A randomized population-based study suggests that offering prostate-specific antigen screening lowers prostate cancer-related mortality.

**Objective:** To determine if prostate cancer screening can reduce mortality from prostate cancer.

**Design:** Population-based, randomized, prospective trial in Sweden initiated in 1994.

**Participants/Methods:** 20,000 men aged 50 to 64 years were randomized to receive an invitation to undergo prostate-specific antigen (PSA) screening once every 2 years versus controls who received no invitation. Men with an increased PSA were invited to undergo further urologic evaluation. Men were invited for screening up to age 69 years.

**Results:** In men randomized to receive an invitation to screening, 76% attended at least 1 screening session. Median follow-up was 14 years. The cumulative incidence of prostate cancer was higher in the screened arm (12.7%) than in the control group (8.2%). The cumulative risk of death due to prostate cancer was lower in the screening group (0.50%) than in the control group (0.90%). Overall, the number needed to screen to prevent one prostate cancer death was 293, and the number needed to diagnose was 12. The overall survival was not different between the 2 groups.

**Conclusions:** Prostate cancer mortality can be reduced by almost half over 14 years with a population-based PSA screening program; however, there is still a substantial risk of over-diagnosis. These results compare favorably to findings from other cancer screening programs.

**Reviewer's Comments:** One of the biggest controversies in urologic oncology is the relative merits of prostate cancer screening with PSA. Ever since PSA was first introduced, the debate has been raging on whether screening for prostate cancer reduces mortality. There are now 3 major prospective, randomized trials addressing this issue. The United States-based PLCO trial suggested screening was not associated with any reduction in prostate cancer mortality, whereas the European ERSPC suggested that there was a mortality reduction. The latter, however, also suggested that the number needed to treat to prevent one prostate cancer death was very large, raising concern about over-diagnosis and over-treatment. This current study by Hugosson et al is now the third major trial. It found that a population-based PSA screening program reduced prostate cancer mortality and suggested that the number needed to diagnose to prevent one prostate cancer death is much lower (12) and is comparable to results for screening programs in other cancers. The differences across trials likely have to do with differences in the baseline population such as patient age, the PSA thresholds to initiate further work-up, the length of follow-up, and the underlying screening rates in the population outside of the study. These differences have meant the debate is sure to continue. While this trial certainly adds more weight to the argument in favor of screening, it is not enough by itself to fully end the debate. (Reviewer-Peter E. Clark, MD).

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**Keywords:** PSA, Prostate Cancer, Screening

**Print Tag:** Refer to original journal article
Active treatment of stage T1 renal tumors is not associated with increased survival in patients aged ≥75 years.

**Objective:** To determine if active intervention for localized renal tumors <7 cm in size in older patients is associated with better survival compared to active surveillance.

**Methods/Participants:** Retrospective cohort analysis of 537 patients aged ≥75 years with a clinically localized renal mass <7 cm. Patients were managed with active surveillance (20%), nephron-sparing therapy such as a partial nephrectomy or thermal ablation (53%), or radical nephrectomy. Survival was compared across interventions, and models were constructed that accounted for differences in age, comorbidity, renal function, and other pertinent variables.

**Results:** At a median follow-up of 3.9 years, a total of 148 patients died (28%). The most common cause of death was secondary to cardiovascular disease (29%), whereas kidney cancer accounted for only 4% of deaths. Patients who underwent active surveillance were older and had greater comorbidities than those who underwent active therapy. Those who had a radical nephrectomy had a higher risk of kidney cancer than those who underwent nephron-sparing therapy. Radical nephrectomy was associated with increased risk of chronic kidney disease (CKD). CKD was associated with an increased risk of cardiovascular death. On multivariate analysis, increasing age and comorbidity were associated with worse all-cause mortality; however, treatment approach was not associated with any difference in survival.

**Conclusions:** In patients aged ≥75 years, active treatment of localized renal tumors <7 cm was not associated with any difference in survival.

**Reviewer's Comments:** The incidence of asymptomatic, small renal masses has been growing at a steady rate. There has been increasing interest in the role for active surveillance, particularly in older patients and those with substantial comorbidities, in managing these lesions. This report by Lane and colleagues has added to that debate by showing, in a large cohort of older patients (aged ≥75 years) followed for almost 4 years, that active treatment of localized renal tumors <7 cm in size is not associated with any improvement in survival. Does this mean that active surveillance should be used in all patients aged ≥75 years with such a mass? Such a blanket statement would overstate the results. This study nicely demonstrates that when a physician carefully assesses a patient and tailors his or her management (considering variables such as age, comorbidities, life expectancy, renal function, and the features of the tumor itself), an individualized approach results in comparable outcomes. This study certainly adds to the argument that, in the properly selected patient, active surveillance is a viable and appropriate strategy; however, it does not necessarily mean that it is the answer for everyone. Clearly, more study is needed to clarify this difficult and complex problem. (Reviewer-Peter E. Clark, MD).

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Objective: To review the impact of α-blockers on the efficacy of shock wave lithotripsy (SWL).

Design: Meta-analysis.

Methods: Randomized clinical trials performed before January 2009 that evaluated the use of α-blockers after SWL were identified. Primary outcomes were stone clearance rate and time to stone clearance.

Results: 7 randomized, controlled trials with a total of 484 patients met the criteria for inclusion. Mean stone sizes treated in each study ranged from 8 to 12 mm. Treatment duration ranged from 14 days to 3 months. All studies evaluated tamsulosin. However, only one study was placebo controlled; the others were not controlled or blinded. Only 2 studies used a strict criteria of "stone free" for success, while others included residual fragments of <3 mm as being successful. Similarly, there was heterogeneity in radiographic follow-up, relying mainly on KUB and ultrasound, with no study using CT as the primary imaging modality. The pooled absolute improvement in stone clearance with tamsulosin at 0.4 mg once daily was 19%. Time to stone clearance improved by 8 days. In addition, pain scores and analgesic use were lower with tamsulosin.

Conclusions: Treatment with tamsulosin after SWL is an effective adjunct.

Reviewer's Comments: A meta-analysis is as good as the studies included in it. Unfortunately, these studies can be criticized for lack of placebo control, lack of blinding and allocation concealment, and heterogeneity of imaging, definition of success, and duration of treatment. Despite these limitations, this study provides sufficient power to demonstrate an advantage in the rate of spontaneous stone expulsion with the use of tamsulosin. Only 3 of the studies reported time to stone passage, and only 4 studies reported pain and analgesia use. The authors do not stratify results based on stone size and recognize discrepancies in results in this regard; some studies claim that tamsulosin is effective only for larger stones, while other say it is effective for small stones or stones of any size. Clearly, further study is warranted, yet the almost 20% difference in stone clearance supports the use of tamsulosin in patients after SWL. (Reviewer-Manoj Monga, MD).

