flow rates in patients with thyroidal dysfunction.

**Conclusions:** Women with hyperthyroidism had lower urinary flow rates and more significant LUTS than their healthy controls. The severity of LUTS is only mild in the majority of patients, with slightly less than 20% having moderate to severe LUTS. Thyroid hormonal supplementation did improve both LUTS and flow rates in those patients with aberrations of same. Mechanistic explanation of this is as of yet undetermined.

**Reviewer’s Comments:** For years, the relationship between thyroid disease and lower urinary tract function has been postulated. This is one of the first prospective studies actually evaluating this association. From a mechanistic pathophysiologic standpoint, the explanations remain undetermined. It has been postulated that specific receptors in the lower urinary tract may be affected by thyroid pituitary axis-based signals, but this has never been fully elucidated and remains non-explicable at this point. This well-designed prospective study does show that there are more symptoms and some objective findings in women with thyroidal dysfunction that are not seen in case controls. Modulation of thyroid function did appear to benefit these individuals. More long-term data are needed to explain and further elucidate this intra-relationship. (Reviewer-Roger R. Dmochowski, MD).

Keywords: LUTS, Hyperthyroidism, Voiding Function

Print Tag: Refer to original journal article
New-Onset Incontinence in Middle-Aged Women Is Usually of Stress Type

Type and Severity of New-Onset Urinary Incontinence in Middle-Aged Women: The Hordaland Women's Cohort.

Jahanlu D, Hunskaar S:

Neurourol Urodyn 2011; 30 (January): 87-92

The majority of middle-aged women who develop urinary incontinence experience pure stress urinary incontinence.

**Objective:** To assess the natural history of new-onset urinary incontinence by type and severity in middle-aged (41 to 45 years of age) women.

**Design/Participants:** Epidemiologic women's cohort analysis beginning in 1997 of 2229 women aged 41 to 45 years.

**Methods:** The women answered postal questionnaires sent in sequence (6 waves) over a period of 10 years.

**Results:** The overall response rate was 95% at inclusion and 87% to 93% in subsequent years. A total of 1274 of the women were continent at baseline and were the baseline analysis group for this assessment. Type and severity of new-onset incontinence and any changes in these were identified at the follow-up periods as noted (usually 2 follow-up visits). Of the 1274 patients continent at baseline, 514 (40.3%) reported new-onset incontinence over the 10-year time frame. The majority of the new-onset cases was stress incontinence in 49.8%, urgency in 18.3%, and mixed incontinence in 20.3%. A majority of these individuals (89.3%) experienced minimal symptoms, with none reporting severe degrees of incontinence after their initial assessment. During a 4-year follow-up period, 212 (62.9%) of 337 women had transient incontinence (resolved spontaneously) and 125 women (37.1%) had urinary incontinence classified as persistent. Of those in the persistent group, 62% described their incontinence as slight (ie, not severe).

**Conclusions:** The study demonstrated that middle-aged women did develop new-onset urinary incontinence. The majority of these women experienced pure stress urinary incontinence with less significant components of urge and mixed symptomatology. One-third of these women developed persistent symptomatology with the likelihood of maintaining the type and severity of incontinence over time. Mixed urinary incontinence was present in the majority of these women.

**Reviewer's Comments:** This is an interesting paper because I, like so many of my colleagues, presume mixed incontinence is the most common type experienced in practice. When postal surveys are done, we are dealing with pure symptoms, and one of the criticisms of this study is that some patients may not be able to elucidate their symptoms well in terms of differentiating between stress and urge. The majority of the patients in this trial had stress incontinence with a much less significant component of mixed. Even a significant percentage of these patients developed incontinence; the overall severity was minimal and tended not to progress with time nor shift in type. These are important findings because they give us some idea of a second wave of women who will be presenting with incontinence over time justifying both a reasonable data set to counsel those women with and create reasonable expectations of what to expect if no therapy is chosen. This is an important study, especially for the generation of baby boomers who are moving through our clanks at this time. (Reviewer-Roger R. Dmochowski, MD).

Keywords: Urinary Incontinence, New-Onset, Middle-Aged Women, Hordaland, Cohort

Print Tag: Refer to original journal article
Acupuncture, Paroxetine Improve Premature Ejaculation Compared to Placebo

**Acupuncture Versus Paroxetine for the Treatment of Premature Ejaculation: A Randomized, Placebo-Controlled Clinical Trial.**

Sunay D, Sunay M, et al:

Eur Urol 2011; January 20 (): epub ahead of print

Paroxetine and acupuncture have a more significant ejaculation-delaying effect than placebo.

**Background/Objective:** Many researchers have used acupuncture in erectile dysfunction studies. This study was designed to determine if acupuncture is effective therapy for premature ejaculation (PE). The authors importantly included an active control (paroxetine) as well as placebo (PL).