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Keywords: Shock Wave Lithotripsy, Medical Expulsive Therapy

Print Tag: Refer to original journal article
More Bang for the Buck -- Differential Renal Function on CT


Morrisroe SN, Su RR, et al:

J Urol 2010; 183 (June): 2289-2293

Computerized tomography-based renal parenchymal volume measurement is an accurate method to determine differential renal function and may diminish the need for nuclear renography in select cases.

Objective: To determine if renal parenchymal volume measurement on CT scan can be used as a surrogate marker for differential renal function.

Design: Retrospective chart and image review.

Participants: 33 patients with chronic obstruction.

Methods: Semi-automated boundary delineation with manual editing was used to determine the parenchymal volume. This was performed by an image analyst, requiring about 15 minutes of a radiologist's time. The differential function by this method was compared to a nuclear renal scan.

Interventions: Contrast-enhanced CT was performed in 23 patients; non–contrast-enhanced CT was performed in 10 patients.

Results: The mean interval between the 2 studies was 1 month. Strong correlations (r=0.90) were found between the 2 studies, independent of the use of contrast enhancement on CT. However, correlations were not as strong for kidneys with <40% function (r=0.76) and kidneys with <30% function (r=0.64).

Conclusions: CT may be used as a surrogate for nuclear renography to determine differential renal function.

Reviewer's Comments: Although the authors report a mean interval of 1 month between studies, they do not report exclusion criteria used for the study. What was the upper limit allowed for the interval between studies? Were patients excluded if they had a ureteral stent or nephrostomy placed during the interval between studies? Were patients excluded if there was interval change in the serum creatinine between studies? This trial spans a 5-year time frame, with evolution of imaging technology from 16- to 64-slice scanners. Although this is a limitation, most likely the improvements in imaging technology would lead to improvements in volume calculation and accuracy of differential function calculation. The authors note that a differential function of ≤10% is commonly used to help guide the need for nephrectomy instead of reconstructive measures. Unfortunately, their study demonstrates that the accuracy of differential function determination diminishes as renal function diminishes. Although overall they demonstrated good correlation, it would be important to repeat this study and look specifically at patients with 0% to 30% function to determine the accuracy of enabling this decision point for urologists (only 5 patients had a differential function in this range in this trial). Although CT scan may provide pertinent information regarding differential function, the nuclear renogram will remain important to define drainage and transit time before and after intervention. (Reviewer-Manoj Monga, MD).

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Keywords: Renal Function, Imaging, CT

Print Tag: Refer to original journal article
Background/Objective: A novel approach to restoring bladder and bowel function in the setting of spina bifida involves creating a skin to central nervous system to bladder reflex arc using lumbar to sacral nerve rerouting. This has been described with high success in China. The authors report their 1-year results in a North-American trial.

Participants: 8 children and 1 adult were enrolled in the study.

Methods: A donor nerve at the level of the lowest ventral root where a reproducible muscle EMG response could be obtained was anastomosed to the proximal stump of the S3 ventral root. An effort was made to harvest only a portion of the donor root to minimize impairment of motor function in the muscles of the lower extremity. Participants were assessed with urodynamics with nerve root stimulation, and bowel function was assessed.

Results: 7 of 9 patients demonstrated an increase in bladder pressure with cutaneous stimulation of the dermatome. Two patients were able to stop intermittent catheterization, and all patients safely stopped anticholinergic therapy. No patient achieved complete urinary continence. Most reported improved bowel function, and 3 experienced new fecal continence after the procedure. Eight patients experienced lower-extremity weakness in the distribution of the donor nerve graft, which generally improved by 1 year, but one patient had persistent foot drop impairing ambulation.

Conclusions: At 1 year, a reflex arc with cutaneous dermatomal stimulation was seen in the majority of patients after lumbar to sacral nerve rerouting. Some improvement in bowel/bladder function was seen, but lower-extremity weakness with persistence was also noted.

Reviewer's Comments: This approach to "re-functionalization" of the urinary tract in patients with spina bifida and spinal cord injury has been followed enthusiastically since Xiao began reporting his experience in 2005. This report is enlightening as its findings are in stark contrast to the 85% success rates initially described. "Success" is a nebulous term, but, with regard to continence, the procedure is disappointing. Long-term follow-up is imperative, but the complication of lifestyle-altering gait impairment balanced against a urodynamic benefit but limited clinical benefit is not an "easy sell" at this point. The study is severely limited by the fact that there is no control group. Improvements in bowel and bladder function may be insignificant compared to controls over a time frame of 1 year. The jury is still out on this approach to the management of patients with spina bifida. Although the procedure is novel and holds promise, it is certainly not mainstream and should be reserved for the setting of a research protocol. This update is also helpful for counseling patients and families who are under the impression that spina bifida can be "cured" with this new approach. (Reviewer-John Gatti, MD).

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Keywords: Spina Bifida, Nerve Rerouting, Continence

Print Tag: Refer to original journal article
Success of DHA Relates to Grade of Reflux

Dextranomer/Hyaluronic Acid for Pediatric Vesicoureteral Reflux: Systematic Review.

Routh JC, Inman BA, Reinberg Y:

Pediatrics 2010; 125 (May): 1010-1019

Lower grades of vesicoureteral reflux have higher success rates with dextranomer/hyaluronic acid injection. A conflict of interest did not appear to affect success in this review.

Background: The literature shows wide variation in the success rates of dextranomer/hyaluronic acid (DHA) injection for vesicoureteral reflux (VUR) in children.

Objective: To assess whether patient or study factors could explain this heterogeneity.

Methods: A literature search was performed from 1990 to 2008. Articles were assessed, and a meta-regression was performed to adjust for patient and study factors. Parameters assessed included patient age, volume of DHA injected, preoperative grade of VUR, study design, country of origin, conflicts of interest disclosure, definition of success, and clinical markers of higher-risk patients such as those with urethral valves, neurogenic bladders, ureteroceles, ureteral duplication, or diverticula.

Results: 1157 reports were identified, of which 89 met inclusion criteria and were reviewed in full; 47 reports were ultimately included in the pooled analysis. A total of 7303 ureters underwent DHA injection, with 5633 (77%) treated successfully based on the authors' definition. The success of injection varied primarily by preoperative reflux grade. After adjusting for VUR grade, other factors (age, injection volume, author conflict of interest) were not significant. The studies were inherently heterogeneous.

Conclusions: The overall success of DHA injection for VUR is 77% after 3 months, with wide variation between studies. Increasing VUR grade was negatively associated with success. There is a need for improved reporting of VUR treatments and comparative studies for different treatment modalities.

Reviewer's Comments: This is an interesting study, as it pools the available data and addresses the issue of reported conflict of interest in regard to its impact on patient outcome. Like other studies, the authors found that the reflux grade is the primary predictor of success, with lower grades responding better. A fairly novel parameter, a reported conflict of interest, did not seem to affect the outcome when adjusted for grade of VUR. Finally, the authors emphasize that uniformity of reporting and comparative studies of different treatment modalities are sorely lacking. (Reviewer-John Gatti, MD).

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Keywords: Dextranomer Hyaluronic Acid Reflux Success

Print Tag: Refer to original journal article
When carefully studied in a large group of patients undergoing either retropubic or transobturator sling procedures, body mass index had no overt effect on outcome.

**Objective:** To assess the impact of weight as defined by body mass index (BMI) on the outcomes and clinical efficacy of mid-urethral tape operations in women with genuine stress urinary incontinence.

**Design:** Prospective random allocation into either the retropubic or transobturator approach with subsequent follow-up.

**Methods:** Initially, 537 women underwent random allocation either to retropubic or transobturator tape procedures for the primary indication of stress urinary incontinence. The patients were followed up for clinical effectiveness for 18 months after intervention. Follow-up visits were scheduled at 1, 4, 6, 12, and 18 months. Patients underwent symptom review and physical examination including supine and standing cough tests. In addition, the use of hygienic pads was included in the definition of care. Success was defined as nullities of incontinence with supine or standing stress tests. Also, the use of hygienic pads was not allowed. Failed was defined as urinary incontinence during an increase of intra-abdominal pressure subjectively, the presence of a positive cough stress test, or the use of pads during the daytime. Patients were considered clinically improved if the cough test was negative but the patient still experienced stress urinary incontinence subjectively and pads were occasionally needed. Of the initial study group, 398 women were actually available at 18 months. Again, the women were stratified by obesity, menopause, and aging. Of those who completed follow-up, there was no difference in the clinical effectiveness of the sling based on BMI or type of mid-urethral sling. Menopausal status and aging did affect the outcome of surgery, however. When segregated into decades of age, patients showed a significant risk of failure at >61 years of age, with both the decades of 60-70 and 70-80 demonstrating higher rates than a younger population of patients. Initially, patients who were postmenopausal on the basis of either surgery or natural menopause demonstrated significant higher failure rates than did premenopausal patients.

**Conclusions:** BMI did not affect the clinical effectiveness of stress incontinence surgery, whereas other variables, including age and menopausal status, had significant impacts.

**Reviewer's Comments:** This is a very significant paper in that it detracts from the commonly held belief that women with increased BMI are at greater risk of failure of interventions for stress incontinence. In this well-designed prospective trial, clearly, BMI had no effect on patients regardless of the type of sling used. The authors did not specifically comment on complications, in which BMI may have played a greater role. Aging and menopausal status apparently did have a significant effect on overall outcomes, which is a very important consideration, especially in patients with multiple comorbidities (in terms of creating reasonable expectations). (Reviewer-Roger R. Dmochowski, MD).

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**Keywords:** Aging, Incontinence Surgery, Menopause, Midurethral Sling, Obesity

**Print Tag:** Refer to original journal article
Bowel Symptoms Common in Pelvic Floor Disorders

Prevalence of Bowel Symptoms in Women With Pelvic Floor Disorders.
Raza-Khan F, Cunkelman J, et al:

Int Urogynecol J 2010; 21 (August): 933-938

There has been a lack of awareness of the true prevalence of bowel condition in women with pelvic organ prolapse, which is now becoming clearly demonstrable in trials such as this one.

Background: Bowel symptoms are highly prevalent in pelvic floor disorders.
Objective: To determine the prevalence of bowel symptoms in women with pelvic floor disorders.
Design: This was a retrospective review of the records of patients who had attended a single clinic over a defined time frame and who had completed 2 bowel questionnaires (a non-validated questionnaire and a validated questionnaire).
Methods: The patients were evaluated in a consecutive fashion over a 24-month period. Patients who entered the clinic completed 2 questionnaires; one was a non-validated questionnaire on symptoms related to liquid, solid, and gas incontinence; pain related to bowel function; difficulties in bowel function and bowel evacuation; and the need for perineal splinting to assist in bowel function. The second questionnaire was the Colorectal-Anal Distress Inventory (CRADI) of the pelvic floor distress inventory. Comorbidities and other demographics were obtained from the study population.
Results: 463 women were assessed in this study. Of this population, only 3% actually presented with defecatory dysfunction or fecal incontinence as the primary complaint; however, 83% of the population answered positively to at least one of the symptoms assessed by the CRADI bowel symptom assessment tool. Most common symptoms were incomplete emptying at the end of bowel movement (56%), straining with movement (55%), and fecal incontinence (54%). A high association was found between the findings in the validated questionnaire and findings in the non-validated questionnaire, which was more extensive in terms of its overall assessment of symptomatology. There did appear to be a strongly significant correlation between trauma related to child-bearing (including perineal tearing and the use of forceps) and increased CRADI score.
Conclusions: Although rarely a primary complaint, bowel and rectal dysfunction and related complaints significantly affect women with pelvic floor disorders.
Reviewer’s Comments: This is a particularly interesting article because, once again, it deals with an aspect of pelvic floor medicine that is not overtly addressed in an adequate fashion—consistent bowel-related function. Several previous trials have documented anywhere from 30% to 50% concomitant bowel function disorder in women with pelvic organ prolapse in a much more diverse population. In this article, 80% of patients had at least one positive bowel symptom that clearly affected the overall perception of outcomes from intervention in individuals who are bothered by those symptoms. This is a very important component to consider in informed consent to avoid discomfiture with overall outcomes of interventions when these specific types of symptoms are not included. (Reviewer-Roger R. Dmochowski, MD).

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Keywords: Pelvic Floor Disorders, Bowel Symptoms, Colorectal-Anal Distress Inventory

Print Tag: Refer to original journal article
The severity of coronary lesions patients with erectile dysfunction (ED) is no different than that observed in patients who do not have ED.

**Background:** Accumulated evidence shows that erectile dysfunction (ED) may be a precursor of coronary artery disease (CAD). Recently, a putative pathophysiologic mechanism, named the "artery size" hypothesis, has been presented to partially explain the association between ED and CAD. This hypothesis proposes that the smaller penile arteries (diameter of 1 to 2 mm) become obstructed from plaque burden earlier than the larger coronary, carotid, or ilio-femoral arteries; therefore, symptomatic ED may be present before a coronary event. Addressing cardiovascular risk early after the presentation of ED and undertaking aggressive intervention to reduce the risk may have long-term symptomatic and prognostic cardiac benefits.

**Objective:** To explore the differences in coronary phenotypes between patients with ED and patients with angina pectoris.