**Design:** Randomized, placebo-controlled clinical trial.

**Participants/Methods:** 90 patients were referred to a urology clinic at a tertiary center with a chief self-reported complaint of PE. Participants were randomized to paroxetine (20 mg/day), acupuncture, or placebo groups. Men were heterosexual, sexually active, and between 28 and 50 years of age. Those with psychiatric or systemic disease, substance abuse, medication, or erectile dysfunction were excluded. The acupuncture and sham acupuncture (ie, placebo) group were each treated twice a week for 4 weeks, and the paroxetine group received daily, early morning doses of 20 mg for 4 weeks.

**Results:** The primary measures were intravaginal ejaculation latency time (IELT) as well as the PE diagnostic tool (PEDT) and were thus used to assess PE changes. The median PEDT scores for paroxetine, acupuncture, and placebo were 17, 16, and 15.5 before treatment and 10.5, 11.0, and 16.0 after treatment. The paroxetine and acupuncture changes were statistically significant. There were significant differences in IELTs of the paroxetine and PL (\( P < 0.001 \)) and the acupuncture and PL (\( P = 0.001 \)) after treatment. Increases in IELT with paroxetine, acupuncture, and PL were 82.7, 65.7, and 33.1 seconds. The extent of ejaculation delay induced by paroxetine was significantly higher than that of acupuncture. The most important limitation of the study was dropouts. Although less effective than daily paroxetine, acupuncture did have a more significant ejaculation-delaying effect than PL.

**Conclusions:** This is an important study because PE is the most frequent male sexual complaint and can have a serious impact on the quality of life for the patient and their partner. Many studies in animals and humans have demonstrated that acupuncture can cause multiple biologic responses.

**Reviewer's Comments:** There are several limitations to this study, including the fact that acupuncture therapies were performed in an outpatient clinic with other patients and the environment was not always suitable. Only 2 IELTs were performed, one at baseline and one after treatment. Therefore, there may be a large discrepancy or a regression to the mean. In addition, there was no follow-up available, thus no residual effect has yet to be determined. (Reviewer-Kevin T. McVary, MD, FACS).

Keywords: Acupuncture, Premature Ejaculation, Erectile Dysfunction

Print Tag: Refer to original journal article
Minority of Men With Prior RT and ADT Respond to PDE5 Inhibitors

Randomized, Double-Blinded, Placebo-Controlled Crossover Trial of Treating Erectile Dysfunction With Sildenafil After Radiotherapy and Short-Term Androgen Deprivation Therapy: Results of RTOG 0215.

Watkins Bruner D, James JL, et al:

J Sex Med 2011; January 14 (): epub ahead of print

In this study, as few as 21% of patients had a treatment-specific response, only improving during sildenafil and not during the placebo phase.

**Objective:** To evaluate sildenafil in the treatment of erectile dysfunction (ED) in prostate cancer patients previously treated with external beam radiation therapy (RT) and neoadjuvant and concurrent androgen deprivation therapy (ADT).

**Design/Methods:** In this randomized, double-blind, placebo-controlled two-way crossover clinical trial, eligible patients received RT/ADT for intermediate risk prostate cancer and currently had ED as measured by the International Index of Erectile Function (IIEF) Q1 (“How often were you able to get an erection during sexual activity?”). The main end point was improvement in erectile function as measured by an IIEF Q1 post-treatment score of ≥4.

**Results:** The study accrued 115 patients (mean age, 70 years), and 61 (55%) completed all 3 IIEF assessments. The sildenafil effect was significant ($P=0.009$), with a difference in probabilities of erectile response of 0.17 (95% CI, 0.06, 0.29) for all patients and 0.21 (0.06, 0.38) for patients receiving ≤120 days of ADT. However, as few as 21% of patients had a treatment-specific response, only improving during sildenafil and not during the placebo phase.

**Conclusions:** This is the first controlled trial to suggest a positive sildenafil response for ED treatment in patients previously treated with RT/ADT. However, only a minority of patients responded to treatment. ADT duration may be associated with the lack of response and requires further study. The overall low response rate suggests the need for study of additional or preventive strategies for ED after RT/ADT for prostate cancer.

**Reviewer’s Comments:** Limitations are numerous in this study, including the small number of men who completed the assessments, making the study prone to a marked bias. Even in that setting, one would have predicted a higher response suggesting that the impact of RT/ADT has a profound effect on erectile function. More importantly, the long-term consequences of RT/ADT on sexual function are not reported here. Whether there is significant recovery in time remains unanswered. (Reviewer-Kevin T. McVary, MD, FACS).

Keywords: Erectile Dysfunction, Prostate Cancer, Sildenafil

Print Tag: Refer to original journal article