**Methods:** The study enrolled 30 ED patients (study group) and 120 age-matched angina patients who had no ED (control group). All patients had angiographically documented CAD. The differences in demographic characteristics, biochemical profiles, and coronary characteristics between the study and control groups were compared.

**Results:** Diabetes mellitus (DM) and obesity (defined by body mass index) were more common in the study group than in the control group. The mean number of lesions and mean number of vessels with the evidence of CAD were significantly different between the study and control groups (2.3 vs 2.2, \( P < 0.001 \); and 2.0 vs 1.8; \( P < 0.001 \)). The distribution of vessel involvement was similar between groups, except for more common involvement of the ramus in the study group. There were no differences in the distribution of lesion sites between the 2 groups. The control group had a higher percentage of type A stenotic lesions than did the study group (16.3% vs 2.9%; \( P = 0.004 \)). Significant differences were also observed in type C lesions (52.9% in the study group vs 38.0% in control group; \( P = 0.026 \)). Fewer calcified, irregular, and bifurcated lesions were present in the study group than in the control group.

**Conclusions:** This study documented coronary phenotypes in ED patients without symptomatic CAD. Although the artery size hypothesis and ED had well been thought to be a precursor of CAD, the severity of coronary lesions in these patients was not more benign than that observed in angina pectoris patients who have no ED. However, addressing cardiovascular risk early after the presentation of ED and undertaking aggressive intervention to reduce the risk may have long-term symptomatic and prognostic cardiac benefits.

**Reviewer’s Comments:** Because of the low prevalence of ED with silent CAD and to avoid a confounding effect of age on the prevalence of ED and CAD, the study recruited patients in an age-matched case-control model. The complexity of CAD could not be compared between patients with angina with and without ED. (Reviewer-Kevin T. McVary, MD).

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Keywords: Erectile Dysfunction, Coronary Artery Disease, Angiography

Print Tag: Refer to original journal article
Who Is Most at Risk for PD After Radical Prostatectomy?

Peyronie's Disease Following Radical Prostatectomy: Incidence and Predictors.
Tal R, Heck M, et al:

J Sex Med 2010; 3 (March): 1254-1261

Peyronie's disease after radical prostatectomy is more common in whites than in other ethnic groups.

Background: Both prostate cancer and Peyronie's disease (PD) are prevalent in men after their fifth decade of life. The evidence to support or refute a link between radical prostatectomy (RP) and PD is limited.

Objective: To define the incidence of PD in men who had RP, and to determine possible predictors of PD development after RP.

Methods: The incidence of PD was determined among men who attended a sexual medicine clinic after they had RP, and predictors of PD development after RP were identified.

Results: The study population included 1011 subjects, and the PD incidence in this population was 15.9%. The mean time to develop PD after RP was 13.9 months. The mean curvature magnitude was 31 degrees. In univariate analysis, younger age (mean age, 59 years in men with PD vs 60 years in men without PD; \( P =0.006 \)) and white race (vs non-white, 18% vs 7%; \( P <0.001 \)) were predictive of PD development after RP, but postoperative erectile function was not a predictor of PD development. On multivariate analysis, younger age (OR, 1.3 for 5-year decrease in age) and white race (OR, 4.1 vs non-white) remained independent significant predictors.

Conclusions: This is the largest reported series of PD after RP. Men presenting with sexual dysfunction after RP have a higher incidence of PD than that found in the general population. No causal information was noted, nor would one expect to see evidence as such using this database. Therefore, these patients should be routinely evaluated for PD. Younger men and men of white race are at increased risk for PD.

Reviewer's Comments: Limitations of this study include the following: (1) causal relationships that could not be addressed; (2) lack of a control group; and (3) a low incidence of cardiovascular comorbidities, as these were drawn from an RP cohort. (Reviewer-Kevin T. McVary, MD).

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Keywords: Peyronie's Disease, Radical Prostatectomy

Print Tag: Refer to original journal article
Does UMFA in Older Adults Increase Ca Risk?

Unmetabolized Serum Folic Acid and Its Relation to Folic Acid Intake From Diet and Supplements in a Nationally Representative Sample of Adults Aged ≥60 y in the United States.

Bailey RL, Mills JL, et al:


Older men do not need extra folic acid in their dietary supplements.

**Background:** Several previous studies have suggested that higher intakes of folic acid (a B-vitamin) may be associated with a higher risk of certain cancers. Unmetabolized serum folic acid (UMFA) may be a good indicator of folic acid exposure, but this had not been tested.

**Objective:** To determine the association between diet and supplemental intake of folic acid and UMFA concentrations in adults aged ≥60 years in the United States.

**Design/Methods:** Excess sera from the National Health and Nutrition Examination Survey 2001 to 2002 were utilized. This study was a cross-sectional, nationally representative survey of 1121 individuals from that large study.

**Results:** UMFA was found in 38% of the population studied. The group that was UMFA+ included a significantly higher number of folic acid supplement consumers than did the group without detectable UMFA. A total of 40% of the UMFA+ group was in the highest intake category of total folic acid. Serum folate concentrations were significantly higher in the UMFA+ group. No difference was found between groups in regard to red blood cell folate, serum homocysteine, or methylmalonic concentration.

**Conclusions:** Monitoring of UMFA levels may be needed in the future because approximately 40% of older adults have detectable levels of this compound after fasting for an average of 10 hours.

**Reviewer’s Comments:** I was told in college biology, public health, and medical school that folic acid was a B vitamin. Therefore, it is water soluble, and if you get too many supplements, this is just "expensive urine." This is really inaccurate because large concentrations of these compounds are not immediately excreted ("expensive blood"). Higher intakes of these water-soluble vitamins can stay in the body longer than it takes the cable repair service to answer the phone (which is a long time). Interestingly, UMFA does not occur after getting folate from natural food sources. However, when getting folic acid from supplements, UMFA increases because the enzymatic system that converts folic acid into a usable form by the body is overwhelmed. Also, keep in mind that, over the past 10 years, almost all of the studies on high-dose folic acid and B vitamin supplements to reduce cardiovascular disease have not been effective. When do we begin to tell patients about this potential problem of overexposure to B vitamins? First, I tell them that B-12 shots are overrated and cost too much, and I tell them to avoid excess folic acid from dietary supplements. Next, I tell them how much money they will save in a year, and then I get a big hug. Afterward, I ask them for that extra money I saved them, and then they laugh at me. (Reviewer-Mark A. Moyad, MD, MPH).

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Keywords: Folic Acid, Diet

Print Tag: Refer to original journal article
Eating Well-Done Meat Does Not Increase Risk of Prostate Cancer

Well-Done Meat Consumption, NAT1 and NAT2 Acetylator Genotypes and Prostate Cancer Risk: The Multiethnic Cohort Study.

Sharma S, Cao X, et al:

Cancer Epidemiol Biomarkers Prev 2010; 19 (July): 1866-1870

Patients need to be educated on the major determinants of heart disease and cancer risk, and should not focus on medical minutiae.

Objective: To determine the association between well-done (red) meat consumption and prostate cancer risk among African-American, Native-Hawaiian and Japanese-American, Latino, and Caucasian men. More African-Americans and Latinos consumed well-done meat compared to the other ethnic groups.

Design: Case-control study of prostate cancer within the Multiethnic Cohort study.

Participants/Methods: A total of 2106 cases were compared to 2063 controls that were genotyped for polymorphisms in NAT1 and NAT2 that impact the liver metabolism or heterocyclic amines, which are thought to raise cancer risk.

Results: No significant associations were found for risk between the groups in terms of well-done meat, NAT1 and NAT2, and prostate cancer risk overall or among advanced prostate cancer cases. Most of the statistical analysis actually demonstrated a nonsignificant lower risk with well-done meat consumers.

Conclusions: These results do not support the hypothesis that exposure to heterocyclic amines is correlated with prostate cancer risk.

Reviewer's Comments: How would you like your steak cooked? Rare to medium rare and you may slightly increase your risk of bacterial exposure and a terrible illness. Or, you can get your meat well-done, but that creates apparently carcinogenic compounds that may give you prostate cancer. Come on folks! Life is a terminal disease. If we continue to slice and dice (pun intended) risk assessment, we will create a patient population that becomes consumed (pun intended again) by every tiny risk factor and begins to ignore the more tangible and obvious immediately life changing risk factors. Do you have any idea how many obese men and women with high cholesterol and hypertension who never exercise and smoke have asked me about well-done meat and carcinogens? I am as serious as a myocardial infarction on this one folks! Artificial sweeteners, mercury in our fish, food dyes, trans-fat, genetically modified products, etc. This is getting ridiculous! We need to begin to triage risk factors for prostate cancer and other diseases for patients. I am not saying that well-done meat does not potentially and ever so slightly increase the risk of prostate cancer, but what I do tell patients is that if they are driving a car going 100 miles per hour toward a wall (major mortality risk factor), then they should not spend any extra time trying to kill a large mosquito (minor mortality risk factor) in the car as opposed to first figuring out how to stop the car! "What if the mosquito has malaria or West Nile Virus?" This is a question I actually received from an anonymous individual! And, you wonder why I need therapy? (Reviewer-Mark A. Moyad, MD, MPH).

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Keywords: Meat Consumptions, NAT1/NAT2 Genotypes, Prostate Cancer

Print Tag: Refer to original journal article
Men who are on a statin prior to surgery for prostate cancer are less likely to have biochemical recurrence after prostatectomy compared to men who are not on a statin prior to surgery.

Objective: To determine if statin use is associated with outcome after radical prostatectomy for clinically localized prostate cancer.

Design: Retrospective cohort study from the Shared Equal Access Regional Cancer Hospital (SEARCH) database.

Participants/Methods: 1319 men were included in the analysis. The biochemical recurrence of prostate cancer was compared between men who were or were not on statin therapy prior to radical prostatectomy after adjusting for other clinical and pathologic variables.

Results: A total of 236 men (18%) were on statin therapy prior to surgery. The median follow-up was 24 months for the statin users and 38 months for the nonusers. Statin users tended to be older, have lower clinical stage, and lower prostate-specific antigen (PSA) levels, but higher biopsy Gleason scores. After adjusting for multiple clinical and pathologic variables, statin users had an approximately 30% lower risk of developing biochemical recurrence after prostatectomy than nonusers. This observation appeared to be dose-dependent, with higher statin dose equivalents correlating with lower risk.

Conclusions: Statin use was associated with a dose-dependent decrease in biochemical recurrence of prostate cancer after radical prostatectomy.

Reviewer's Comments: Statin therapy has become one of the most prevalent prescription medications in the United States over the last decade due to its proven benefits in reducing cardiovascular mortality. There is a growing body of evidence suggesting that statins may have benefits outside of their known cholesterol-lowering properties. Among these is reducing the risk of developing malignancies, including prostate cancer. Now in this study by Hamilton and colleagues, statin therapy was found to reduce the risk of PSA recurrence after prostatectomy by 30%. This is encouraging, and if confirmed, it could warrant a prospective trial in the future. However, at this point, the evidence is not nearly strong enough to endorse the use of statins beyond their current indications regarding hypercholesterolemia. The reader should bear in mind something the authors themselves readily acknowledge. This was a retrospective study, and the 2 groups (statin users and nonusers) were not balanced. There were differences in PSA, stage, Gleason score, and follow-up between the groups. Even though the authors carefully worked to statistically account for these differences, there remains the distinct possibility that the association is actually due to unaccounted for confounders between the groups and not due to an actual biologic or therapeutic effect. Nevertheless, if these findings are upheld in other patient cohorts, then perhaps a prospective, randomized trial in this setting would be justified in the future. (Reviewer-Peter E. Clark, MD).

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Keywords: Prostate Cancer, Radical Prostatectomy, Biochemical Recurrence, Statins

Print Tag: Refer to original journal article
The odds of undergoing a lymphadenectomy at the time of robotic cystectomy increases with surgeon experience and volume.

**Objective:** To determine the factors associated with performing a lymphadenectomy at the time of robotic-assisted radical cystectomy (RARC).

**Methods:** Retrospective analysis of the International Robotic Cystectomy Consortium database of 527 patients who underwent RARC across 15 institutions between 2003 and 2009. Predictors for undergoing a lymphadenectomy, defined as the removal of at least 10 nodes, were analyzed.

**Results:** Overall, 83% of patients underwent lymphadenectomy at the time of RARC. The mean number of nodes examined was approximately 18. On multivariate analysis, the factors independently associated with a higher probability of undergoing a lymphadenectomy at the time of RARC were T stage <T4, increasing sequential case number, and higher surgeon volume.

**Conclusions:** The overall rate of lymphadenectomy and the median number of nodes examined at RARC are comparable to published rates across open series. The odds of undergoing lymphadenectomy appear to be influenced by the learning curve.

**Reviewer’s Comments:** In the last 20 years, it has become clear that performing a lymphadenectomy at the time of radical cystectomy for invasive bladder cancer ought to be the gold standard. Although there is considerable debate regarding the relative merits of so-called extended versus standard lymphadenectomy, there is general consensus that a bilateral pelvic lymph node dissection of some sort ought to be done in the overwhelming majority of cases. The introduction of RARC has fueled a new debate as to its relative merits compared to the traditional open operation. Part of that debate centers on the quality of the lymph node dissection that can be achieved at the time of RARC. This study by Hellenthal and colleagues speaks to this issue by supporting several important points. One is that when a surgeon is committed to performing a lymphadenectomy by any method, including RARC, this can be achieved with nodal counts that are comparable to other published series. This encouraging finding is tempered, however, by the additional finding that the odds a surgeon will have that commitment is heavily influenced by where that individual is on the learning curve and by how many RARCs they are doing. The inexperienced, low-volume robotic surgeon is much less likely to do a proper lymph node dissection. This has important implications on how we ought to be implementing this new technology and how we disseminate it in a responsible and safe way for all patients. It also emphasizes that it is critical as surgeons that we first strive to perform the proper operation and then consider what technique/approach we ought to utilize to achieve that. This study shows that when the surgeon is committed to such an approach, it can be achieved, but that early in the learning curve we may be falling short. (Reviewer-Peter E. Clark, MD).

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Keywords: Cancer, Robot-Assisted Radical Cystectomy, Pelvic Lymphadenectomy

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Ureteroscopy is the primary procedure for midureteral and distal ureteral stones, while the majority of urologists would still consider shock wave lithotripsy for proximal ureteral stones.

Objective: To discuss the results of a survey of practicing U.S. urologists in regard to the treatment of patients with ureteral calculi.

Methods: An e-mail survey was sent to members of the American Urological Association (AUA) and the Endourology Society from late 2007 to early 2008.

Results: Over 50% of the respondents were from the United States, with 15% from Europe and 12% from Asia. The holmium laser was available to 99% of U.S. urologists and 80% of urologists in Europe and Asia, but only 63% of the urologists in South America. For North American urologists, the decision to utilize ureteroscopy for ureteral stones (4 to 15 mm) was independent of stone size, but did vary based on stone location: distal (95%); midureteral (75%); and proximal (40%). Non-North American urologists similarly stratified the use of ureteroscopy to stone location: distal (80%); midureteral (70%); and proximal (25%).

Conclusions: The use of ureteroscopy has expanded since last evaluated in a 2004 survey, when only 15% of U.S. urologists reported utilizing ureteroscopy for proximal ureteral stones.

Reviewer's Comments: The international sample of urologists responding to the questionnaire may not be reflective of the general practicing urologist in those countries, as they are selected by their membership in international organizations (AUA) or membership in societies for physicians with a specific interest and/or expertise in endourology (Endourology Society). As such, the survey may overestimate the availability of holmium laser in these countries and the penetrance of advanced endoscopic procedures. The authors did not stratify responses based on gender of the patient. One might anticipate that a higher percentage of urologists may tackle a midureteral or proximal ureteral stone in a female than in a male patient due to the ability to access the stone with a semi-rigid ureteroscope. Interestingly, non-North American urologists were more likely (15%) than North American urologists (4%) to stent only for a small 4-mm stone. This may represent a higher inclination to give the patient an opportunity to pass the stone spontaneously once stented, which is a two-edged sword as it may increase the likelihood for a secondary procedure down the road. (Reviewer-Manoj Monga, MD).

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Keywords: Ureteral Calculi, Ureteroscopy, Shock Wave Lithotripsy

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Ureteroscopic Ultrasound Probe Sizes Up the Problem

Ureteroscopic Ultrasound Technology to Size Kidney Stone Fragments: Proof of Principle Using a Miniaturized Probe in a Porcine Model.

Sorensen MD, Shah AR, et al:

J Endourol 2010; 24 (June): 939-942

The development of a small ultrasonic probe capable of determining stone size may help improve the safety of ureteroscopic stone extraction.

Background: Ureteral avulsion is a serious complication of ureteroscopy, occurring in approximately 1 in 300 procedures.

Objective: To develop a ureteroscopic ultrasound probe capable of measuring stone size.

Design: Ex vivo study using porcine kidneys.

Methods: Stones ranging in size from 3 to 7 mm were placed in the lower pole of a freshly sectioned porcine kidney and submerged in saline. A 2 MHz, 3.6F hydrophone transducer was connected to a pulse receiver that provided the excitation pulse and received and recorded the return signal using a digital oscilloscope. This rigid probe was inserted directly into the lower calyx through the renal pelvis. Stone compositions tested were calcium oxalate monohydrate, cystine, and calcium hydrogen diphosphate.

Results: An excellent correlation was found between ultrasound-determined thickness and caliper measurements. All measurements were accurate to within 1 mm, and 67% were accurate to within 0.5 mm.

Conclusions: A 3.6F ultrasound probe is capable of sizing stone fragments to within 1 mm.

Reviewer's Comments: The authors report a good correlation with stone-size to within 1 mm. As a 0.5 mm discrepancy represents a 1.5F difference for stone extraction through a 12F inner diameter ureteral access sheath, one could argue that the limit for error be placed at 0.5 mm, in which case, the probe is accurate in only two-thirds of the cases. Though the authors tested stones 3 to 7 mm in size, the critical clinical question is posed by those stones 4 to 5 mm in size. A report to the operator that the stone is less than or greater than 4.5 mm in size is required with a high level of accuracy. The authors utilized a rigid probe, but they do not state what length probe was utilized or if it would be easy to modify to the typical 42-cm length of a rigid ureteroscope or preferably to a flexible configuration for a flexible ureteroscope. One limitation of the device is that it provides unidimensional sizing capabilities; if the largest dimension of the stone was not captured, then the risk of engaging a stone too large to extract would not be mitigated. Often air bubbles are transmitted to the collecting system through the irrigation fluid; one might anticipate that interference with the stone-fluid interface may pose a challenge in these cases for stone sizing. The technology provides the potential sizing stones prior to engaging them in a basket, thereby decreasing the risk of ureteral injury. This would be particularly appealing for stones that are impacted or partially embedded. In addition, this technology may aid in the identification of submucosal calculi and calculi in a calyceal diverticulum, as well as facilitate unroofing with the holmium laser. (Reviewer-Manoj Monga, MD).

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Keywords: Stone Size, Measuring, Ureteroscopy, Ultrasound

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Objective: To determine if the Children's Oncology Group (COG) guidelines for primary germ cell tumors are being utilized and if they are applicable to all pediatric ovarian malignancies.

Methods: A single institution retrospective chart review was performed over a 15-year period to identify all operative ovarian masses in children from birth to 19 years of age.

Results: 424 children were identified, with 46 (11%) having malignancies. Malignancies included germ cell tumors (GCTs; 50%), sex cord-stromal (SCS; 28%) tumors, epithelial tumors (17%), and lymphoma/leukemia (4%). The majority were low stage (I). Complete COG staging was unusual, noted in only 24%. Advanced stages had visible findings, which guided biopsy. Site-directed biopsies were positive for disease in 40%. Random biopsies were uniformly negative (n=38). Two of the 4 recurrences had complete COG staging. There were 4 mortalities, all of which had complete COG staging. Follow-up was a mean of 3.6 years, with 17% lost to follow-up.

Conclusions: COG staging is not consistently followed and does not appear to affect outcome. Advanced cases were visibly obvious, whereas random sampling was uniformly negative and did not affect stage.

Reviewer's Comments: This report is an interesting assessment of the use of the COG staging protocol, which is less aggressive than the Federation of Gynecology and Obstetrics (FIGO) guidelines used in adults. In general, the pathology drives the staging approach, with more indolent tumors (GCT and SCS) seeming more appropriate for the COG approach, and more aggressive tumors (epithelial/adenocarcinoma) thought to be better served by the FIGO approach. It appears that the lesser approach was efficacious in this series, as random biopsies and peritoneal washings were negative in all cases, and advanced disease was suggested by clinical findings to guide site-specific biopsies. Although compliance in only 25% of cases appears quite low, this is an increase compared to other series and will likely improve over time. The study was retrospective with all its inherent biases, but overall, it suggests that the COG protocol is reasonable in children with ovarian tumors. (Reviewer-John Gatti, MD).

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Keywords: Pediatrics, Ovary, Malignancy, Staging, COG Guidelines

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Essentially all grade III blunt renal trauma injuries in children can be managed nonoperatively, while nearly all grade V injuries require surgery and grade IV injuries are a mixed bag.

**Objective:** To review the impact and management of major blunt renal trauma in children in the context of long-term function and morphology of the affected kidney.

**Participants/Methods:** 36 children with major blunt renal trauma presented to a single institution over a 3-year span (2004 to 2007); 20 were male, 16 were female, and their average age was 6 years. A total of 37 renal units were involved (grade III, 13; grade IV, 14; and grade V, 10). The mean follow-up was 14 months (range, 3 to 38 months). Management was initially nonoperative unless the patient was vitally unstable hemodynamically or multiple organ injury required exploration. Fourteen patients had associated non-renal injuries. Most injuries were the result of falls and motor vehicle collisions. Grade I & II renal injuries were excluded from the study.

**Results:** 13 patients (36%) underwent surgical intervention, including 9 of the 10 grade V injuries and 4 of the 14 grade IV injuries. In 7 cases, lacerations were repaired, in 4 cases, partial nephrectomy was performed, and in 2 cases, nephrectomy was required. At follow-up, no significant change in renal function was noted, and no hypertension was observed. The nonoperative group included all grade III injuries, 10 grade IV injuries, and 1 grade V injury. Eighteen of the 24 (75%) had no adverse sequela. The remaining 6 had lower pole infarction (1), renal atrophy (1), persistent subcapsular collection (2), recurrent hematuria requiring embolization (1), and there was 1 death related to central nervous system injury. Overall, a decrease in function or infarction was seen in approximately 10%.

**Conclusions:** The outcome of the described management strategy for major renal trauma was favorable. Longer follow-up is needed regarding long-term renal function and hypertension. While the authors recommend a conservative approach to major renal injuries in children, nonoperative management of grade V injuries carries a high risk of failure.

**Reviewer’s Comments:** The authors present their experience with a conservative approach to major (grade III through grade V) blunt renal trauma in children. In general, all grade III injuries did well without major operations, and 9 of the 10 grade V injuries required operations. Grade IV injuries continue to be variable, and it must be noted, that approximately 70% did not require open operations, but that 50% did require stents. As long as the patient is stable, conservative management of grade V injuries is reasonable, but the deck is certainly stacked against it. The authors should be lauded that nephrectomy was only performed in 2 cases, emphasizing their bias toward renal repair. (Reviewer-John Gatti, MD).

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Keywords: Pediatrics, Blunt Renal Trauma, Management

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Simulator Use Improves Cystoscopy Skills in Trainees

Transfer of Cysto-Urethroscopy Skills From a Virtual-Reality Simulator to the Operating Room: A Randomized Controlled Trial.

Schout BMA, Ananias HJK, et al:

BJU Int 2010; 106 (July): 226-231

The use of virtual reality simulators for cystoscopic skill training demonstrates earlier skill acquisition and improved performance of procedures in actual patient care as compared to trainees with no prior exposure to this technology.

Objective: To assess whether the performance of cystoscopy is improved with preclinical practical skill training using simulator technologies for purposes of technology exposure.

Design: Prospective randomized assessment of a trainee group, with randomization prior to pre-cystoscopy virtual reality simulation versus the absence thereof prior to clinical exposure.

Participants/Methods: 100 trainees in Holland were placed into a randomized trial to determine whether or not the use of a specific virtual reality simulator, the URO Mentor, would help with the acquisition of clinical skills. Trainees underwent real-time performance rating by supervisors, who were unaware of the training status, using a global rating scale. Overall, those who had received simulator training performed significantly better in terms of their real-time performance using the above noted scale. Training did not appear to have any affect in the individuals regarding their surgical preference of surgical specialty. Interestingly, training was associated with the perceived stress by the training. The URO Mentor actually consisted of a flexible and semi-rigid cysto- and ureteroscope. This has been previously investigated for construct validity, but had yet to be examined in a controlled environment. The simulator allowed the trainee to acquire manual dexterity with the instrument in a real-time environment. The Global Rating Scale assessed 5 different domains on a scale of 1 to 5, including respect for tissue, time and motion, handling of endoscope, flow of procedure and forward planning, and knowledge of procedure.

Conclusions: Overall, these results show that simulator training had clear benefit for trainees in terms of subsequent performance in patient care. The authors concluded that this virtual reality system globally benefitted the trainees in terms of all 5 aspects of the Global Rating Scale, and they recommend the use of this for early level trainees prior to exposure to patient care.

Reviewer's Comments: Real-time simulation is increasingly being used for a variety of surgical skills. These include suture and ligation type trainers, laparoscopic trainers, and, more recently, vaginal surgery trainers. These trainers have shown benefit for other indications and have demonstrated superiority in terms of the exposure of individuals with skill development and those who have had prior exposure to these real-time systems. The currently mentioned system is a relatively new one that had yet to be evaluated in a randomized controlled setting, and as might be expected, the trainees actually performed in a superior fashion to those who have utilized the simulator. (Reviewer-Roger R. Dmochowski, MD).

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Keywords: RCT, Simulation, Training, Transfer, Cysto-Urethroscopy, Validation

Print Tag: Refer to original journal article
Objective: To assess what would constitute a minimum set of outcome measures (OMs) for postoperative evaluation of stress incontinent women.

Design: Prospective, electronically based, survey assessment, tool-based method.

Methods: Members of a urologic society underwent a short (11 item) online, electronically based survey to determine use of OMs in daily practice.

Results: The survey was administered over 2 separate 10-day periods to the same members of the society. Overall response rates were approximately 30% for the first distribution and 25% for the second distribution. There was no tendency for any one geographic area to be represented over another. The majority of respondents had been in practice ≤15 years and performed between 5 and 15 cases per month. The overall distribution was slightly oriented toward university-based practices (56%) versus group private settings (approximately 30%). Consistency was noted in the use of types of questionnaire, with the Urogenital Distress Inventory being used in isolated fashion between 40% and 52% and a combination of that plus the Incontinence Impact Questionnaire by a smaller minority (30% to 34%). Tests commonly used included urinalysis and post-void residual (approximately one-third of the responders), physical examination with some form of prolapse grading by 38% to 55%, and cough stress test by slightly >50%. Imaging was not routinely done, and urodynamics was only done if complications were encountered (complications were not specified). Most common tests not preferred included the Q-tip assessment, bladder diary, longer questionnaires, the pelvic organ prolapse quantification scale, and the 24-hour pad test.

Conclusions: The authors concluded that minimal OM sets have yet to be ideally determined; however, the similarity of findings suggests a tendency toward minimalistic OM assessment tools.

Reviewer's Comments: This article is an interesting analysis of current practice in assessment of outcomes related to urinary incontinence interventions in women. It clearly shows that the preference for most physicians is to do a limited outcome assessment, with examination and questionnaire-based assessment being the most commonly used assessments. Surprisingly, urodynamics was utilized relatively infrequently, which is in some contradistinction to reported utilization of urodynamics in national databases that have recently come to light. This article is interesting, as it really does reflect common practice and should form a basis for our determination of OM sets to be used for purposes of documentation in the soon to be developed national outcomes data sets that are a measure part of new national legislation. (Reviewer-Roger R. Dmochowski, MD).

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Keywords: Anti-Incontinence Procedure, Outcome Measure, Survey

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There is a negative correlation between patients’ preoperative expectations and their ultimate satisfaction with inflatable penile prosthesis surgery for erectile dysfunction.

**Background:** Penile implant has been successfully used as an effective form of treatment for erectile dysfunction (ED) for several decades. Some have proposed that the high expectations prior to implant surgery diminish satisfaction.

**Objective:** To understand the role that preoperative counseling and patients’ realistic understanding of inflatable penile prosthesis (IPP) surgery play in determining postoperative satisfaction.

**Participants/Methods:** 33 patients received IPP surgery from June 2008 through March 2009. All devices were Coloplast Titan implants. Patients were counseled for surgery in the office at least once. At the office visit, 45 minutes was spent reviewing the pros and cons of surgery, including the major risks, and what to expect during the recovery phase and beyond. A uniform message was given to each patient. Upon leaving the office, the survey was given to the patient to complete, and the score was recorded. A scatter plot is used to visually evaluate the relationship between patients’ preoperative composite expectation scores and their postoperative satisfaction scores.

**Results:** There was a negative linear relationship between preoperative expectations and postoperative satisfaction ($r$ value, $-0.489$; $R^2$ value, 0.239).

**Conclusions:** Preoperative counseling plays a role in initial postoperative satisfaction in patients undergoing IPP implantation. The significant correlation between expectations and satisfaction demonstrates that emphasis needs to be placed on appropriate and complete preoperative counseling. The $R^2$ value implies that postoperative satisfaction decreases with enhanced expectation, and that 23.9% of the variation in the postoperative evaluation score can be attributed to the variation in the preoperative expectation score. Thus, there exists some correlation between patients’ preoperative expectations and their ultimate satisfaction with the procedure. This negative linear relationship is fairly strong (albeit with a small sample size), but the correlation between lower preoperative expectations and immediate postoperative expectations is significant.

**Reviewer’s Comments:** Every study has some limitations, and this useful, but pilot, study is no exception. These include that a larger sample size was needed, and the authors did not use a validated questionnaire. (Reviewer-Kevin T. McVary, MD.)

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Keywords: Erectile Dysfunction, Surgery, Penile Prosthesis

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PTX May Have Useful Role in Management of PD


Shindel AW, Lin G, et al:

J Sex Med 2010; 7 (June): 2077-2085

Both elastin and collagen are upregulated by transforming growth factor-β1 in tunica albuginea-derived fibroblasts.

Background: Transforming growth factor-β1 (TGF-β1) has been implicated in the pathogenesis of Peyronie’s disease (PD) and also plays a role in collagen and elastin metabolism. Pentoxifylline (PTX) antagonizes the effects of TGF-β1 and has been utilized clinically for the management of PD.

Objective: To study the effects of TGF-β1 and PTX on collagen metabolism and elastogenesis in tunica albuginea-derived fibroblasts (TADFs).

Methods: TADFs from men with PD (PT) and without PD were cultured and treated with TGF-β1 and PTX as monotherapy at differing concentrations and time points. Combination treatment (TGF-β1 followed by PTX and vice versa) was also investigated. The authors used in vitro methods of a cell proliferation assay, enzyme-linked immunosorbent assay (ELIZA), and immunohistochemistry (IHC) to assess the impact of TGF-β1 and PTX on TADF with respect to elastin and collagen I metabolism.

Results: PTX inhibited fibroblast proliferation at doses of 100 µM. TGF-β1 stimulated elastogenesis and collagen I fiber deposition in TADF in a dose- and time-dependent fashion. Pretreatment with PTX dramatically attenuated TGF-β1-mediated elastogenesis and collagen fiber deposition in TADFs from men with and without PD. Interestingly, production of collagen I was higher in untreated Peyronie’s tunica cells relative to normal tunica cells. Furthermore, PTX attenuated collagen production to levels similar to untreated control TADF in PT cells but not in normal cells, suggesting important intrinsic differences between Peyronie’s and normal cells.

Conclusions: Both elastin and collagen are upregulated by TGF-β1 in TADF. This likely contributes to the PD phenotype. Pretreatment with PTX attenuates both collagen fiber deposition and elastogenesis in TADF exposed to TGF-β1; these effects suggest a useful role for PTX in the management of PD.

Reviewer’s Comments: This was an in vitro study design; the behavior of cultured monolayers of fibroblasts in vitro may not be representative of what occurs in the more complex in vivo environment. Furthermore, the Principal Investigator did not assess collagen III metabolism, which has been shown to play a role in PD in vivo. PTX treatment had to be applied prior to the application of TGF-β1 for maximal efficacy, while patients with PD typically present after disease is already manifest. (Reviewer-Kevin T. McVary, MD).

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Keywords: Peyronie’s Disease, Transforming Growth Factor-β1, Pentoxifylline

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